PART I

The ACTION of HYDRAZINES on
SEMICARBAZONES
and
THIOSEMICARBAZONES.

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I desire to record my deep gratitude to Professor Wilson, my Supervisor, for his excellent advice and encouraging interest.

Wm Baird,

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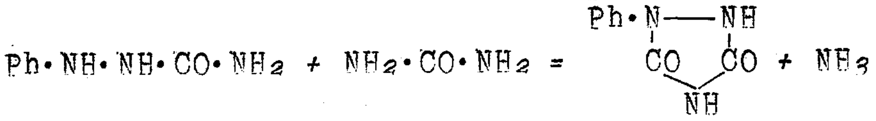
Introduction and Theoretical.

In the year 1887, Pinner (B. 20, 2358) showed that phenylhydrazine reacted with carbamide to give products depending on the proportions used, the reaction being accompanied by the evolution of ammonia. When one molecule of phenylhydrazine reacted with one or two of carbamide the product was found to be α-phenylsemicarbazide*, formed according to the equation

$$Ph\cdot NH\cdot NH_2 + NH_2\cdot CO\cdot NH_2 = Ph\cdot NH\cdot NH\cdot CO\cdot NH_2 + NH_3.$$

When a larger excess of carbamide was used, phenylurazole was obtained, α-phenylsemicarbazide being assumed as an intermediate product, thus:-



In 1888, Skinner and Ruhemann (J.C.S. 53, 550) gave an account of the action of phenylhydrazine on certain carbamide derivatives. With

* Nomenclature – $\underset{\alpha}{NH_2}\cdot\underset{\beta}{NH}\cdot\underset{\gamma}{CO}\cdot\underset{\delta}{NH_2}$.

equimolecular quantities of phenylhydrazine and urethane, α-phenylsemicarbazide was again formed, ethyl alcohol being eliminated -

$$PhNH{\cdot}NH_2 + NH_2{\cdot}CO{\cdot}OEt = PhNH{\cdot}NH{\cdot}CO{\cdot}NH_2 + EtOH.$$

By using two molecules of phenylhydrazine to one of urethane, diphenylcarbohydrazide, ethyl alcohol, and ammonia, were formed -

$$2\ PhNH{\cdot}NH_2 + NH_2{\cdot}CO{\cdot}OEt = (PhNH{\cdot}NH{\cdot})_2CO + EtOH + NH_3.$$

Borsche (B.1901, 34, 4299; 1904, 37, 3177; 1905, 38, 831) found that in general, semicarbazones reacted with arylamines giving rise to δ-arylsemicarbazones, thus :-

$$RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2 + NH_2Ar = RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NHAr + NH_3.$$

These compounds on hydrolysis with dilute hydrochloric acid gave the δ-arylsemicarbazide hydrochloride from which the free base could be obtained by the action of weak alkalies -

$$RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NHAr + H_2O + HCl = RR'CO + HCl,\ NH_2{\cdot}NH{\cdot}CO{\cdot}NHAr.$$

From the results of those researches, it was thought possible that hydrazines would react with semicarbazones to give δ-aminosemicarbazones and ammonia -

$$RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2 + NH_2{\cdot}NHR'' = RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHR'' + NH_3.$$

Knöpfer (Monatsh. 1910, 31, 87) investigated the mutual replacement of semicarbazide and phenylhydrazine residues, the reactions being carried out in boiling alcoholic or acetic acid solution. He studied mainly aromatic aldehydic derivatives and found that usually a state of equilibrium was set up, this being independent of the temperature -

$$RCH{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2 + NH_2NHPh \rightleftharpoons RCH{:}N{\cdot}NHPh + NH_2{\cdot}NH{\cdot}CO{\cdot}NH_2$$

With about five molecules of the decomposing reagent, the replacement was usually complete, but no regularities were detected; no formation of δ-anilinosemicarbazone was reported.

In 1924, Sutherland and Wilson (J.C.S. 125, 2145) showed that benzophenone and acetophenone semicarbazones heated with phenylhydrazine in the presence of toluene as a solvent, gave the corresponding δ-anilinosemicarbazones -

$$Ph_2C{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2 + NH_2{\cdot}NHPh = Ph_2C{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHPh + NH_3.$$

Hydrolysis of these compounds with dilute hydrochloric acid gave the ketone and δ-anilinosemicarbazide hydrochloride,

$$Ph_2C{:}N\cdot NH\cdot CO\cdot NH\cdot NHPh + H_2O + HCl =$$
$$Ph_2CO + HCl,NH_2\cdot NH\cdot CO\cdot NH\cdot NHPh,$$

and with stronger acid the δ-anilinosemicarbazide hydrochloride was split up into phenylhydrazine hydrochloride, hydrazine hydrochloride, and carbon dioxide, thus :-

$$PhNH\cdot NH\cdot CO\cdot NH\cdot NH_2,HCl + H_2O + 2\ HCl =$$
$$PhNH.NH_2,HCl + N_2H_4,2\ HCl + CO_2.$$

To prove the correctness of their scheme, the base, δ-anilinosemicarbazide, was synthesised from β-carbethoxyphenylhydrazine and hydrazine hydrate,

$$PhNH\cdot NH\cdot CO\cdot OEt + NH_2NH_2,H_2O = PhNH\cdot NH\cdot CO\cdot NH\cdot NH_2 + EtOH + H_2O.$$

The author first investigated the action of phenylhydrazine on acetone semicarbazone under conditions similar to those used for acetophenone and benzophenone semicarbazones. The reaction was however essentially one of replacement of the semicarbazide residue by a phenylhydrazine residue,

$$Me_2C{:}N\cdot NH\cdot CO\cdot NH_2 + NH_2\cdot NHPh =$$
$$Me_2C{:}N\cdot NHPh + NH_2\cdot NH\cdot CO\cdot NH_2 ,$$

and even under varied conditions, the yield of acetone-δ-anilinosemicarbazone never exceeded 5%. The semicarbazide thus formed usually decomposed into hydrazodicarbonamide and hydrazine, and the hydrazine decomposed into nitrogen and ammonia (Curtius, B. 1894, 27, 57) -

$$2\ NH_2\cdot NH\cdot CO\cdot NH_2 = NH_2\cdot CO\cdot NH\cdot NH\cdot CO\cdot NH_2 + NH_2NH_2 ;$$
$$3\ NH_2NH_2 = 4\ NH_3 + N_2 .$$

Hence, when a hydrazine reacts with a semicarbazone, the evolution of ammonia does not necessarily mean that δ-anilinosemicarbazone is being formed.

In view of the widely differing behaviour of acetone and acetophenone semicarbazones, it was decided to make a general study of the behaviour of semicarbazones, both aldehydic and ketonic, on heating with phenylhydrazine. In all, the semicarbazones of seven aldehydes and fourteen ketones have been investigated.

The semicarbazones of acetaldehyde, furfuraldehyde, benzaldehyde*, anisaldehyde*, piperonal*,

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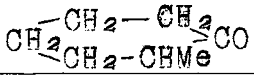
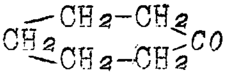
* Investigated by others.

and cinnamaldehyde*, gave only replacement products, whereas *n*-heptaldehyde gave a little δ-anilinosemicarbazone.

The behaviour of the ketonic semicarbazones varied in each case, and in general δ-anilinosemicarbazone was formed together with replacement products. The following table shows the yields of δ-anilinosemicarbazone obtained from different ketonic semicarbazones, and also the molecular weight of the ketone.

KETONE.	MOL. WT.	YIELD.
Me_2CO	58.	5%.
$MeEtCO$	72.	Nil.
$MePrCO$	86.	"
Et_2CO	86.	2%.
$Me(Me_3C)CO$	100.	60%.
 $CH_2{<}\begin{matrix}CH_2-CH_2\\CH_2-CHMe\end{matrix}{>}CO$	112	10%.
 $CH_2{<}\begin{matrix}CH_2-CH_2\\CH_2-CH_2\end{matrix}{>}CO$	98.	12%.
$(MeCH_2CH_2)_2CO$	114.	13%.
$(Me_2CH)_2CO$	114.	90%.
Ph_2CO	182.	95%.
$MePhCO$	120.	95%.
$Me(PhCH_2)CO$	134.	13%.
$Me(PhCH_2CH_2)CO$	148.	8%.
$(PhCH_2)_2CO$	210.	95%.

It is quite evident from the table that the molecular weight of the ketone has little or no influence in determining the course of the reaction; *e.g.*, the semicarbazones of acetone (58), acetophenone (120), and benzylacetone (148) give yields of 5%, 95%, and 8%, of their respective δ-anilinosemicarbazones.

From an examination of the general schemes shown by the equations

$$\begin{array}{l} RR'\underset{\times}{C}{:}N\cdot NH\cdot CO\cdot NH_2 \\ \quad + NH_2\cdot NHPh \end{array} \begin{array}{l} \nearrow RR'C{:}N\cdot NH\cdot CO\cdot NH\cdot NHPh + NH_3 \qquad (1) \\ \searrow RR'C{:}N\cdot NHPh + NH_2\cdot NH\cdot CO\cdot NH_2 \qquad (2), \end{array}$$

it will be seen that in order to have replacement, (2), the phenylhydrazine molecule must approach the ketonic carbon atom (marked × in equation), whereas for δ-anilinosemicarbazone formation, (1), it must approach the NH_2 group of the semicarbazone. Now if the groups R and R' are sufficiently bulky they will hinder the approach of the phenylhydrazine molecule to the ketonic carbon atom, thus hindering replacement; and consequently δ-anilinosemicarbazone formation will be increased, the NH_2group of the semicarbazone being always easily accessible. The experimental results agree well with this supposition.

With the nonphenylated ketones, as expected, the yield of δ-anilinosemicarbazone is small except with methyl *tert*-butyl ketone and di*iso*propyl ketone where there is a concentration of methyl groups on one or both of the α-carbon atoms. The di*iso*propyl ketone semicarbazone gives a yield of 90%, whereas with di-*n*-propyl ketone semicarbazone the yield is 13%.

Considering the monophenylated ketones, it is obvious that reaction (1) should be more pronounced when the phenyl group is contiguous to the ketonic carbon atom than when it is removed from it by one or two CH_2 groups. This is borne out experimentally by the semicarbazones of acetophenone, methyl benzyl ketone, and benzylacetone, which give yields of 95%, 13%, and 8% of their respective δ-anilinosemicarbazones.

With the diphenylated ketones, reaction (1) is pronounced with both benzophenone and dibenzyl ketone semicarbazones, the attachment of a phenyl group to both of the α-carbon atoms evidently strongly inhibiting reaction (2).

Now if we consider a hydrazine of the type $R''R'''N\cdot NH_2$, reacting with a semicarbazone according to the general schemes (1) and (2), (page 9), we would expect that just as the ketonic groups R and R' tend to hinder the hydrazine from approaching the ketonic carbon atom, so would the groups R" and R''' of the hydrazine, if sufficiently bulky, tend to hinder replacement and consequently increase the yield of δ-aminosemicarbazone. The following table indicates the main results, the yields given being those of the δ-aminosemicarbazones.

KETONE.	HYDRAZINE.	YIELD.
Acetone.	$PhNH{\cdot}NH_2$.	5%.
"	p-$MeC_6H_4NH{\cdot}NH_2$	9%.
"	$MePhN{\cdot}NH_2$	52%.
"	$Ph_2N{\cdot}NH_2$	80%.
Benzylacetone.	$PhNH{\cdot}NH_2$	8%.
"	p-$MeC_6H_4NH{\cdot}NH_2$	Nil.
"	$MePhN{\cdot}NH_2$	65%.

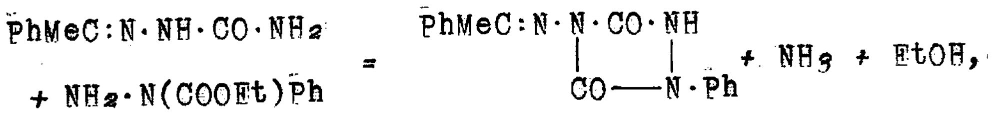
We see from the table that with acetone semicarbazone there is an increase in the yield of δ-aminosemicarbazone from phenylhydrazine through methylphenylhydrazine to diphenylhydrazine, in accordance with the theory. p-Tolylhydrazine naturally behaves like phenylhydrazine as the methyl group is too far away to influence the course of the reaction to any extent.

Thus, in general, if a hydrazine reacts with a semicarbazone, the reaction will proceed according to the equations

$$\begin{array}{lll} RR'C{:}N\cdot NH\cdot CO\cdot NH_2 & \nearrow RR'C{:}N\cdot NH\cdot CO\cdot NH\cdot NR''R''' + NH_3 & (1) \\ \quad + NH_2\cdot NR''R''' & \searrow RR'C{:}N\cdot NR''R''' + NH_2\cdot NH\cdot CO\cdot NH_2 & (2), \end{array}$$

and the extent in any direction will be determined by the steric effect of the groups R, R', R", and R'''.

The interaction of α-carbethoxy-α-phenylhydrazine and acetophenone semicarbazone was investigated in the expectation that it would proceed according to the scheme



$$\begin{array}{lcl} PhMeC{:}N\cdot NH\cdot CO\cdot NH_2 & & PhMeC{:}N\cdot \underset{|}{N}\cdot CO\cdot \underset{|}{NH} \\ \quad + NH_2\cdot N(COOEt)Ph & = & \qquad\quad CO \text{——} N\cdot Ph \quad + NH_3 + EtOH, \end{array}$$

giving the acetophenone derivative of 4-phenyl-1-aminourazole. The product was, however, acetophenone-

δ-carbethoxyanilinosemicarbazone, formed thus :-

$$\begin{array}{l}\mathrm{PhMeC{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2} \\ \quad + \mathrm{NH_2{\cdot}N(COOEt)Ph}\end{array} = \mathrm{PhMeC{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}N(COOEt)Ph} + \mathrm{NH_3},$$

and efforts to eliminate ethyl alcohol from this compound were unsuccessful. The constitution was established by hydrolysis into acetophenone and δ-carbethoxyanilinosemicarbazide hydrochloride, further hydrolysis giving hydrazine, phenylhydrazine, and ethyl alcohol, in a manner similar to benzophenone-δ-anilinosemicarbazone (page 5).

The action of phenylhydrazine on thiosemicarbazones was investigated in the hope that they would react in a manner similar to semicarbazones, and so give δ-anilinothiosemicarbazones -

$$\begin{array}{l}\mathrm{RR'C{:}N{\cdot}NH{\cdot}CS{\cdot}NH_2} \\ \quad + \mathrm{NH_2{\cdot}NHPh}\end{array} = \mathrm{RR'C{:}N{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NHPh} + \mathrm{NH_3}$$

The thiosemicarbazones of acetone, acetophenone, and dibenzyl ketone were used, but in all cases only replacement products were formed -

$$\mathrm{RR'C{:}N{\cdot}NH{\cdot}CS{\cdot}NH_2} + \mathrm{NH_2{\cdot}NHPh} =$$
$$\mathrm{RR'C{:}N{\cdot}NHPh} + \mathrm{NH_2{\cdot}NH{\cdot}CS{\cdot}NH_2}.$$

As the semicarbazones of acetophenone and dibenzyl ketone gave very good yields of δ-anilinosemicarbazone, we may assume that a thiosemicarbazide residue is more easily replaced than a semicarbazide residue.

Attempts were made to synthesise the free base, δ-anilinothiosemicarbazide, but they were without success. Fischer (A. 1878, <u>190</u>, 114) showed that phenylhydrazine phenyldithiocarbazinate could loose hydrogen sulphide to give diphenylthiocarbohydrazide, thus :-

$$PhNH\cdot NH\cdot CS\cdot SH,NH_2\cdot NHPh = PhNH\cdot NH\cdot CS\cdot NH\cdot NHPh + H_2S.$$

This reaction was extended and modified by other investigators; *e.g.*, Stolle and Bowles (B. 1908, <u>41</u>, 1099) prepared thiocarbohydrazide from hydrazine dithiocarbazinate, using litharge to remove the hydrogen sulphide.

In an analogous manner it was hoped to obtain δ-anilinothiosemicarbazide from hydrazine phenyldithiocarbazinate,

$$PhNH\cdot NH\cdot CS\cdot SH,NH_2NH_2 = PhNH\cdot NH\cdot CS\cdot NH\cdot NH_2 + H_2S,$$

but none was obtained.

As amines act on semicarbazones giving rise to δ-substituted semicarbazones, it was thought that aniline would react with thiocarbohydrazide to form δ-anilinothiosemicarbazide,

$$NH_2\cdot NH\cdot CS\cdot NH\cdot NH_2 + NH_2Ph = PhNH\cdot NH\cdot CS\cdot NH\cdot NH_2 + NH_3,$$

but the method proved unsuccessful.

EXPERIMENTAL.

Phenylhydrazine and Acetone Semicarbazone.

5.4 g. of phenylhydrazine and an equivalent quantity , 5.7 g., of acetone semicarbazone (Thiele and Stange, A. 1894, 283, 18) were heated under reflux with 30 ccs. of dry toluene in a bath at 80-90° for a period of 3½ hours. The semicarbazone gradually dissolved, but no ammonia was evolved. Towards the end of the heating, a thin film of an insoluble substance separated on the walls of the boiling tube in which the materials were contained.

The insoluble material was filtered off, washed with a little hot toluene, and recrystallised from water. Small silvery leaves M.P. 245-246° were obtained, insoluble in ether, benzene, acetone and light petroleum, and almost insoluble in alcohol. From these properties, the substance was thought to be hydrazodicarbonamide, and a mixture with an authentic specimen showed no depression of melting point.

The toluene mother liquor, on cooling, deposited crystals which were filtered off and recrystallised from absolute alcohol, giving yellowish prisms M.P. 95°. After decolourising with charcoal, large colourless prisms M.P. 96° were obtained; these were very soluble in water and reduced Fehling's solution even in the cold, thus corresponding to semicarbazide.

Found:- N = 56.20%; 55.94%.

CH_5ON_3 requires N = 56.00%.

To prove its identity further, it was dissolved in alcohol and a few drops of hydrochloric acid added; on cooling, needles of semicarbazide hydrochloride M.P. 175° were obtained.

The toluene mother liquor was cooled in ice for a few days, and the solid thus obtained filtered off and recrystallised from absolute alcohol. Yellowish granules M.P. 167° were thus obtained, and further crystallising and decolourising gave almost white plates M.P. 169°; the melting point seemed to vary slightly with the rate of heating. The compound was *acetone-δ-anilinosemicarbazone** $Me_2C:N\cdot NH\cdot CO\cdot NH\cdot NHPh$.

* *This type is used to denote new compounds.*

Found :- N = 27.28%; 27.35%.

$C_{10}H_{14}ON_4$ requires N = 27.18%.

To prove the constitution of the compound, it was hydrolysed by boiling for ½ hour, under reflux, with dilute hydrochloric acid. Some of the liquid was distilled off, and the distillate was found to contain acetone by the nitroprusside test*. The residual liquid was taken to dryness by distillation under reduced pressure, and the solid washed out with ether. This solid was recrystallised from a mixture of absolute alcohol and light petroleum, and gave leaflets M.P. 193° (decomp.). This product was identified as δ-anilinosemicarbazide hydrochloride by comparison with an authentic specimen, and by means of the benzylidene derivatives; hence the constitution of the original substance is proved. The method adopted for the preparation of the benzylidene derivative, and used successfully in other cases, was as follows. The hydrochloride was dissolved in water, a few drops of alcohol and one drop of benzaldehyde added, and the mixture shaken

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* On adding acetone to a freshly prepared ammoniacal solution of sodium nitroprusside, and shaking, a violet colouration is produced.

vigorously until a solid separated. This was filtered off, the filtrate treated with another drop of benzaldehyde, and the process repeated until no more solid was obtained.

The acetone-δ-anilinosemicarbazone was insoluble in light petroleum, cold water, benzene, and ether, sparingly soluble in cold alcohol and acetone, and moderately soluble in hot alcohol, benzene, and acetone. It reduced Fehling's solution only after prolonged boiling, and was blackened by copper sulphate solution. The yield was 5%.

The toluene was removed from the mother liquor, by distillation under reduced pressure, and the residual oil cooled in ice, but no further solid was obtained. The oil was therefore distilled under reduced pressure, and a fraction B.P. 139°/37 mm. was obtained, this being within 1° of the boiling point of acetone phenylhydrazone, at that pressure. The distillate, a pale yellowish oil, did not reduce Fehling's solution, and on cooling in a freezing mixture it gave long needles. These were filtered off, washed with a little light petroleum, and dried in an evacuated desiccator. The crystals were quite white, melted at about 35°, and quickly turned to a brown oil on exposure. It would therefore appear to be acetone phenylhydrazone, and this was confirmed by hydrolysis, acetone and phenylhydrazine being identified. The phenylhydrazine could not be purified as hydrochloride, and was therefore converted to its benzylidene derivative which crystallised easily.

Hence the main products of the reaction were semicarbazide and acetone phenylhydrazone, while acetone-δ-anilinosemicarbazone was only formed to a small extent. The hydrazodicarbonamide was doubtless due to the decomposition of some of the semicarbazide.

(2) A similar reaction was carried out using benzene as a solvent, the benzene being refluxed vigorously for 34 hours, at the end of which time ammonia was still being evolved.

The large quantity of insoluble material was filtered off and identified as hydrazodicarbonamide.

Some of the benzene was removed under reduced pressure, and on cooling the residual liquid, acetone-δ-anilinosemicarbazone separated out of solution to the extent of about 5%.

The mother liquor was then fractionated under reduced pressure as in the previous experiment, and acetone phenylhydrazone was again the only product.

(3) This reaction was carried out without the use of a solvent, the materials being heated at 120-130° for 11 hours.

The products were found to be the same as before, the yield of δ-anilinosemicarbazone being 5%.

(4) In the preparation of triphenylrosaniline by heating aniline and rosaniline, ammonia being split off, the yield is increased by the addition of benzoic acid which seems to act as a catalyst. Since the reaction is similar to the one being tried, it was thought that the addition of benzoic acid might increase the yield of δ-anilinosemicarbazone.

The previous reaction was therefore repeated with the addition of 0.5 g. of benzoic acid, but the results were the same.

(5) Since mainly replacement had so far taken place, it was thought that an increase in temperature and the previous heating of the reactants to that temperature before mixing, might raise the yield of δ-anilinosemicarbazone.

5.4 g. of phenylhydrazine were therefore added to a gently refluxing solution of 5.7 g. of acetone semicarbazone in 30 ccs. of xylene. The temperature of the bath was maintained at 140°, until the evolution of ammonia ceased, the time required being 3½ hours.

On working up as before, the reaction products were the same, the yield of acetone-δ-anilinosemicarbazone being slightly smaller, namely 3%.

(6) The above reaction was repeated, using a paraffin fraction B.P. 160-170°. The evolution of ammonia ceased after ½ hour.

The products were as before, and the yield of δ-anilinosemicarbazone was 2%.

Phenylhydrazine and Methyl ethyl ketone Semicarbazone

4.32 g. of phenylhydrazine, 5.16 g. of methyl ethyl ketone semicarbazone (Scholtz, B. 1898, 29, 610) and 20 ccs. of toluene were heated under reflux in a bath at 80-90° until an insoluble material commenced to separate. This required about 4 hours heating.

The insoluble was filtered off while hot, washed with toluene and recrystallised from water. As in the case of acetone semicarbazone, it was found to be hydrazodicarbonamide.

The toluene solution, on cooling, gave crystals, which, after recrystallising and decolourising, were identified as semicarbazide.

Most of the toluene was distilled off from the mother liquor, under reduced pressure, and the residual oil cooled in ice for three days, but no more solid was obtained. It was therefore fractionated at 100 mm. (methyl ethyl ketone phenylhydrazone, Arnold, B.1897, 30, 1016, boils at 190°/100 mm.) and the fraction B.P. 188-192° collected. This was hydrolysed by boiling with dilute hydrochloric acid, and a portion of the liquid distilled off. This was found to contain methyl ethyl ketone by the nitroprusside test* and by its odour. Phenylhydrazine was found in the residual liquid, being separated and identified by means of its benzylidene derivative as in the case of acetone phenylhydrazone.

(2) The above experiment was repeated, the heating being continued for 10 hours.

The products were mainly hydrazodicarbonamide and methyl ethyl ketone phenylhydrazone. A little semicarbazide was also produced, but no other substances were found.

(3) 4.32 g. of phenylhydrazine, 5.16 g. of the semicarbazone and 5 ccs. of toluene were heated in a bath at 130° for 4 hours.

The products were only hydrazodicarbonamide and methyl ethyl ketone phenylhydrazone, no trace of other products being found.

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* As for acetone, page 18.

Phenylhydrazine and Methyl propyl ketone Semicarbazone.

4.44 g. of phenylhydrazine, 6.00 g. of methyl propyl ketone semicarbazone (Bouveault and Bougert, Bl. 1902, (3), <u>27</u>, 1083), and 20 ccs. of toluene, were heated under reflux in a bath at 130°, for 9 hours. Ammonia was evolved, and an insoluble product separated.

This insoluble was filtered off, and found to be hydrazodicarbonamide as in previous cases.

The toluene was removed from the filtrate under reduced pressure and the oily residue cooled in ice for about 40 hours. No solid separated, and the addition of light petroleum produced no precipitate. The solvent was therefore distilled off and the residue fractionated under reduced pressure. A fraction B.P. 188-193°/90 mm. was obtained, and was found by hydrolysis to be methyl propyl ketone phenylhydrazone (Fischer, A. 1886, <u>236</u>, 132).

No other products were obtained.

Phenylhydrazine and Diethyl ketone Semicarbazone.

4.0 g. of phenylhydrazine, 5.4 g. of diethyl ketone semicarbazone (Dilthey, B. 1901, 34, 2122), and 20 ccs. of toluene, were heated under reflux in a bath at 130° for 7 hours. Ammonia was evolved, and a large quantity of insoluble material separated.

This insoluble substance was filtered off, washed with a little hot toluene, and found to be, as in previous cases, hydrazodicarbonamide.

The toluene was removed from the filtrate by distillation under reduced pressure, and to the residual oil was added twice its volume of light petroleum. On cooling in ice, a little solid was obtained, and this was filtered off and recrystallised from alcohol. Colourless plates, M.P. 180-182° were thus obtained, but the quantity was too small to permit of further investigation. The mother liquor on standing, deposited more solid, and this was filtered off. On recrystallising from alcohol, 0.2 g. of *diethyl ketone-δ-anilinosemicarbazone,* $Et_2C{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHPh$, was obtained in the form of white needles, M.P. 140-141°.

Found :- N = 24.16%.

$C_{12}H_{18}ON_4$ requires N = 23.93%.

0.1 g. of the compound was hydrolysed by boiling with dilute hydrochloric acid, and some of the liquid distilled off. Diethyl ketone was identified in the distillate by its odour and semicarbazone. The residual liquid was taken to dryness under reduced pressure, and the residue identified as δ-anilinosemicarbazide hydrochloride by comparison with an authentic specimen, and by means of its benzylidene derivative. Hence the constitution of the original compound was proved.

The compound was fairly soluble in alcohol, and insoluble in light petroleum. The yield was 2%.

The solvent was removed from the original mother liquor, and the remaining oil distilled under reduced pressure. A fraction B.P. 130°/6 mm. was obtained, and found by hydrolysis to be diethyl ketone phenylhydrazone (Planoher, G. 1898, 28, ii, 387).

Phenylhydrazine and Methyl *tert*-butyl ketone Semicarbazone.

3.6 g. of phenylhydrazine, 5.2 g. of the semicarbazone (Carlinfanti, G. 1897, 27, ii, 387), and 20 ccs. of toluene, were heated under reflux in a bath at 130° till the evolution of ammonia ceased; this required 7½ hours.

The small quantity of insoluble material which had formed, was filtered off and identified as before as hydrazodicarbonamide.

Most of the toluene was then removed under reduced pressure, and the solid which separated on cooling was filtered off and recrystallised from alcohol. Feathery needles were thus obtained, and these proved to be *methyl* tert-*butyl ketone-δ-anilinosemicarbazone*, $Me(Me_3C)C:N\cdot NH\cdot CO\cdot NH\cdot NHPh$, M.P. 179°.

Found :- N = 22.54%; 22.69%.

$C_{13}H_{20}ON_4$ requires N = 22.58%.

On hydrolysis with dilute hydrochloric acid, it gave methyl *tert*-butyl ketone and δ-anilinosemicarbazide hydrochloride, identified as before.

It was insoluble in water and light petroleum, slightly soluble in cold alcohol, more soluble in cold benzene, and easily soluble in ether, hot benzene, and alcohol. It reduced Fehling's solution after considerable boiling, probably because of hydrolysis, for the odour of the ketone was quite distinct. The yield was 60%.

As the yield of δ-anilinosemicarbazone was large, phenylhydrazone, if formed, could only be present in small quantity. Hence instead of distilling, it was decided to remove impurities which would vitiate the results of hydrolysis. The mother liquor from the crude δ-anilinosemicarbazone was therefore treated with light petroleum till no more precipitate was obtained, and the petroleum solution washed with dilute acetic acid and water to remove unchanged phenylhydrazine. The solvent was then distilled off and the residual oil hydrolysed, methyl *tert*-butyl ketone and phenylhydrazine being identified by the usual means.

Phenylhydrazine and *cyclo*Hexanone Semicarbazone.

3.6 g. of phenylhydrazine, 5.2 g. of the semicarbazone (Zelinsky, B. 1897, 30, 1541), and 20 ccs. of toluene were heated under reflux till the evolution of ammonia ceased; this required 4 hours at 135°.

The insoluble material produced, was filtered off and found to be hydrazodicarbonamide.

The filtrate was cooled in ice and as no solid was obtained the toluene was removed under reduced pressure, and the almost solid residue washed out with a little cold alcohol. On recrystallising from alcohol it gave a white amorphous mass , M.P. 194°, of cyclo*hexanone-δ-anilinosemicarbazone,*

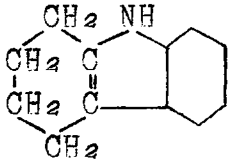

$CH_2<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>C:N\cdot NH\cdot CO\cdot NH\cdot NHPh.$

Found :- N = 22.95%; 22.90%.

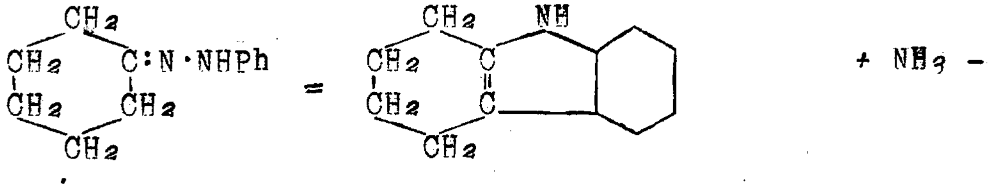
$C_{13}H_{18}ON_4$ requires N = 22.77%.

Slightly soluble in hot alcohol, acetone, and methyl ethyl ketone, from which it separated in an amorphous form, it gave plates M.P. 192° from methyl alcohol, in which it was only slightly soluble. Easily soluble in pyridine, it crystallised from a mixture of alcohol and pyridine in plates, M.P. 192°. A mixture of the two forms melted at 192°. The yield was 12%.

The alcohol was distilled off from the mother liquor of the crude δ-anilinosemicarbazone, and the residual oil cooled in ice. The pasty solid obtained was crystallised from aqueous alcohol, giving long needles, M.P. 77-78°. These, on treating with hot dilute sulphuric acid, gave tetrahydrocarbazole,



, thus conforming to the behaviour of *cyclo*hexanone phenylhydrazone under the same treatment-



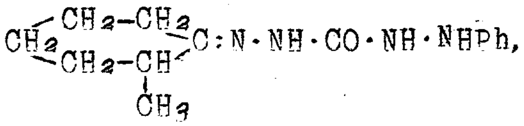
(Baeyer, A. 1894, <u>278</u>, 105).

Phenylhydrazine and 1-Methyl*cyclo*hexan-2-one Semicarbazone.

3.21 g. of phenylhydrazine, 4.86 g. of the semicarbazone* (Zelinsky, B. 1897, 30, 1542), and 20 ccs. of toluene were heated under reflux for 8 hours, in a bath at 130°. Ammonia was evolved.

The insoluble material was filtered off while still hot, washed with hot toluene, and identified as in other cases, as hydrazodicarbonamide.

The filtrate, on cooling in ice, deposited crystals which after several crystallisations from alcohol gave white needles of *1-methylcyclohexan-2-one δ-anilinosemicarbazone*,



$$CH_2\begin{matrix}\diagup CH_2-CH_2\diagdown\\ \diagdown CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}\diagup\end{matrix}C:N\cdot NH\cdot CO\cdot NH\cdot NHPh,$$

M.P. 182-183°. The yield was 10%.

Found :- N = 21.54%.

$C_{14}H_{20}ON_4$ requires N = 21.59%.

It was hydrolysed by boiling with dilute hydrochloric acid, and a portion of the liquid distilled off. This distillate was found to contain

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*For preparation of the ketone see appendix, P. 135

1-methyl*cyclo*hexan-2-one by its odour and semicarbazone. The residual liquid was found to contain δ-anilinosemicarbazide hydrochloride, by the usual methods.

The toluene was distilled off from the mother liquor under reduced pressure, and the oily residue cooled in ice. The crystals thus obtained were extracted with light petroleum, and filtered. The residue was found to be δ-anilinosemicarbazone. The solvent was removed from the filtrate in an evacuated desiccator, leaving a solid residue. By analogy with previous experiments, this was expected to be 1-methyl*cyclo*hexan-2-one phenylhydrazone, but this compound has been previously described as an oil B.P. 204-205°/ 30 mm. by Plancher (R.A.L. 1900, 9, 221). The solid was recrystallised from warm aqueous alcohol, and gave white needles M.P. 45-46° identical with a prepared specimen of 1-methyl*cyclo*hexan-2-one phenylhydrazone*. The compound quickly turned to a brown oil on exposure.

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* See appendix, P. 138.

Phenylhydrazine and Di-*n*-propyl ketone Semicarbazone

3.6 g. of phenylhydrazine, 5.7 g. of di-*n*-propyl ketone semicarbazone (Dilthey, B. 1901, 34, 2123), and 10 ccs. of toluene, were heated in a bath at 130° for 5½ hours. Ammonia was evolved, and an insoluble compound separated.

This insoluble was filtered off, washed with hot toluene, and identified as hydrazodicarbonamide.

The filtrate was cooled in ice, but as nothing separated, the toluene was distilled off under reduced pressure. On cooling the residue in ice, crystals were obtained, and the separation was aided by the addition of light petroleum. After filtering and recrystallising from absolute alcohol, they gave beautiful silky matted needles M.P. 152° which were proved to be *di-n-propyl ketone-δ-anilinosemicarbazone*, $(CH_3\cdot CH_2\cdot CH_2)_2C:N\cdot NH\cdot CO\cdot NH\cdot NHPh$.

Found :- N = 21.48%; 21.42%.

$C_{14}H_{22}ON_4$ requires N = 21.38%.

On hydrolysis with dilute hydrochloric acid di-*n*-propyl ketone and δ-anilinosemicarbazide hydrochloride were obtained, being identified in the usual manner.

The compound was insoluble in water and light petroleum, slightly soluble in cold alcohol, and very soluble in benzene, ether, acetone, and hot alcohol. The yield was 13%.

The solvent was removed from the mother liquor and the residual oil fractionated at 7 mm. and the portion boiling about 159° collected - di-*n*-propyl ketone phenylhydrazone (Arbusow, C. 1913, 2, 1474) has B.P. 159-160°/7 mm. The fraction obtained was identified as di-*n*-propyl ketone phenylhydrazone by hydrolysis.

Phenylhydrazine and Di*iso*propyl ketone Semicarbazone.

3.1 g. of phenylhydrazine, 4.9 g. of di-*iso*-propyl ketone* semicarbazone**, and 20 ccs. of toluene, were heated under reflux in a bath at 135° for 6½ hours. Ammonia was evolved, and no insoluble product separated.

The solution on cooling deposited crystals, and these were filtered off and washed with a little cold toluene. After two recrystallisations from absolute alcohol, colourless prismatic needles of *diisopropylketone-δ-anilinosemicarbazone*, $[(CH_3)_2CH]_2C{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHPh$, were obtained, M.P. 181°. The yield was 90%.

Found :- N = 21.46%; 21.47%.

$C_{14}H_{22}ON_4$ requires N = 21.37%.

The compound was hydrolysed by boiling with

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* The ketone was prepared from *iso*butyric acid by the manganous oxide method of Sabatier and Mailhe (C.R. 1914, <u>158</u>, 832).

** See appendix P. 136.

dilute hydrochloric acid, the liquid extracted with ether and separated. Di*iso*propyl ketone was identified in the ethereal extract by means of its semicarbazone, and δ-anilinosemicarbazide hydrochloride was obtained from the aqueous part by the usual means.

On concentrating the toluene mother liquor, a little more δ-anilinosemicarbazone was obtained.

No other products were found.

Phenylhydrazine and Methyl benzyl ketone Semicarbazone.

3.6 g. of phenylhydrazine, 6.4 g. of methyl benzyl ketone semicarbazone (Wolff, Bock, Lorentz, and Trappe, A. 1902, 325, 146), and 20 ccs. of toluene were heated under reflux in a bath at 130° for 7 hours. Ammonia was evolved, and an insoluble substance separated.

This insoluble product was filtered off, and identified as hydrazodicarbonamide as before.

The toluene was removed from the filtrate under reduced pressure, and some light petroleum added to the oily residue. After cooling in ice, a solid was obtained, and this was filtered off and recrystallised from alcohol. The resultant crystals melted at 88°, and were extracted with hot light petroleum since methyl benzyl ketone phenylhydrazone (Frenkler, A. 1888, 248, 110) melts at 83° and is soluble in that solvent. The insoluble portion was filtered off and recrystallised from alcohol, giving, finally, colourless glistening plates of *methylbenzyl-*

ketone-δ-anilinosemicarbazone, $Me(PhCH_2)C:N\cdot NH\cdot CO\cdot NH\cdot NHPh$, M.P. 171-172°. The yield was 13%.

Found :- N = 19.93%; 19.90%.

$C_{16}H_{18}ON_4$ requires N = 19.86%.

On hydrolysis with dilute hydrochloric acid it gave methyl benzyl ketone and δ-anilinosemicarbazide hydrochloride which were separated and identified as in the previous experiment.

The petroleum filtrate from the crude δ-anilinosemicarbazone deposited crystals on cooling, and these after filtration were found to melt at 83°. They were further proved by hydrolysis to consist of methyl benzyl ketone phenylhydrazone.

Phenylhydrazine and Benzylacetone Semicarbazone.

2.7 g. of phenylhydrazine, 5.0 g. of benzylacetone semicarbazone (Klages, B. 1904, 37, 2313), and 10 ccs. of toluene, were heated under reflux in a bath at 125° for 8 hours. Ammonia was evolved, and a large quantity of insoluble material formed.

The insoluble was filtered off, washed with toluene, and identified as hydrazodicarbonamide.

The filtrate was cooled in ice but nothing separated, and so the toluene was distilled off under reduced pressure. The residue on cooling gave crystals which were filtered off and recrystallised from alcohol. Silky needles of *benzylacetone-δ-anilinosemicarbazone*, $Me(PhCH_2\cdot CH_2)C:N\cdot NH\cdot CO\cdot NH\cdot NHPh$, M.P. 162°, were thus obtained.

Found :- N = 19.14%; 18.97%.

$C_{17}H_{20}ON_4$ requires N = 18.92%.

It was insoluble in water and light petroleum, slightly soluble in cold alcohol, and easily soluble in ether, benzene, and hot alcohol. While the first crop separated in the form of needles, the substance came down from the mother liquor, on standing, in small plates of the same melting point. It turned slightly yellow on standing, and was blackened by boiling Fehling's solution though no reduction took place. The yield was 8%.

It was hydrolysed by boiling with dilute hydrochloric acid giving benzylacetone and δ— anilinosemicarbazide hydrochloride, these being separated and identified in the usual manner.

Unsuccessful attempts were made to obtain, from the original mother liquor from the crude δ-anilinosemicarbazone, benzylacetone phenylhydrazone in a solid condition - Schlenk (J. Pr. 1908, ii, <u>78</u>, 60) describes it as melting at 59°. All traces of solvent were therefore removed, and the residual oil hydrolysed. Benzylacetone and phenylhydrazine were obtained, thus proving the presence of benzylacetone phenylhydrazone.

Phenylhydrazine and Dibenzyl ketone Semicarbazone.

2.06 g. of phenylhydrazine, 5.10 g. of dibenzyl ketone semicarbazone (Senderens, C.R. 1910, 150, 1337), and 20 ccs,of toluene, were heated in a bath at 130° for 4 hours, the evolution of ammonia having ceased after that time. After about ½ hour of heating, a white crystalline solid commenced to separate, and by the time the reaction was finished, an almost solid mass was formed.

This product was filtered off and recrystallised from a mixture of alcohol and pyridine, and gave a mass of white needles, M.P. 205°, which proved to be *dibenzylketone-δ-anilinosemicarbazone*, $(PhCH_2)_2C:N\cdot NH\cdot CO\cdot NH\cdot NHPh$.

Found :- N = 15.85%; 15.77%.

$C_{22}H_{22}ON_4$ requires N = 15.62%.

The compound was insoluble in water, light petroleum, and benzene, and only slightly soluble in the usual solvents except pyridine and glacial acetic acid . The yield was 90%.

On hydrolysis with dilute hydrochloric acid, it gave dibenzyl ketone and δ-anilinosemicarbazide hydrochloride, identified in the usual manner.

Since the semicarbazone, phenylhydrazone, and semioxamazone of this ketone exist in dimorphous forms, it was thought that the δ-anilinosemicarbazone might also possibly give two forms. Attempts to get different crystals by crystallising from dilute, concentrated, cold, and hot solutions, etc., were unsuccessful, though some of the crops examined under the microscope seemed to contain plates as well as needles.

No other products were obtained on working up the toluene solution.

Phenylhydrazine and Acetaldehyde Semicarbazone.

5.40 g. of phenylhydrazine, 5.05 g. of the semicarbazone (Thiele and Bailey, A. 1898, 303, 79), and 30 ccs. of toluene, were heated under reflux in a bath at 130° for 6 hours. A little ammonia was evolved, the semicarbazone dissolved gradually, and an insoluble product separated.

This insoluble material was filtered off, washed with a little hot toluene and extracted with alcohol. The residue was found to be, as in previous cases, hydrazodicarbonamide.

The alcoholic extract was concentrated, and finally gave crystals which were identified as unchanged acetaldehyde semicarbazone.

The toluene was removed from the mother liquor under reduced pressure, and the oily residue cooled in ice till crystals were obtained. These were recrystallised from light petroleum, and gave leaves, M.P. 59-60°; by recrystallising from alcohol, the M.P. was raised to 75°. This corresponds to the behaviour of acetaldehyde phenylhydrazone (Laws and Sidgwick, J.C.S. 1911, 99, 2085). It was therefore recrystallised from 75% alcohol containing a little hydrochloric acid, and the product M.P. 58° was identical with a prepared specimen of the β form of acetaldehyde phenylhydrazone.

No other products were isolated.

Phenylhydrazine and *n*-Heptaldehyde Semicarbazone.

4.3 g. of phenylhydrazine, 6.8 g. of the semicarbazone (Semmler, B. 1909, 42, 1162), and 20 ccs. of toluene, were heated in a bath at 125° for 8 hours. Ammonia was evolved during this period, and an insoluble product separated.

This insoluble material was filtered off and identified as hydrazodicarbonamide.

The toluene was distilled off from the filtrate under reduced pressure, and a solid was obtained by cooling the residue in ice. This was filtered off, washed with light petroleum, and crystallised several times from alcohol. Small white lustrous balls of fine needles, M.P. 176°, were finally obtained, and these proved to be n-*heptaldehyde-δ-anilinosemicarbazone*, $CH_3(CH_2)_5CH{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHPh$.

Found :- N = 21.46%; 21.55%.

$C_{14}H_{22}ON_4$ requires N = 21.37%.

The substance was insoluble in light petroleum, and sparingly soluble in cold alcohol. The yield was 8%.

The compound was hydrolysed by boiling with dilute hydrochloric acid for a short time, and *n*-heptaldehyde and δ-anilinosemicarbazide hydrochloride were separated and identified in the usual manner.

The solvent was distilled off from the filtrate of the crude δ-anilinosemicarbazone and the residue fractionated under reduced pressure. A fraction B.P. 180-190°/14 mm. was obtained, and a portion hydrolysed by boiling with dilute hydrochloric acid. The odour of *n*-heptaldehyde could not be detected, but phenylhydrazine was found. Hydrolysis with dilute sulphuric acid for a few moments, however, revealed the presence of the aldehyde. Some *n*-heptaldehyde phenylhydrazone (Reisenegger, B. 1883, 16, 663) was prepared, and behaved exactly as the above; it gave B.P. 184-187°/14 mm.

Phenylhydrazine and Furfuraldehyde Semicarbazone.

3.6 g. of phenylhydrazine, 5.1 g. of furfuraldehyde semicarbazone (Knöpfer, Monatsh. 1910, 31, 95), and 20 ccs. of toluene, were heated under reflux in a bath at 135° for 10 hours. Ammonia was evolved and an insoluble product separated.

The insoluble was filtered off, extracted with alcohol, and found to be hydrazodicarbonamide. Nothing was obtained from the alcoholic extract.

The toluene was removed under reduced pressure, leaving a clear viscous mass which crystallised by cooling overnight in ice. On recrystallising from aqueous alcohol, yellowish plates M.P. 95-96° were obtained. These were identified, by comparison with an authentic specimen, as furfuraldehyde phenylhydrazone (Fischer, B. 1884, 17, 574).

No other products were obtained.

α-Methyl-α-phenylhydrazine and Acetophenone Semicarbazone.

3.87 g. of α-methyl-α-phenylhydrazine, 5.10 g. of acetophenone semicarbazone (Stobbe, A. 1899, 308, 123), and 17 ccs. of toluene, were heated under reflux in a bath at 125-130° for 8 hours. Ammonia was evolved, and the semicarbazone gradually dissolved to give a clear solution.

A solid separated from the solution on cooling, and this was filtered off and washed with a little cold toluene, giving an almost white mass. On crystallising from absolute alcohol it gave colourless prisms of *acetophenone-δ-methylanilino-semicarbazone*, MePhC:N·NH·CO·NH·NMePh, M.P. 196°.

Found :- N = 19.94%; 19.99%.

$C_{16}H_{18}ON_4$ requires N = 19.86%.

The compound was sparingly soluble in cold alcohol, ether, acetone, and benzene, moderately soluble in cold chloroform, pyridine, glacial acetic acid, hot alcohol and benzene, and easily soluble in hot pyridine and glacial acetic acid. It was precipitated from solution in pyridine and acetic acid by the addition of water. The yield, increased slightly by working up the toluene mother liquor, was 85%.

0.5 g. of the acetophenone-δ-methylanilinosemicarbazone was hydrolysed by boiling with 10 ccs. of dilute hydrochloric acid, under reflux, until a clear solution was obtained; this necessitated 5 minutes boiling. The solution was extracted with ether and separated. The ethereal part was distilled free from ether and the residual oil identified as acetophenone by its odour and semicarbazone. The aqueous portion was taken to dryness under reduced pressure, and the semi-oily residue treated with ether, thus causing it to become quite solid. The solid was then washed out with ether and dissolved in absolute alcohol in which it was found to be rather soluble. On adding dry ether or light petroleum to the solution, *δ-methylanilinosemicarbazide hydrochloride*, $PhMeN \cdot NH \cdot CO \cdot NH \cdot NH_2, HCl$, was precipitated sometimes as a white solid, M.P. 181°, and sometimes as an oil which solidified on standing and scratching.

Found :- Cl = 16.31%; N = 25.81%.

$C_{18}H_{13}ON_4Cl$ requires Cl = 16.38%; N = 25.86%.

An attempt was made to prepare the base δ-methylanilinosemicarbazide from its hydrochloride, by dissolving 0.3 g. in a little absolute alcohol and adding the theoretical quantity of sodium ethoxide. The precipitated sodium chloride was filtered off and the filtrate concentrated to a pasty mass in an evacuated desiccator. On treating this with chloroform the odour of carbylamine was noticed, showing that decomposition must have taken place, and so the attempt was given up.

αα-Diphenylhydrazine and Acetophenone Semicarbazone.

5.00 g. of αα-diphenylhydrazine, 4.90 g. of acetophenone semicarbazone, and 20 ccs. of toluene, were heated under reflux in a bath at 135-140° for 8½ hours. Ammonia was evolved during that period, and the semicarbazone seemed to dissolve gradually and be replaced by small colourless crystals.

After cooling, the product was filtered off, washed with alcohol in which they seemed to be almost insoluble, and recrystallised from a mixture of pyridine and alcohol. Thick colourless hexagonal plates of *acetophenone-δ-diphenylaminosemicarbazone*, $MePhC:N\cdot NH\cdot CO\cdot NH\cdot NPh_2$, M.P. 236-237°, were thus obtained.

Found :- N = 16.31%; 16.35%.

$C_{21}H_{20}ON_4$ requires N = 16.28%.

The compound was insoluble in ether, alcohol, and benzene, and easily soluble in hot pyridine and glacial acetic acid. It gave a blueish-green colour with concentrated sulphuric acid, and was not acted upon by Fehling's solution or copper sulphate. The yield, increased slightly by concentrating the toluene mother liquor, was 90%.

1.0 g. of the acetophenone-δ-diphenylamino-semicarbazone was boiled with 40 ccs. of 12% hydrochloric acid for 2 hours. The unchanged substance was filtered off and the filtrate extracted with ether and separated. The ethereal part was found to contain acetophenone by the usual means. The aqueous portion was taken to dryness under reduced pressure and the residue washed out with ether. It was extracted with a little hot absolute alcohol and filtered. The residue, the amount of which was small, was converted into its benzylidene derivative which was found to be benzal azine, and so the residue must have been hydrazine hydrochloride. Dry ether was added to the filtrate from the hydrazine hydrochloride and the precipitate filtered off. It was of a greenish colour, was very soluble in water, and proved to be a hydrochloride. Instead of trying to purify this hydrochloride, as the presence of the hydrazine hydrochloride showed that the hydrolysis had gone further than desired (Cf. δ-anilinosemicarbazide hydrochloride. page 5), it was converted into its benzylidene derivative, these compounds being usually easily purified.

This benzylidene derivative on crystallising from alcohol gave white silky needles, M.P. 234-235°, of *benzylidene-δ-diphenylaminosemicarbazone*, $PhCH:N\cdot NH\cdot CO\cdot NH\cdot NPh_2$.

Found :- N = 17.02%.

$C_{20}H_{18}ON_4$ requires N = 16.97%.

It was insoluble in light petroleum, slightly soluble in ether, and moderately soluble in boiling alcohol. It gave a blueish-green colour with concentrated sulphuric acid.

p-Tolylhydrazine and Acetone Semicarbazone.

5.0 g. of *p*-tolylhydrazine, 5.0 g. of acetone semicarbazone, and 20 ccs. of toluene, were heated under reflux for 9 hours in a bath at 135°. Ammonia was evolved, and an insoluble product formed during the course of the reaction.

This insoluble was filtered off, washed with toluene, and identified as hydrazodicarbonamide.

A little light petroleum was added to the filtrate which was then allowed to stand in ice with occasional scratching for two days. The solid thus obtained was filtered off, and after two crystallisations from alcohol melted at 168-169°. By further recrystallisation from alcohol and benzene, the melting point was raised to 175-176°. The substance was probably *acetone-δ-p-toluidinosemicarbazone*, $Me_2C:N\cdot NH\cdot CO\cdot NH\cdot NH\cdot C_6H_4\cdot CH_3$.

Found :- N = 24.98%; 24.85%.

$C_{11}H_{16}ON_4$ requires N = 25.46%.

The experiment had to be repeated to obtain sufficient for the second analysis, and on account of the small yield (9%, crude) it was decided not to proceed further with it.

The toluene was distilled off under reduced pressure from the mother liquor and the oily residue crystallised by cooling in ice. On recrystallising from light petroleum, yellow crystals of acetone-*p*-tolylhydrazone (Raschen, 1887, 239, 227) were obtained, being identified by hydrolysis into acetone and *p*-tolylhydrazine.

α-Methyl-α-phenylhydrazine and Acetone Semicarbazone.

5.00 g. of the hydrazine, 4.71 g. of acetone semicarbazone, and 20 ccs. of toluene, were heated under reflux in a bath at 135° for 8 hours. Ammonia was evolved, and an insoluble product separated.

The insoluble material was filtered off, washed with a little hot toluene, and identified as hydrazodicarbonamide.

The toluene filtrate, on cooling, deposited crystals which were filtered off and recrystallised from alcohol. Elongated masses of diamond plates, M.P. 194°, were thus obtained, and these were identified as *acetone-δ-methylanilinosemicarbazone*, $Me_2C:N\cdot NH\cdot CO\cdot NH\cdot NMePh$.

Found :- N = 25.58%; 25.48%.

$C_{11}H_{16}ON_4$ requires N = 25.45%.

It was sparingly soluble in ether, cold alcohol, and hot water, and moderately soluble in hot alcohol. It reduced Fehling's solution slightly on boiling, and was unaffected by copper sulphate. The yield was 52%.

The toluene was distilled off from the mother liquor under reduced pressure and light petroleum added to the oily residue. The solid which separated proved to be more acetone-δ-methylanilinosemicarbazone. The solvent was removed from the mother liquor and the residual oil distilled under reduced pressure, but the quantity was too small to determine the boiling point. The distillate was hydrolysed and acetone and α-methyl-α-phenylhydrazine identified by the usual means, thus showing the presence of acetone methylphenylhydrazone.

αα-Diphenylhydrazine and Acetone Semicarbazone.

6.31 g. of αα-diphenylhydrazine, 3.83 g. of acetone semicarbazone, and 20 ccs. of toluene, were heated under reflux in a bath at 135° for 7 hours. Ammonia was evolved and the semicarbazone dissolved gradually to give a clear solution.

The toluene solution deposited crystals on cooling and these were filtered off. On recrystallising from alcohol, needles of *acetone-δ-diphenylaminosemicarbazone*, $Me_2C:N\cdot NH\cdot CO\cdot NH\cdot NPh_2$, M.P. 186-187°, were obtained.

Found :- N = 19.96%; 19.86%.

$C_{16}H_{18}ON_4$ requires N = 19.86%.

The needles on standing in cold alcohol were converted into colourless prisms of the same melting point, and this change was greatly accelerated by heat. There was no depression of melting point on mixing the two forms. The compound gave a pale blueish-green colour with concentrated sulphuric acid, and a very deep blue colour when the acid contained a trace of nitric acid. With copper sulphate solution, an alcoholic solution of the compound gave a pale light blue colour which gradually changed to a violet purple, very like dilute permanganate. Ferric chloride gave a similar permanganate colour much more rapidly. The colour of the solution with copper sulphate was unaffected by boiling, whereas that with ferric chloride was changed to a brownish-red.

By distilling off the toluene from the mother liquor, under reduced pressure, and adding alcohol to the residue, a little more of this compound was obtained. The total yield was 80%, and no other products were found.

p-Tolylhydrazine and Benzylacetone Semicarbazone.

3.05 g. of *p*-tolylhydrazine, 5.13 g. of benzylacetone semicarbazone (Kessler and Rupe, B. 1912, 45, 29; by the reduction of benzylideneacetone semicarbazone), and 20 ccs. of toluene, were heated under reflux for 9 hours in a bath at 135°. Ammonia was evolved and an insoluble product separated.

The insoluble material was filtered off, treated in the usual amnner, and identified as hydrazodicarbonamide.

The toluene filtrate was cooled in ice and the crystals which separated after 24 hours were filtered off and recrystallised from alcohol. Pale yellow needles of *benzylideneacetone* p-*tolylhydrazone*, $Me(PhCH{:}CH)C{:}N{\cdot}NH{\cdot}C_6H_4Me$, M.P. 172-174°, were thus obtained, showing that the method of preparation of the semicarbazone was not altogether satisfactory. It was identified by comparison with an authentic specimen*.

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* See appendix, P. 139.

The toluene was removed from the mother liquor by distillation under reduced pressure, and the residual oil cooled in ice till it crystallised. After several crystallisations from light petroleum, a crop of crystals M.P. 74-78° was obtained, and this appeared to be *benzylacetone* p-*tolylhydrazone*, $Me(PhCH_2 \cdot CH_2)C:N \cdot NH \cdot C_6H_4 \cdot Me$.

Found :- N = 11.27%.

$C_{17}H_{20}N_2$ requires N = 11.11%.

It was further identified by hydrolysis with dilute hydrochloric acid, benzylacetone and *p*-tolylhydrazine being separated and identified in the usual manner. The compound was rather unstable, turning, on exposure, to a reddish oil, and decomposing even in solution.

α-Methyl-α-phenylhydrazine and Benzylacetone Semicarbazone.

4.07 g. of α-methyl-α-phenylhydrazine, 6.82 g. of benzylacetone semicarbazone, and 14 ccs. of toluene, were heated under reflux for 7 hours in a bath at 135°. A considerable evolution of ammonia occurred, and practically no insoluble material was formed.

The solution was cooled but no crystals were obtained, so the toluene was distilled off under reduced pressure. The clear viscous oil thus obtained did not crystallise on freezing, so it was dissolved in ether and the solution evaporated in a vacuum desiccator. The solid thus formed was extracted with alcohol, a little insoluble substance, M.P. 213°, being left; the quantity was too small to permit of further treatment. The alcoholic solution on cooling deposited crystals of *benzylacetone-δ-methylanilinosemicarbazone*, $Me(C_6H_5CH_2 \cdot CH_2)C:N \cdot NH \cdot CO \cdot NH \cdot NMePh$, in the form of acicular rosettes, M.P. 113°

Found :- N = 18.09%; 18.12%.

$C_{18}H_{22}ON_4$ requires N = 18.06%.

The yield was 65%, and no other products were obtained.

α-Methyl-α-phenylhydrazine and *n*-Heptaldehyde Semicarbazone.

4.07 g. of α-methyl-α-phenylhydrazine, 5.70 g. of *n*-heptaldehyde semicarbazone, and 20 ccs. of toluene, were heated under reflux in a bath at 135-140° for 7 hours. A little ammonia was evolved.

The insoluble substance which separated during the reaction was filtered off while hot and washed with a little hot toluene. It was identified as hydrazodicarbonamide.

As nothing separated from the toluene solution on cooling, the solvent was distilled off under reduced pressure and light petroleum added to the viscous residual oil. Only a very small quantity of solid separated, and this was filtered off; it was not treated further. The solvent was distilled off from the filtrate and the residual oil washed with dilute acetic acid and water, extracted with ether, and dried over anhydrous potassium carbonate. The ether was then removed and the oil fractionated under reduced pressure. A fraction B.P. 169-172°/5 mm. was obtained and this proved to be n-*heptaldehyde methylphenylhydrazone*, $CH_3(CH_2)_5CH:N\cdot NMePh$.

Found :- N = 12.76%.

$C_{14}H_{22}N_2$ requires N = 12.84%.

It was an almost colourless liquid which did not reduce Fehling's solution on boiling. On hydrolysis with dilute hydrochloric acid it gave the aldehyde and methylphenylhydrazine hydrochloride, both being identified in the usual manner.

α-Carbethoxy-α-phenylhydrazine and Acetophenone Semicarbazone.

5.0 g. of α-carbethoxy-α-phenylhydrazine (Rupe and Gebhardt, B. 1899, 32, 11), 4.9 g. of acetophenone semicarbazone, and 15 ccs. of toluene, were heated in a bath at 135°. The boiling tube containing the reactants was fitted with a reflux condenser, the top of which was joined to a wash-bottle containing a little dilute sulphuric acid, and the wash-bottle was attached to the pump and a very slight suction maintained. Ammonia was soon evolved, and after about 4 hours heating the semicarbazone had all dissolved. About 5 hours later, a white substance commenced to separate, and after about 10 hours heating the evolution of ammonia ceased.

The liquid in the wash-bottle was distilled and the first small quantity of distillate tested for alcohol but none was found. Some of the toluene was then distilled off, extracted with water and the aqueous part tested for alcohol, but without success.

After cooling, the product was filtered off and recrystallised from alcohol, giving *acetophenone-δ-carbethoxyanilinosemicarbazone*, MePhC:N·NH·CO·NH·N(CO_2Et)Ph, in the form of white rosettes of acicular plates M.P. 192°

Found :- N = 16.46%; 16.50%; C = 63.36%; H = 5.90%.
$C_{18}H_{20}O_3N_4$ requires N = 16.47%; C = 63.53%; H = 5.88%.

The acicular plates on standing in contact with their mother liquor or alcohol gradually changed into thick colourless plates of the same melting point, and these on recrystallisation from alcohol were converted to acicular plates. A mixture of the dimorphous forms showed no depression of melting point.

1.0 g. of the substance was hydrolysed by boiling with 20 ccs. of dilute hydrochloric acid for 4 minutes, a clear solution with a little oil on top being obtained. A portion of the liquid was distilled off, the distillate separated from the oil and tested for alcohol but none was found. The oil was identified as acetophenone by its odour and semicarbazone. The residual liquid was extracted with ether to remove the acetophenone still remaining, separated, and the aqueous part taken to dryness under reduced pressure. The residue was washed out with ether and dissolved in a little hot absolute alcohol. It did not crystallise and was therefore precipitated by the addition of ether, separating as a white amorphous solid M.P. 190°. Several attemps were made to crystallise this compound, identified as *δ-carbethoxyanilinosemicarbazide hydrochloride*, $Ph(CO_2Et)N\cdot NH\cdot CO\cdot NH\cdot NH_2,HCl$, but were unsuccessful.

Found*:- Cl = 12.86%; 12.89%.

$C_{10}H_{15}O_3N_4Cl$ requires Cl = 12.91%.

A benzylidene derivative, *benzylidene-δ-carbethoxyanilinosemicarbazone*, $PhCH{:}N\cdot NH\cdot CO\cdot NH\cdot N(CO_2Et)Ph$, was prepared in the usual manner from the hydrochloride. It crystallised from alcohol in white silky needles M.P. 158° with decomposition.

Found :- N = 17.00%; 17.06%.

$C_{17}H_{18}O_3N_4$ requires N = 17.18%.

* By Volhard method.

As it was desired to split up the δ-carbethoxyanilinosemicarbazide hydrochloride into alcohol, hydrazine, and phenylhydrazine, in order to prove its constitution, about 2.5 g. were boiled under reflux with 30 ccs. of concentrated hydrochloric acid for 2 hours. The uncondensed products were led into a wash-bottle containing water.

Portions were distilled from the acid solution and the liquid in the wash-bottle and tested for alcohol, but none was found.

The residual liquid from the hydrolysis was taken to dryness under reduced pressure and the solid dissolved in hot alcohol. On cooling and concentrating in vacuo, a small amount of a sparingly soluble compound separated. This was found to be hydrazine hydrochloride by its melting point and by its benzylidene derivative.

The alcoholic mother liquor was further concentrated and another crop obtained. This was filtered off and extracted with a little absolute alcohol, and filtered free from a little hydrazine hydrochloride. The solution was evaporated to small bulk as no crystals could be obtained, diluted with water, and a benzylidene derivative prepared after adding potassium acetate to remove the strong acid. This was recrystallised and identified as benzylidene-δ-carbethoxyanilinosemicarbazone, thus showing the presence of δ-carbethoxyanilinosemicarbazide hydrochloride.

The mother liquor was now taken to dryness, and the residue proved to be more δ-carbethoxyanilinosemicarbazide hydrochloride, being identified by its benzylidene derivative as above.

Since the above experiment had proved unsuccessful, 1.5 g. of the δ-carbethoxyanilinosemicarbazide hydrochloride were refluxed with 30 ccs. of 50% potassium hydroxide. Ammonia was evolved, and after that had ceased a portion of the liquid was distilled off and tested for alcohol but none was found.

About 2 g. of the hydrochloride were therefore distilled slowly with 40 ccs. of 40% sulphuric acid. Alcohol was detected in the distillate by means of the iodoform test. After distilling off about a third of the liquid, it was allowed to cool and the crystals which separated out were filtered off. These were dissolved in water and a benzylidene prepared in the usual manner. This was identified as benzal azine by comparison with an authentic specimen. Caustic soda was added to the mother liquor to partly neutralise the acid, and the precipitated bisulphate filtered off. The filtrate was treated with potassium acetate and benzaldehyde, the product being identified as benzylidene phenylhydrazone. Consequently the products of hydrolysis were alcohol, hydrazine, and phenylhydrazine, thus proving the constitution.

An attempt was made to split off alcohol from acetophenone-δ-carbethoxyanilinosemicarbazone, thus giving the acetophenone derivative of 4-phenyl-1-aminourazole (which was expected from the reaction described on P. 67), by heating it above its melting point. 1.0 g. of the compound was heated at 195° for 1¼ hours. The molten mass set on cooling to a clear resin which was dissolved in alcohol. Yellowish crystals separated from the solution, and after filtration they were extracted with hot light petroleum and filtered. The residue after recrystallising from alcohol was found to be unchanged starting material. The petroleum solution on cooling gave yellow plates M.P. 121° which were found by hydrolysis to be methyl phenyl ketazine.

The experiment was repeated, heating being carried out at 200-205° for 4 hours. The melt was treated as before, and the only product identified was methyl phenyl ketazine. A small quantity of an insoluble substance M.P. 236° was also isolated, but not identified.

Phenylhydrazine and Acetone Thiosemicarbazone.

4.32 g. of phenylhydrazine, 5.24 g. of acetone thiosemicarbazone (Freund and Schander, B. 1902, 35, 2604), and 20 ccs. of toluene, were heated under reflux for 6½ hours in a bath at 135°. A little ammonia was evolved, and a change in the form of the crystals suspended in the toluene appeared to take place. The mass of crystals was stirred up after an hour to ensure a greater surface.

The undissolved material was filtered off while still hot, and washed with a little hot toluene. The product melted at 182°, and this was unchanged by recrystallisation from alcohol. It was identified as thiosemicarbazide by comparison with an authentic specimen.

The first crop deposited from the toluene on cooling was recrystallised from alcohol and then from water. The crystals so obtained melted at 179° which is the melting point of acetone thiosemicarbazone, and it was identified as such by comparison with an authentic specimen.

The toluene was removed from the mother liquor by distillation under reduced pressure, and a few crystals separated from the oily residue on cooling in ice. These were filtered off but the quantity was too small to permit of identification.

The filtrate was fractionated under reduced pressure, and a fraction B.P. 139-142°/17 mm. was obtained. This was shown to be acetone phenylhydrazone by hydrolysis, acetone and phenylhydrazine being identified in the usual manner.

No other products were isolated.

Phenylhydrazine and Acetophenone Thiosemicarbazone.

2.70 g. of phenylhydrazine, 4.82 g. of acetophenone thiosemicarbazone (Neuberg and Neimann, B. 1902, 35, 2052), and 20 ccs. of toluene, were heated under reflux for 5 hours in a bath at 135°. After about ½ hour a clear solution was obtained and in about 1 hour a white crystalline solid commenced to separate out. The odour of ammonia and sometimes that of hydrogen sulphide, was noticed. A yellow distillate, probably a polysulphide of ammonium, formed in the condenser.

After cooling overnight, the crystals were filtered off, washed with alcohol, and recrystallised from alcohol. Glistening plates M.P. 177-178° were thus obtained. These were recrystallised from water and then melted at 182°, and were identified as thiosemicarbazide by comparison with an authentic specimen.

The toluene was removed from the mother liquor by distillation under reduced pressure, and the rather resinous residue cooled in ice till it crystallised. It was dissolved in hot absolute alcohol and the product obtained on cooling was obviously a mixture of yellowish crystals with an orange coloured amorphous substance. The mixture was extracted with a little cold carbon disulphide and filtered. The residue was the orange coloured substance, M.P. 171-172°, but the quantity was too small to permit of further treatment.

The carbon disulphide was removed from the filtrate in a vacuum desiccator and the residue recrystallised from alcohol. Almost white crystals M.P. 104-105° were thus obtained and they were identified as acetophenone phenylhydrazone by their behaviour and by comparison with an authentic specimen* (Reisenegger, B. 1883, 16, 662).

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* Acetophenone phenylhydrazone was found to give coloured solutions with some halogen-containing solvents. See appendix P.

Phenylhydrazine and Dibenzyl ketone Thiosemicarbazone.

1.80 g. of phenylhydrazine, 4.72 g. of dibenzyl ketone thiosemicarbazone (Appendix P. 142) and 20 ccs. of toluene were heated under reflux for 4 hours in a bath at 130-135°. Some ammonia was evolved and towards the end of the reaction some hydrogen sulphide was formed. Crystals separated from the clear solution during the reaction.

These crystals were filtered off, washed with a little hot toluene, and recrystallised from alcohol. Crystals M.P. 182° were obtained, and were identified as thiosemicarbazide by comparison with an authentic specimen.

The toluene filtrate was cooled in ice and the crystals which separated were filtered off, washed with toluene and recrystallised from alcohol, and then from light petroleum. Needles M.P. 128-129° were thus obtained, and these proved to be dibenzyl ketone phenylhydrazone (Francis, J.C.S. 1899, 75, 868), being identified by comparison with an authentic specimen. The second crop of crystals from the alcoholic mother liquor of the crude dibenzyl ketone phenylhydrazone, after several recrystallisations from alcohol, melted at 165-166°, and was found to be unchanged dibenzyl ketone thiosemicarbazone.

The toluene was removed from the mother liquor under reduced pressure, the residue cooled in ice and recrystallised from alcohol, but only more dibenzyl ketone phenylhydrazone was found.

Attempts to Synthesise
δ-Anilinothiosemicarbazide

(1) From Hydrazine Phenyldithiocarbazinate.

17 g. of hydrazine phenyldithiocarbazinate (Losanitch, J.C.S. 1921, <u>119</u>, 765) and the theoretical quantity of freshly precipitated lead carbonate were suspended in 250 ccs. of water and stirred vigorously for 1½ hours. As no appreciable darkening of the lead carbonate was taking place, the temperature was slowly raised to 60° and maintained at 60-70° for a further period of 1½ hours.

The quite black solid was filtered off and extracted with water, alcohol, and finally with acetic acid. Nothing was obtained from these extracts. The filtrate was cooled in ice but nothing separated out, and therefore the solution was concentrated under reduced pressure till a solid formed. After cooling, this was filtered off and recrystallised from water. It separated first as an oil and crystallised on cooling further; the product melted at 133-134°. It was recrystallised from absolute alcohol giving colourless glistening leaves M.P. 136°. Further crystallisation raised the melting point to 149° but the substance then looked less pure. An analysis of the crop M.P. 136° was carried out as the quantity did not permit of further treatment.

Found :- N = 29.14%.
δ-Anilinothiosemicarbazide requires N = 30.77%.

The mother liquor on further concentration gave more crystals, and these were filtered off and recrystallised from water. A product M.P. 169° with decomposition was thus obtained, and this was converted into its benzylidene derivative by boiling with benzaldehyde in alcoholic solution. Yellowish needles M.P. 192-194° separated on cooling and these were identified as dibenzylidene thiocarbohydrazone by analysis and by comparison with an authentic specimen.

Found :- N = 19.68%.
$C_{14}H_{14}N_4S$ requires N = 19.85%.

Hence the compound M.P. 169° was thiocarbohydrazide,

$(NH_2 \cdot NH)_2CS$.

The mother liquor from the crude thiocarbohydrazide was then treated with benzaldehyde and the product after purification was identified as benzylidene phenylhydrazone, thus showing the presence of free phenylhydrazine.

No other products were isolated.

The experiment was repeated, heating being carried out on a boiling water bath for 1 hour, but the same results were obtained with the exception that no substance melting at 136° was found.

Another experiment was tried using litharge instead of lead carbonate, 15 g. of the salt, 20 g. of litharge, and 150 ccs. of water, being heated at 50-60° for $\frac{3}{4}$ hour. On working up as before, a large quantity of unchanged salt was obtained, and the attempt was abandoned.

(2). From Thiocarbohydrazide and Aniline.

0.74 g. of thiocarbohydrazide (Stolle and

Bowles, B. 1908, 41, 1099), 0.65 g. of aniline, and 20 ccs. of toluene, were heated under reflux for 4 hours at 130-135°.

The solid was filtered off and found to be unchanged thiocarbohydrazide.

The experiment was therefore repeated using xylene, the bath being heated to 165°. Ammonia was evolved and also some hydrogen sulphide, and what appeared to be sulphur separated out. After 2 hours the insoluble material was filtered off, extracted with water, and a benzylidene derivative prepared from the extract. This melted at 193-194° and was probably dibenzylidene thiocarbohydrazone (which melts at 193-194° - Stolle and Bowles, B. 1908, 41, 1100). The toluene mother liquor gave a little of a compound, M.P. 172°, which was not identified, on account of the small quantity.

PART II

The THERMAL DECOMPOSITION of the δ-AMINOSEMICARBAZONES.

Introduction and Theoretical.

It was shown by Scholtz (B. 1896, 29, 611), Borsche (B. 1901, 34, 4297), and others, that semicarbazones decompose on heating to give azine and hydrazodicarbonamide, thus :-

$$\begin{array}{c} \mathrm{RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2} \\ + \\ \mathrm{RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2} \end{array} = \begin{array}{l} \mathrm{RR'C{:}N} \\ \qquad\quad | \\ \mathrm{RR'C{:}N} \end{array} + \begin{array}{l} \mathrm{NH{\cdot}CO{\cdot}NH_2} \\ | \\ \mathrm{NH{\cdot}CO{\cdot}NH_2} \end{array}$$

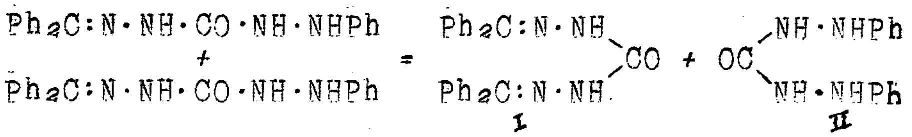
Curtius and Burkhardt (J.Pr. 1898, [2], 58, 223) further found that δ-phenylsemicarbazide decomposes on heating, giving hydrazine and hydrazodicarbonanilide, according to the equation

$$\begin{array}{c} \mathrm{NH_2{\cdot}NH{\cdot}CO{\cdot}NHPh} \\ + \\ \mathrm{NH_2{\cdot}NH{\cdot}CO{\cdot}NHPh} \end{array} = \begin{array}{l} \mathrm{NH_2} \\ | \\ \mathrm{NH_2} \end{array} + \begin{array}{l} \mathrm{NH{\cdot}CO{\cdot}NHPh} \\ | \\ \mathrm{NH{\cdot}CO{\cdot}NHPh} \end{array}$$

From those results it was thought that the δ-aminosemicarbazones would decompose on heating to give azine and a substituted hydrazidicarbonhydrazide, thus :-

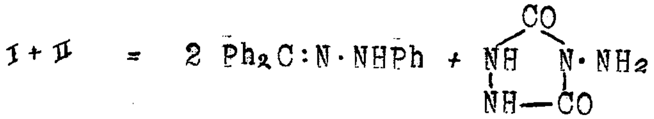
$$\begin{array}{c} \mathrm{RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHR''} \\ + \\ \mathrm{RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NHR''} \end{array} = \begin{array}{l} \mathrm{RR'C{:}N} \\ \qquad\quad | \\ \mathrm{RR'C{:}N} \end{array} + \begin{array}{l} \mathrm{NH{\cdot}CO{\cdot}NH{\cdot}NHR''} \\ | \\ \mathrm{NH{\cdot}CO{\cdot}NH{\cdot}NHR''} \end{array}$$

When, however, benzophenone-δ-anilinosemicarbazone was heated at 160–165° for 3 hours, besides some unchanged δ-anilinosemicarbazone, benzophenone carbohydrazone, (I), and an uncrystallisable resinous product were obtained. The resin gave colours with copper sulphate and ammonia similar to those given by diphenylcarbohydrazide, (II). Hence the reaction would appear to have followed the course shown by the equation



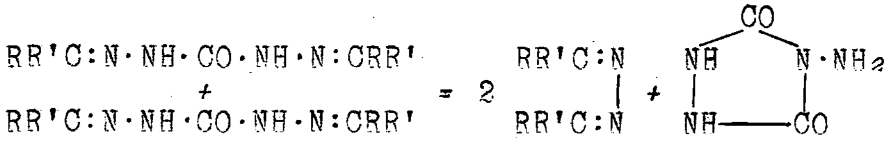
$$\begin{array}{c} Ph_2C{:}N\cdot NH\cdot CO\cdot NH\cdot NHPh \\ + \\ Ph_2C{:}N\cdot NH\cdot CO\cdot NH\cdot NHPh \end{array} = \underset{I}{\left.\begin{array}{c} Ph_2C{:}N\cdot NH \\ Ph_2C{:}N\cdot NH \end{array}\right\rangle CO} + \underset{II}{OC\left\langle\begin{array}{c} NH\cdot NHPh \\ NH\cdot NHPh \end{array}\right.} \qquad (1)$$

When the heating was carried out at a higher temperature and for a longer period, the only product identified was benzophenone phenylhydrazone. This must therefore have been formed by the interaction of the benzophenone carbohydrazone and the diphenylcarbohydrazide. To test this supposition, equimolecular quantities of the carbohydrazone and diphenylcarbohydrazide were heated in a manner similar to the δ-anilinosemicarbazone, and the products were benzophenone phenylhydrazone and N-aminourazole, thus agreeing with the theory. The interaction is shown by the equation



(2)

All the other δ-anilinosemicarbazones on heating gave the phenylhydrazone and N-aminourazole, and sometimes also a little azine. This latter was presumably formed by the partial decomposition of the intermediate carbohydrazone according to the scheme shown by Brown, Pickering, and Wilson, (J.C.S. 1927, 131, 108) –

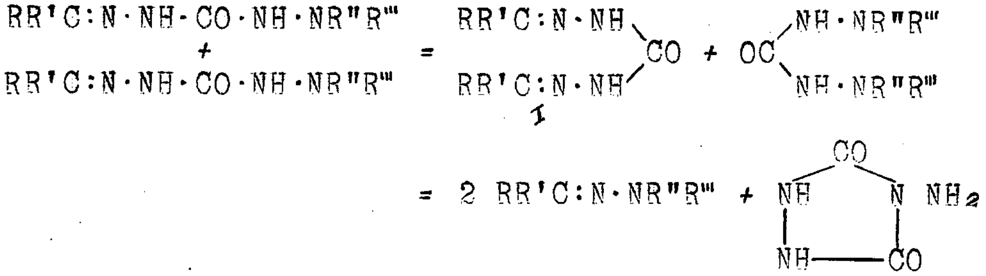


(3)

When acetone carbohydrazone and diphenylcarbohydrazide were heated together in equimolar quantities, acetone phenylhydrazone, N-aminourazole, and dimethyl ketazine were formed, thus showing that reactions (2) and (3) take place at the same time.

When acetone-δ-diphenylaminosemicarbazone was heated above its melting point, it decomposed and gave tetraphenylcarbohydrazide, N-aminourazole, dimethyl ketazine and acetone diphenylhydrazone, thus conforming to the behaviour of the δ-anilinosemicarbazones.

Consequently we may say that in general, δ-aminosemicarbazones decompose on heating, in two stages, according to the equations



(1)

(2),

and usually the intermediate carbohydrazone, (1), decomposes to a certain extent at the same time as reaction (2) is taking place, according to equation (3) on page 88.

The compounds actually isolated would seem to depend on the temperature at which the reaction is carried out and on the relative stability of the products of the different stages; the reaction temperature is of course limited by the melting point of the δ-aminosemicarbazone. E.g., benzophenone carbohydrazone was the only carbohydrazone isolated, presumably because it is fairly stable, and has a high melting point, (223-225°), and also because benzophenone-δ-anilinosemicarbazone has a fairly low melting point, namely 161°, thus enabling the decomposition to take place at a low temperature.

In the case of benzylidene-δ-anilinosemicarbazone, special precautions had to be adopted to isolate the phenylhydrazone as it decomposed at the temperature of the reaction, giving stilbene, benzylideneaniline, etc. (Chattaway, Cumming, and Wilsdon, J.C.S. 1911, 99, 1952).

EXPERIMENTAL.

Benzophenone-δ-anilinosemicarbazone.

2 g. of benzophenone-δ-anilinosemicarbazone (Sutherland and Wilson, J.C.S. 1924, 125, 2147) were heated at 180-185° for 1 hour. After cooling, the hard yellowish melt was treated with ether in order to promote crystallisation. The crystals were filtered off, washed with ether, and recrystallised from alcohol, and gave fine white needles, M.P. 223-225°. These were identified as benzophenone carbohydrazone by analysis and comparison with an authentic specimen.

Found :- N = 13.22%.
$C_{27}H_{22}ON_4$ requires N = 13.39%.

The alcoholic mother liquor from the benzophenone carbohydrazone, on concentration, gave crystals M.P. 155°, which were recrystallised from alcohol and identified as unchanged benzophenone-δ-anilinosemicarbazone, M.P. 161°.

The mother liquor gave a violet precipitate with copper sulphate and a scarlet colour with ammonia, which would seem to indicate that it contained diphenylcarbohydrazide (Skinner and Ruhemann, J.C.S. 1888, 53, 551). The solution was therefore concentrated in a vacuum desiccator, but only a resinous mass was left. This was treated with ether and other solvents but could not be obtained in a crystalline form. An attempt was made to isolate the diphenylcarbohydrazide by its mercuric chloride derivative, but the precipitate obtained could not be purified.

Another reaction was therefore carried out by heating 3 g. of the δ-anilinosemicarbazone for 3 hours at 160-165°. The melt was treated with ether and the crystals filtered off, washed with ether, and recrystallised from alcohol. The product turned pink in the air like diphenylcarbohydrazide and was fractionally crystallised from alcohol, but only benzophenone carbohydrazone and unchanged substance were isolated.

2 g. of benzophenone-δ-anilinosemicarbazone were heated for 7 hours in a bath at 180-185°. The melt when cold was a hard clear resin, and was dissolved in ether. On removing the ether in vacuo,

a semi-crystalline solid was obtained, and this was treated with cold alcohol and filtered. The residue was recrystallised from alcohol, giving yellowish crystals M.P. 134° which were recrystallised from alcohol and decolourised with charcoal. The product was almost white and melted at 136-137° (which is the melting point of benzophenone phenylhydrazone). It was insoluble in water and slightly soluble in light petroleum. On hydrolysis with dilute hydrochloric acid it gave benzophenone and phenylhydrazine. The former was extracted with ether and identified by means of its phenylhydrazone, and the latter was separated and identified as the benzylidene derivative in the usual manner. Hence the compound M.P. 136-137° was benzophenone phenylhydrazone, and this was confirmed by comparison with a prepared specimen.

No other products were identified.

Acetophenone-δ-anilinosemicarbazone.

2.0 g. of acetophenone-δ-anilinosemicarbazone (Sutherland and Wilson, J.C.S. 1924, 125, 2146) were heated in a bath at 220-225° for 2 hours. A small quantity of a gas resembling ammonia was evolved.

When cold, the mass was extracted with ether and the solvent removed in a vacuum desiccator. This was repeated in order to promote crystallisation, the mass again taken up with ether, filtered, and the residue washed with ether. The residue was extracted with boiling alcohol, and the insoluble portion recrystallised twice from water. Colourless prisms, M.P. 273-274°, were obtained. Their aqueous solution was strongly acid to litmus, gave a white precipitate with silver nitrate, and gave a red colouration with ferric chloride. From these properties it was thought to be N-aminourazole, and this was confirmed by analysis.

Found :- N =48.33%.

$C_2H_4O_2N_4$ requires N = 48.28%.

The alcoholic extract from the crude N-aminourazole was concentrated and yellowish crystals, M.P. 121°, were obtained. These were identified as methyl phenyl ketazine by comparison with an authentic specimen.

The solvent was removed from the ethereal extract of the melt and the residue recrystallised from alcohol. The first crop which was filtered off melted at 90-91° and decomposed on standing to give a dark oil smelling of acetophenone, thus resembling acetophenone phenylhydrazone in behaviour. The second crop was recrystallised from light petroleum and the resultant product was found to be acetophenone phenylhydrazone by comparison with an authentic specimen.

No other products were found.

Acetone-δ-anilinosemicarbazone.

2.0 g. of acetone-δ-anilinosemicarbazone (Appendix, P. 132) were heated in a small distillation flask immersed in a bath at 180°. To the flask was connected a similar one to act as a receiver, and this was connected to the pump. The apparatus was evacuated every hour till no more liquid distilled over.

The semi-resinous residue in the flask was extracted with boiling absolute alcohol, filtered, and the residue washed several times with hot alcohol. After recrystallisation from water it was identified as N-aminourazole by its reactions and by comparison with an authentic specimen.

The alcoholic filtrate was taken to dryness under reduced pressure, and the resinous residue treated with ether, frozen, etc., but it could not be crystallised. The alcoholic solution gave the usual colourations of diphenylcarbohydrazide with copper sulphate and ammonia.

The distillate was too small in quantity to be successfully fractionated, and was therefore hydrolysed by boiling with dilute hydrochloric acid. By distilling off part of the liquid it was found to contain acetone by the nitroprusside test. The residual liquid was taken to dryness under reduced pressure and the residue dissolved in water. This solution was treated with benzaldehyde in the usual manner till exhausted. The product was filtered off and recrystallised from alcohol and then from light petroleum, the crystals filtered off and well washed with the latter solvent. The compound thus obtained was identified as benzylidene phenylhydrazone by comparison with a prepared specimen; the quantity was small. The light petroleum filtrate was concentrated till crystals were obtained and these were recrystallised from alcohol and identified as benzal azine.

Hence the distillate was a mixture of acetone phenylhydrazone and dimethyl ketazine.

Methyl *tert.*-butyl ketone δ-Anilinosemicarbazone.

3 g. of the δ-anilinosemicarbazone (page 28) were heated under conditions exactly similar to those used for the acetone-δ-anilinosemicarbazone.

The semi-resinous residue was extracted with boiling alcohol and the insoluble part filtered off, recrystallised from water and identified as N-aminourazole as before.

The distillate was hydrolysed by boiling with dilute hydrochloric acid and a portion of the liquid distilled off. This distillate was found to contain methyl *tert.*-butyl ketone by its odour and by its semicarbazone. The residual liquid, on cooling, deposited crystals which were filtered off and identified as phenylhydrazine hydrochloride by their benzylidene derivative. The mother liquor from them was taken to dryness under reduced pressure and the residue extracted with a little hot absolute alcohol and filtered. The insoluble residue was found to be hydrazine hydrochloride by its melting point and that of its benzylidene derivative.

Hence the distillate contained methyl *tert.*-butyl ketone phenylhydrazone and methyl *tert.*-butyl ketazine*.

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* See appendix, P. 140.

Benzylidene-δ-anilinosemicarbazone.

3 g. of benzylidene-δ-anilinosemicarbazone (Appendix, P. 134) were heated in a flask of the Anschütz type to which was attached a small receiver. The temperature was maintained at about 220° for 1 hour, the apparatus being kept evacuated. A liquid distilled up and solidified in the collar of the flask.

The contents of the flask were extracted several times with absolute alcohol and the residue filtered off. This was identified as N-aminourazole as in previous cases.

The alcoholic extract on cooling, gave crystals of benzylidene phenylhydrazone.

No other products were found.

Acetone-δ-diphenylaminosemicarbazone.

2 g. of acetone-δ-diphenylaminosemicarbazone (page 59) were heated at 190-195° for 4 hours in a small flask fitted with a receiver; the apparatus was kept evacuated. A liquid distilled over and a black residue remained.

This residue, which was expected to be N-aminourazole, was extracted with boiling absolute alcohol and filtered. As the filtrate deposited crystals on cooling, it was decided to extract the N-aminourazole, if present, from the residue with hot water. This residue, therefore, after boiling with water and filtration, was recrystallised from alcohol and the first alcoholic extract added. It gave white needles, M.P. 241-242°, which were identified as tetraphenylcarbohydrazide (Acree, B. 1903, <u>36</u>, 3157).

Found :- N = 14.44%; 14.27%.

$C_{25}H_{22}ON_4$ requires N = 14.21%.

The compound remained white on standing whereas Acree states that it turns blue.

The aqueous extract of the crude tetraphenylcarbohydrazide was taken to dryness under reduced pressure. There was not sufficient residue to give a melting point, but its aqueous solution was acid to litmus and gave a white precipitate with silver nitrate and a red colouration with ferric chloride. Hence it was N-aminourazole.

The distillate was hydrolysed with dilute hydrochloric acid, and a small quantity of liquid distilled off. This distillate was found to contain acetone by the nitroprusside test. The residual liquid on cooling deposited crystals which were filtered off. They did not give a benzylidene derivative when treated in the usual way, but with a trace of nitric acid in sulphuric acid they gave a deep blue colour the same as diphenylhydrazine. An attempt was made to obtain the free base from the hydrochloride by means of alkali and to prepare the benzylidene derivative from the base*, but the quantity was too small to give a satisfactory derivative. The mother liquor from the above was concentrated and gave hydrazine hydrochloride, identified as usual. Hence the distillate was a mixture of acetone diphenylhydrazone and dimethyl ketazine.

* See appendix, P. 141.

The Action of Diphenylcarbohydrazide on Benzophenone Carbohydrazone.

0.18 g. of diphenylcarbohydrazide (Barnebey and Wilson, J.Am.C.S. 1913, 35, 156) and 0.30 g. of benzophenone carbohydrazone (page 91) were intimately mixed and heated for 5 hours at 180-185° - i. e., under conditions similar to those used for the decomposition of benzophenone-δ-anilinosemicarbazone.

The cold mass was extracted with ether and allowed to stand for a short time to promote crystallisation. The small quantity of insoluble material was filtered off and found to be N-aminourazole by its reactions.

The ethereal filtrate was taken to dryness and the residue recrystallised from alcohol several times. Crystals, M.P. 136-137° were finally obtained and these were identified as benzophenone phenylhydrazone by comparison with a prepared specimen.

The action of Diphenylcarbohydrazide on Acetone Carbohydrazone.

2.07 g. of diphenylcarbohydrazide and 1.45 g. of acetone carbohydrazone (Brown, Pickering, and Wilson, J.C.S. 1927, 131, 108) were ground intimately together and heated in exactly the same manner as acetone-δ-anilinosemicarbazone (page 97).

The residue in the flask was extracted several times with boiling absolute alcohol and the insoluble part identified as N-aminourazole as in previous cases.

The distillate was hydrolysed by boiling with dilute hydrochloric acid, and a portion of the liquid distilled off. This distillate was found to contain acetone by the nitroprusside test. The residual liquid was taken to dryness under reduced pressure, and the residue extracted with boiling absolute alcohol and filtered. The residue was shown to be hydrazine hydrochloride by its melting point and that of its benzylidene derivative. The alcoholic filtrate was concentrated to small volume and, after diluting with water, a benzylidene derivative was prepared in the usual manner. This was found to be benzylidene phenylhydrazone.

Hence the distillate would appear to have been a mixture of acetone phenylhydrazone and dimethyl ketazine.

The products of the reaction were the same as those obtained from the decomposition of the acetone-δ-anilinosemicarbazone.

PART III

The ACTION of AMINES on THIOSEMICARBAZONES.

Introduction and Theoretical.

It was shown by Borsche (B. 1901, 34, 4299; 1904, 37, 3177; 1905, 38, 831) that arylamines reacted with semicarbazones to give ammonia and a δ-arylsemicarbazone, thus :-

$$RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NH_2 + NH_2Ar = RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NHAr + NH_3.$$

These compounds on hydrolysis with dilute hydrochloric acid gave the ketone and the δ-arylsemicarbazide hydrochloride, from which the free base could be obtained by the action of weak alkalies -

$$RR'C{:}N{\cdot}NH{\cdot}CO{\cdot}NHAr + H_2O + HCl = RR'CO + HCl,NH_2{\cdot}NH{\cdot}CO{\cdot}NHAr.$$

This reaction was extended to aliphatic amines and amines with the NH_2 group in a side chain by Wilson, Hopper, and Crawford (J.C.S. 1922, 121, 866).

It has now been found that amines react with thiosemicarbazones in a similar manner giving ammonia and δ-substituted thiosemicarbazones -

$RR'C{:}N{\cdot}NH{\cdot}CS{\cdot}NH_2 + NH_2R'' = RR'C{:}N{\cdot}NH{\cdot}CS{\cdot}NHR'' + NH_3.$

Aliphatic amines, aromatic amines, and amines with the NH_2 group in a side chain, all reacted in the normal manner.

On hydrolysis with dilute hydrochloric acid they gave the ketone and the δ-substituted thiosemicarbazide hydrochloride –

$$RR'C{:}N{\cdot}NH{\cdot}CS{\cdot}NHR'' + H_2O + HCl = RR'CO + HCl,NH_2{\cdot}NH{\cdot}CS{\cdot}NHR''.$$

Sometimes a little *iso*thiocyanate and hydrazine hydrochloride were formed by the decomposition of the δ-substituted thiosemicarbazide hydrochloride, as was shown in the case of δ-phenylthiosemicarbazide by Pulvermacher (B. 1894, 27, 616) –

$$R''NH{\cdot}CS{\cdot}NH{\cdot}NH_2,HCl + HCl = R''N{:}C{:}S + NH_2NH_2,2\,HCl.$$

The free bases were obtained from their respective hydrochlorides by the action of water, barium carbonate, or sodium carbonate.

To prove their constitution, it was shown that the compound obtained from the action of aniline on acetone thiosemicarbazone was identical with acetone-δ-phenylthiosemicarbazone prepared from acetone and δ-phenylthiosemicarbazide (Stephen and Wilson, J.C.S. 1926, 129, 2534). Also the δ-benzylthiosemicarbazide synthesised in a manner similar to δ-phenylthiosemicarbazide (Pulvermacher, B. 1894, 27, 615), namely from benzyl *iso*thiocyanate and hydrazine hydrate,

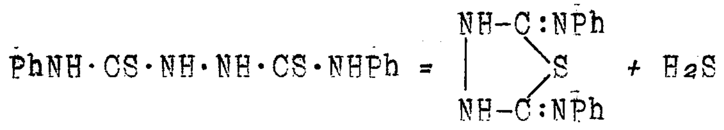
$$PhCH_2N{:}C{:}S + NH_2NH_2,H_2O = PhCH_2NH\cdot CS\cdot NH\cdot NH_2 + H_2O,$$

was the same as that obtained from the acetone derivative produced by the action of benzylamine on acetone thiosemicarbazone.

In some of the reactions, notably that of β-naphthylamine on acetone thiosemicarbazone, a little insoluble material was formed, and this was supposed to be due to the decomposition of the δ-thiosemicarbazone. Pulvermacher (B. 1894, 27, 616) showed that δ-phenylthiosemicarbazide decomposed on heating to give s-diphenylthiocarbamylhydrazide –

$$2\ PhNH\cdot CS\cdot NH\cdot NH_2 = PhNH\cdot CS\cdot NH\cdot NH\cdot CS\cdot NHPh + N_2H_4.$$

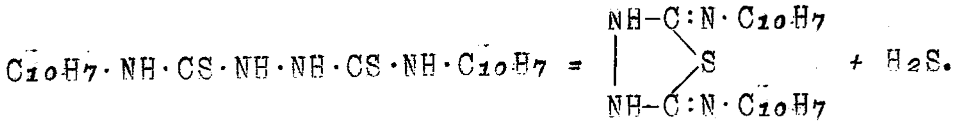
This decomposed further on heating to give a compound shown by Busch and Schmidt (B. 1913, 46, 2241) to be diphenyliminotetrahydrothiodiazole, hydrogen sulphide being evolved –



Presumably acetone-δ-β-naphthylthiosemicarbazone would, on heating, decompose in a similar way giving dimethyl ketazine and s-di-β-naphthylthiocarbamylhydrazide

$$2\ Me_2C:N\cdot NH\cdot CS\cdot NH\cdot C_{10}H_7 = Me_2C:N\cdot N:CMe_2 + C_{10}H_7\cdot NH\cdot CS\cdot NH\cdot NH\cdot CS\cdot NH\cdot C_{10}H_7,$$

which latter could then decompose to give hydrogen sulphide and di-β-naphthyliminotetrahydrothiodiazole



The insoluble product from the β-naphthylamine and acetone thiosemicarbazone gave an analysis corresponding to di-β-naphthyliminotetrahydrothiodiazole.

The acetone-δ-β-naphthylthiosemicarbazone when boiled with dilute hydrochloric acid gave mainly a large quantity of an insoluble product and a small amount of hydrazine hydrochloride. The insoluble product was probably s-di-β-naphthylthiocarbamylhydrazide and it was presumably formed, together with the hydrazine hydrochloride, by the decomposition of the δ-β-naphthylthiosemicarbazide hydrochloride,

$$\begin{array}{c} \mathrm{C_{10}H_7\cdot NH\cdot CS\cdot NH\cdot NH_2,HCl} \\ + \\ \mathrm{C_{10}H_7\cdot NH\cdot CS\cdot NH\cdot NH_2,HCl} \end{array} = \begin{array}{r} \mathrm{C_{10}H_7\cdot NH\cdot CS\cdot NH} \\ | \\ \mathrm{C_{10}H_7\cdot NH\cdot CS\cdot NH} \end{array} + \begin{array}{l} \mathrm{NH_2,HCl} \\ | \\ \mathrm{NH_2,HCl} \end{array}$$

EXPERIMENTAL.

Aniline and Acetone Thiosemicarbazone.

1.86 g. of aniline, 2.62 g. of acetone thiosemicarbazone, and 20 ccs. of toluene, were heated under reflux for 20 hours at 125-130°. As some unchanged substance separated out on cooling, the heating was continued at 130-135° for 17 hours, at the end of which period the evolution of ammonia had again ceased. A small quantity of an insoluble substance separated, and towards the end of the reaction some hydrogen sulphide was evolved.

The insoluble material was filtered off, washed, and recrystallised from alcohol. It gave leaves M.P. 245°, but the quantity was too small to permit of further treatment.

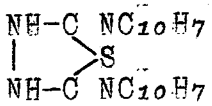
As nothing separated from the filtrate on cooling, the toluene was distilled off under reduced pressure. The clear yellow resinous residue obtained was dissolved in hot alcohol, and on cooling, crystals were deposited. After recrystallisation, these were identified as acetone-δ-phenylthiosemicarbazone by comparison with an authentic specimen. More of this compound was obtained by concentrating the mother liquor and adding light petroleum. The total yield did not exceed 30%.

The residual mother liquor was distilled under reduced pressure but only a little dimethyl ketazine was found.

β-Naphthylamine and Acetone Thiosemicarbazone.

5.72 g. of β-naphthylamine, 5.24 g. of acetone thiosemicarbazone, and 30 ccs. of toluene, were heated under reflux for 18 hours in a bath at 125-130°. Ammonia was evolved and an appreciable quantity of an insoluble substance separated out.

The insoluble material was filtered off and washed with a little hot toluene. It was then extracted with boiling alcohol, in which it was insoluble, and recrystallised from a mixture of alcohol and pyridine. It separated as an amorphous white solid which began to decompose at 266° and melted finally at 275°. It was thought to be *di-β-naphthyliminotetrahydrothiodiazole*,



$$\begin{array}{l} NH-C\ \ NC_{10}H_7 \\ |\qquad >S \\ NH-C\ \ NC_{10}H_7 \end{array}$$

Found :- N = 15.52%.

$C_{22}H_{16}N_4S$ requires N = 15.22%.

A solid separated from the toluene solution on cooling in ice and scratching. This was filtered off and after several recrystallisations from alcohol melted at 147-149°; after recrystallisation from benzene and again from alcohol, yellowish plates, M.P. 150-151°, of *acetone-δ-β-naphthylthiosemicarbazone*, $Me_2C:N \cdot NH \cdot CS \cdot NH \cdot C_{10}H_7$, were obtained.

Found :- N = 16.41%.

$C_{14}H_{15}N_3S$ requires N = 16.34%

The compound existed in dimorphous forms, since, when recrystallised from benzene, it gave an apparently amorphous form M.P. 137-138° which returned to the higher melting form on recrystallisation from alcohol. The yield was about 65% in the crude condition but decreased rapidly on purification. The mother liquors darkened as though decomposition were taking place.

About 1 g. of the compound was boiled with 40 ccs. of 6% hydrochloric acid, under reflux, for 1 hour. A large amount of insoluble material was formed and this was filtered off. It was insoluble in water and alcohol, and was recrystallised from a mixture of alcohol and pyridine. It formed a slightly pinkish solid which began to decompose at 220° and finally melted at 252°. It was thought to be s-*di-β-naphthylthiocarbamylhydrazide*, $C_{10}H_7 \cdot NH \cdot CS \cdot NH \cdot NH \cdot CS \cdot NH \cdot C_{10}H_7$.

Found :- $N = 13.71\%$.

$C_{22}H_{18}N_4S_2$ requires $N = 13.93\%$.

The filtrate from the crude s-di-β-naphthyl thiocarbamylhydrazide was found to contain acetone by the usual method.

The remaining liquid was taken to dryness under reduced pressure, and the residue extracted with hot absolute alcohol and filtered. The residue was found to be hydrazine hydrochloride by its melting point and that of its benzylidene derivative. The alcoholic filtrate was concentrated and found to contain a hydrochloride, but the amount was too small to permit of identification.

n-Heptylamine and Acetone Thiosemicarbazone.

4.60 g. of *n*-heptylamine, 5.24 g. of acetone thiosemicarbazone, and 30 ccs. of toluene, were heated under reflux for 21½ hours in a bath at 125-130°. Ammonia was evolved, and the thiosemicarbazone dissolved to give a perfectly clear solution.

No crystals separated from the solution on cooling, and so the solvent was distilled off under reduced pressure, a clear viscous oil being left. This crystallised on cooling and was dissolved in a little hot absolute alcohol. On cooling this solution in ice , crystals were obtained and these were filtered off and recrystallised from light petroleum. They gave thin glistening plates of *acetone-δ-heptylthiosemicarbazone*, $Me_2C:N\cdot NH\cdot CS\cdot NHC_7H_{15}$, M.P. 74-74.5°. A further crystallisation raised the melting point to 75°, and the substance possessed the same melting point after recrystallisation from aqueous alcohol. It sometimes separated as needles.

Found :- N = 18.37%.

$C_{11}H_{23}N_3S$ requires N = 18.34%.

The compound was easily soluble in ether, carbon tetrachloride, alcohol, and benzene. The yield was increased by concentrating the mother liquor in vacuo and adding light petroleum, and amounted finally to 65%. No other products were isolated.

About 1 g. of the acetone-δ-heptylthiosemicarbazone was hydrolysed by boiling under reflux with 20 ccs. of 6% hydrochloric acid for 10 minutes, a perfectly clear solution resulting. A small quantity of the liquid was distilled off and found to contain acetone by the nitroprusside test. Crystals separated from the residual liquid on cooling, and these were filtered off and recrystallised from light petroleum containing a little alcohol. Silvery leaflets, M.P. 135-136° were obtained and identified as *δ-heptylthiosemicarbazide hydrochloride*, $C_7H_{15}NH\cdot CS\cdot NH\cdot NH_2,HCl$.

Found :- N = 18.52%.

$C_8H_{20}N_3SCl$ requires N = 18.62%.

It was sparingly soluble in hot water and melted under it; the solution was acid. This was thought to be due to partial hydrolysis into the base which was found to be a low melting solid. It was insoluble in benzene and light petroleum, and easily soluble in alcohol. The yield was about 80%.

The benzylidene derivative, *benzylidene-δ-heptylthiosemicarbazone*, $PhCH{:}N{\cdot}NH{\cdot}CS{\cdot}NHC_7H_{15}$, was prepared from the above hydrochloride in the usual manner. It tended to separate as an oil, but solidified on cooling in ice. It was recrystallised from light petroleum, giving white matted needles M.P. 73°.

Found :- N = 15.25%.
$C_{15}H_{22}N_3S$ requires N = 15.16%.

It was easily soluble in alcohol, ether, and benzene, and turned yellow on standing.

0.5 g of δ-heptylthiosemicarbazide hydrochloride was dissolved in aqueous alcohol and an excess of sodium carbonate added. The liquid was then boiled till the evolution of gas ceased, and the solid filtered off. The filtrate was taken to dryness under reduced pressure, and the residue extracted with hot light petroleum and filtered. The crystals separating from the filtrate were filtered off and recrystallised from light petroleum, giving silky glistening acicular plates of *δ-heptylthiosemicarbazide*, $C_7H_{15}NH \cdot CS \cdot NH \cdot NH_2$, M.P. 54.5-55°.

Found :-   N = 22.26%.

$C_8H_{19}N_3S$ requires N = 22.22%.

It was easily soluble in alcohol and benzene.

Benzylamine and Acetone Thiosemicarbazone.*

5.35 g. of benzylamine, 6.55 g. of acetone thiosemicarbazone, and 10 ccs. of toluene, were heated under reflux for 20 hours in a bath at 125-127°. A product separated on cooling, and this was filtered off.

It was recrystallised several times from methyl alcohol, and then from alcohol and benzene. From benzene it separated in yellowish thin square plates, and from alcohol in prismatic needles, both forms melting at 148°. It was identified as *acetone-δ-benzylthiosemicarbazone*, $PhCH_2 \cdot NH \cdot CS \cdot NH \cdot N{:}CMe_2$.

Found :- $S = 14.44\%$.

$C_{11}H_{15}N_3S$ requires $S = 14.48\%$.

The yield, increased by concentrating the toluene mother liquor, was 65%.

1.0 g. of the compound was hydrolysed by boiling with 20 ccs. of 2% hydrochloric acid for

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* The author is indebted to Dr. Burns for the preliminary work of this reaction.

20 minutes. The liquid was found to contain acetone by the usual means. The residual liquid, which had a cress-like odour presumably due to benzyl *iso*thiocyanate, deposited crystals on cooling, and these were filtered off. The filtrate was taken to dryness under reduced pressure, the residue washed out with ether and added to the crystals already obtained. On extracting with a little hot absolute alcohol and filtering, a small amount of residue identified as hydrazine hydrochloride was obtained.

The filtrate, on cooling, gave colourless plates, M.P. 189° (decomp.), of *δ-benzylthiosemicarbazide hydrochloride*, $PhCH_2NH\cdot CS\cdot NH\cdot NH_2,HCl$.

Found :- Cl = 16.16%.

$C_8H_{12}N_3SCl$ requires Cl = 16.32%.

The compound was insoluble in benzene and ether, and dissolved in water to give an acid solution. The yield was 87%.

Benzylidene-δ-benzylthiosemicarbazone, $PhCH:N\cdot NH\cdot CS\cdot NH\cdot CH_2Ph$, was prepared from the hydrochloride in the usual way. It was fairly soluble in alcohol, and best recrystallised from a mixture of alcohol and light petroleum. It formed long matted needles, M.P. 133-134°.

Found :- N = 15.72%.

$C_{15}H_{15}N_3S$ requires N = 15.61%.

0.8 g. of the δ-benzylthiosemicarbazide hydrochloride was boiled with 20 ccs. of water for 5 minutes. A slight odour of cress, doubtless due to benzyl *iso*thiocyanate, was noticed. On cooling, glistening leaves separated out, and these were filtered off and recrystallised from absolute alcohol. Silvery glistening leaves of ***δ-benzylthiosemicarbazide***, $PhCH_2 \cdot NH \cdot CS \cdot NH \cdot NH_2$, M.P. 130°, were obtained. The fact of the base being obtainable in this way shows that the hydrochloride is very easily hydrolysed.

Found :- N = 23.19%.

$C_8H_{11}N_3S$ requires N = 23.20%.

The base was sparingly soluble in cold water, easily soluble in hot water, alcohol, and benzene. Its aqueous solution gave a white precipitate with silver nitrate, soluble in hot water and separating from solution on cooling. It was turned violet by hot copper sulphate and gave a brown oil on boiling; the odour of the mustard oil was also very distinct.

The yield was 76%.

The base was synthesised by mixing equimolecular quantities of benzyl *iso*thiocyanate (Hofmann, B. 1868, 1, 201) and 100% hydrazine hydrate in ice cold alcoholic solution. Heat was evolved and crystals separated out on cooling. These were filtered off and recrystallised from alcohol, giving tabular prisms, M.P. 130°, of δ-benzylthiosemicarbazide. On recrystallising from benzene, it gave glistening leaves of the same melting point, identical with the base previously obtained. The benzylidene-δ-benzylthiosemicarbazone was also the same as that described before. The yield was good.

Benzylamine and Acetophenone Thiosemicarbazone.

3.06 g. of benzylamine, 5.50 g. of acetophenone thiosemicarbazone, and 20 ccs. of toluene, were heated under reflux in a bath at 125-130° until the evolution of ammonia ceased. There was a little insoluble material formed, and the heating lasted for 42 hours.

The insoluble substance was filtered off, and was neglected owing to the small amount.

Crystals separated from the toluene solution on cooling, and these were filtered off and recrystallised from alcohol, creamy acicular plates, M.P. 157-159°, being obtained. Recrystallisation from benzene gave a white mass of fine needles having the same melting point, and a further crystallisation from alcohol gave colourless plates M.P. 160-161°. These were identified as *acetophenone-δ-benzylthiosemicarbazone*, $\mathrm{MePhC{:}N{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}CH_2Ph}$. More was obtained from the toluene mother liquor, the total yield being 87%.

Found :- $N = 14.91\%$; $S = 11.21\%$.

$C_{16}H_{17}N_3S$ requires $N = 14.84\%$; $S = 11.31\%$.

1.0 g. was boiled with 20 ccs. of 6% hydrochloric acid for 4½ hours. At the end of that time quite a large amount of the substance was unchanged, and this was filtered off. The filtrate had the odour of acetophenone, and this substance was removed by extracting the liquid, while still hot, with carbon tetrachloride. After cooling, the crystals which were deposited were filtered off and identified as δ-benzylthiosemicarbazide hydrochloride by comparison with an authentic specimen. The filtrate was taken to dryness under reduced pressure, and the residue extracted with a little hot alcohol. The insoluble part was found to be hydrazine hydrochloride.

rac. α-Phenylethylamine and Acetone Thiosemicarbazone.

4.84 g. of α-phenylethylamine, 5.24 g. of acetone thiosemicarbazone, and 30 ccs. of toluene, were heated in a bath for 35½ hours, the temperature being 125-130°. Ammonia was evolved and a little insoluble material separated.

This insoluble substance was filtered off, but was not identified as the quantity was too small.

The filtrate was cooled in ice but no solid formed, and therefore the toluene was removed under reduced pressure. The clear viscous residual oil set to a straw coloured resin on cooling, and this was dissolved in a little hot absolute alcohol. The crystals which were obtained by cooling the solution in ice, were recrystallised from alcohol, giving tabular prisms, M.P. 89-90°, of *acetone-δ-α-phenylethylthiosemicarbazone,* $Me_2C{:}N{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}CHMePh$.

Found :- $N = 18.00\%$; $S = 13.76\%$.

$C_{12}H_{17}N_3S$ requires $N = 17.87\%$; $S = 13.62\%$.

The compound was fairly soluble in cold benzene and almost insoluble in light petroleum.

1.0 g. of the compound was hydrolysed by boiling with 20 ccs. of 6% hydrochloric acid for 17 minutes, under reflux, and a small quantity of the liquid then distilled off. The distillate was found to contain acetone by the nitroprusside test. A small quantity of oil separated from the remaining liquid on cooling; this was separated off and neglected as the quantity was very small. The main portion of the liquid was taken to dryness under reduced pressure, and the residue extracted with hot absolute alcohol and filtered free from a very small quantity of insoluble material. No crystals separated from the filtrate, and the addition of benzene produced no precipitate. The solution was therefore concentrated in vacuo, and small colourless plates of *δ-α-phenylethylthiosemicarbazide hydrochloride*, $PhMeCH\cdot NH\cdot CS\cdot NH\cdot NH_2,HCl$, M.P. 157-158°, were obtained.

Found :- Cl = 15.49%.

$C_9H_{14}N_3SCl$ requires Cl = 15.32%.

The compound was insoluble in benzene and ether, and easily soluble in alcohol. The yield was 80%.

Benzylidene-δ-α-phenylethylthiosemicarbazone, PhCH:N·NH·CS·NH·CHMePh, was obtained from the hydrochloride in the usual manner. It tended to separate as an oil, but became quite solid on standing. It was very soluble in alcohol and was crystallised from light petroleum, giving colourless plates M.P. 128-129°..

Found :- N = 15.00%.
$C_{16}H_{17}N_3S$ requires N = 14.84%.

An attempt was made to prepare the base by boiling 0.7 g. of the hydrochloride with 20 ccs. of water for 5 minutes. A slight odour of cress was noticed, and on cooling, a turbidity was produced by the separation of a small quantity of an oil, but no crystals were obtained. Some barium carbonate was therefore added and the liquid boiled till the evolution of gas ceased. The solid was filtered off and the filtrate taken to dryness under reduced pressure. The residue was extracted with benzene, filtered, the filtrate dried over sodium sulphate, and then the solvent removed in a vacuum desiccator. The oily residue obtained solidified on standing, and the solid, on crystallisation from light petroleum, gave small crystals, M.P. 84°, of *δ-α-phenylethylthiosemicarbazide*, PhMeCH·NH·CS·NH·NH$_2$.

Found :- N = 21.62%.

$C_9H_{13}N_3S$ requires N = 21.54%.

The base was very soluble in alcohol and benzene.

It is possible that the oil which separated from the aqueous solution of the hydrochloride, and that formed in the hydrolysis of the acetone-δ-α-phenylethylthiosemicarbazone, mentioned above, was the base just described.

APPENDIX.

Acetone-δ-anilinosemicarbazone.

The following method was adopted for the preparation of this compound in an appreciable quantity as the yield from the ordinary reaction was very small. It is similar to that used for the preparation of the semicarbazones, namely from the hydrochloride of the base, potassium acetate, and acetone. The method of preparation of the δ-anilinosemicarbazide hydrochloride (Sutherland and Wilson, J.C.S. 1924, 125, 2146) was altered slightly.

3.3 g. of acetophenone-δ-anilinosemicarbazone were hydrolysed by boiling for 20 minutes with 75 ccs. of 6% hydrochloric acid. While still hot, the acetophenone was removed by three extractions with carbon tetrachloride. The hydrochloride which separated on cooling was filtered off and the remainder obtained by evaporating the filtrate to dryness under reduced pressure.

The total amount of hydrochloride was dissolved in a minimum of water, 10 ccs. of acetone added to the solution, and then a slight excess

(4 g.), of potassium acetate was added in small quantities, the liquid being shaken after each addition till solution was effected. Acetone-δ-anilinosemicarbazone commenced to separate almost immediately, and after cooling in ice for 5 hours it was filtered off, thoroughly washed with water, dried, and recrystallised from alcohol. It was found to be identical with that previously obtained. The yield, calculated on the acetophenone-δ-anilinosemicarbazone, was 94%.

Methyl ethyl ketone-δ-anilinosemicarbazone.

This compound, which could not be obtained by the action of phenylhydrazine on methyl ethyl ketone semicarbazone, was prepared by the method described above. 1.5 g. of the hydrochloride were dissolved in 30 ccs. of water, 3 ccs. of the ketone added and the solution cooled in ice. The product was filtered off and more obtained from the filtrate by the addition of 2 g. of potassium acetate. The whole was recrystallised from alcohol and gave almost white plates, M.P. 137°, of *methylethylketone-δ-anilinosemicarbazone*, MeEtC:N·NH·CO·NH·NHPh.

Found :- N = 25.42%.

$C_{11}H_{16}ON_4$ requires N = 25.45%.

The yield of the crude product was almost theoretical.

Benzylidene-δ-anilinosemicarbazone.

The method previously described (Sutherland and Wilson, J.C.S. 1924, 125, 2146) was altered for the preparation of a large quantity. The hydrochloride was dissolved a a minimum of water, and a very slight excess of benzaldehyde together with sufficient alcohol to give a clear solution added. After being cooled in ice for ½ hour, and shaken vigorously occasionally, the solid was filtered off and washed with water and then with alcohol. The compound was obtained practically pure by further washing with hot alcohol. The yield was 95%.

1-Methyl*cyclo*hexan-2-one.

The ketone was prepared by the method used for the 1:3 compound by Knoevenagel and Tübben (A. 1897, 297, 154).

170 g. of Beckmann's chromic acid mixture were added to 25 g. of 1-methyl*cyclo*hexan-2-ol and the mixture well shaken. After it had started to cool it was heated on a water bath for ½ hour. After cooling, the ketone was separated off and the acid portion extracted with ether. The ketone was added to the ethereal solution and the whole washed with caustic soda and then with water. The crude ketone was purified by means of its bisulphite compound in the usual manner.

Di*iso*propyl ketone Semicarbazone.

The melting point of this compound, presumably always prepared in the same manner, varies from 136° to 157° in different references. Salkind (C. 1906, ii, 316) gives 136-137° as does also Mereschkowski (C. 1914, i, 1814), whereas Henderson, Henderson, and Heilbron (B. 1914, 47, 887) give 142°, Haller and Bauer (C.R. 1910, 150, 662) give 143-144°, Blaise and Marcilly (Bl. 1904, [3], 31, 114) give 151-152°, and Staudinger (B. 1911, 44, 529) gives 157°.

That prepared by the author in the usual manner melted at 143-144°. The semicarbazone from the di*iso*propyl ketone obtained by the hydrolysis of the δ-anilinosemicarbazone melted at 157° after three crystallisations from alcohol. A mixture of this with that melting at 143-144° melted at 152-153°, and when the low melting specimen was recrystallised and the solution seeded with the high melting, the product melted at 151-152°. The specimen melting at 157°, on standing a few days, was changed to that melting at 143-144°. As there was only a small quantity it was not investigated further. There was no obvious difference in the crystalline form of the two specimens.

1-Methyl*cyclo*hexan-2-one Phenylhydrazone.

1-methyl*cyclo*hexan-2-one was heated on a boiling water bath with a very slight excess of phenylhydrazine for 1 hour. After cooling, the product was dissolved in ether, washed with dilute acetic acid, then with water, and finally dried over calcium chloride. On removing the ether in an evacuated desiccator, solid 1-methyl*cyclo*hexan-2-one phenylhydrazone was obtained. This was recrystallised from warm aqueous alcohol and gave almost white needles, M.P. 45-46°, identical with the product obtained from the reaction described on page 82.

Found :- N = 13.68%.
$C_{13}H_{18}N_2$ requires N = 13.87%.

It was very soluble in the usual organic solvents, and an attempt to distill it at 30 mm. was not very successful, the temperature rising from 195-209°. The distillate did not crystallise on cooling, though it became very viscous.

Benzylideneacetone
p-tolylhydrazone.

1.5 g. of benzylideneacetone and a slight excess (1.4 g.) of *p*-tolylhydrazine were heated under reflux with 15 ccs. of alcohol for 1 hour. *Benzylideneacetone p-tolylhydrazone*, Me(PhCH:CH)C:N·NH·C_6H_4Me, separated on cooling, and was purified by two recrystallisations from alcohol. It gave pale yellow needles, M.P. 172-173°.

Found :- N = 11.21%.
$C_{17}H_{18}N_2$ requires N = 11.20%.

Methyl *tert.*-butyl ketazine

2.5 g. of 100% hydrazine hydrate and 11.0 g. of methyl *tert.*-butyl ketone were heated under reflux with 10 ccs. of alcohol for 2 hours. After drying over anhydrous potassium carbonate it was distilled and a fraction B.P. 213-216° was obtained.

On redistillation under reduced pressure, *methyl* tert.*-butyl ketazine*, $Me(Me_3C)C{:}N{\cdot}N{:}C(CMe_3)Me$, was obtained. It was an almost colourless oil with an odour similar to that of crude acetamide and boiled at 103°/17 mm. The yield was 77%.

Found :- N = 14.33%.

$C_{12}H_{24}N_2$ requires N = 14.20%.

On hydrolysis with dilute hydrochloric acid it gave the ketone and hydrazine hydrochloride.

Acetone Diphenylhydrazone.

6.1 g. of diphenylhydrazine were refluxed with 6 ccs. of acetone for 2½ hours, dried over calcium chloride and distilled under reduced pressure. A fraction B.P. 156°/5 mm. was obtained. It was a yellowish oil which did not crystallise on freezing, and the nitrogen content was about 1% below that required for acetone diphenylhydrazone. It was therefore redistilled but the boiling point was as before and the nitrogen content still lower. A black residue was left in the flask, and it would appear, therefore, that decomposition was taking place. The oil was hydrolysed and acetone detected in the usual manner. The solution deposited crystals on cooling and these were filtered off. They did not give a benzylidene derivative by the usual method, and so the free base was liberated and the benzylidene derivative prepared from that. This was identified as benzylidene diphenylhydrazone, and therefore the oil must have been largely acetone diphenylhydrazone.

Dibenzyl ketone
Thiosemicarbazone.

2.1 g. of dibenzyl ketone in 15 ccs. of alcohol and 0.91 g. of thiosemicarbazide in a minimum of water were heated under reflux for $\frac{3}{4}$ hour. Crystals of *dibenzyl ketone thiosemicarbazone*, $(PhCH_2)_2C{:}N{\cdot}NH{\cdot}CS{\cdot}NH_2$, separated on cooling and were recrystallised from alcohol and then from benzene. It formed silvery glistening leaves, M.P. 135-166°. The yield was 85%.

Found :- N = 14.86%.

$C_{16}H_{17}N_3S$ requires N = 14.84%.

The action of Carbon Tetrachloride on Acetophenone Phenylhydrazone.

When acetophenone phenylhydrazone was dissolved in carbon tetrachloride and the solution allowed to stand, it gradually turned yellow through red with a violet fluorescence to a deep violet. Chloroform, ethylene dichloride, ethyl iodide, and chlorobenzene, gave similar colourations.

4 g. of acetophenone phenylhydrazone were dissolved in 60 ccs. of carbon tetrachloride, the solution warmed to 35° and then allowed to stand for 24 hours. Hydrochloric acid gas and carbonyl chloride were evolved, the latter being detected by its conversion of aniline into carbanilide. No change occurred when the solution was kept in an atmosphere of carbon tetrachloride.

When the coloured solution was taken to dryness, a deep violet pasty mass was left. This was extracted for 3 hours in a Sohxlet apparatus with light petroleum, a brownish violet mass being obtained. All attempts to crystallise this product were without success. It appeared to be a hydrochloride and was therefore dissolved in absolute alcohol and the solution saturated with dry hydrochloric acid gas. The deep violet solution obtained was taken to dryness in a vacuum desiccator and the residue washed out with dry ether saturated with hydrochloric acid. A deep violet crystalline solid was obtained, the analysis of which varied considerably each time it was prepared.

An attempt was made to prepare the free base by treating the hydrochloride with dilute sodium hydroxide and extracting with ether. On removing the ether a reddish resinous mass was obtained but could not be crystallised. It gave a picrate, chloroplatinate, perchlorate, benzoyl and nitrobenzoyl derivatives, but none of these could be obtained pure.

As it was not in the direct line of research the investigation was abandoned.

Contractions used.

A.	Justus Jiebig's Annalen der Chemie.
B.	Berichte der Deutschen chemischen Gesellschaft.
Bl.	Bulletin de la Société chimique de France.
C.	Chemisches Zentralblatt.
C.R.	Comptes rendues de L'Académie des Sciences.
G.	Gazzetta chimica italiana.
J.C.S.	Journal of the Chemical Society.
J.Am.C.S.	Journal of the American Chemical Society.
J.Pr.	Journal für praktische Chemie.
Monatsh.	Monatshefte für Chemie.
R.A.L.	Atti della Reale Academia Lincei.