Chemistry. — *On the Preparation and Properties of Some Ortho-Diamino-Cyclohexanes.* By F. M. JAEGER and J. A. VAN DIJK.

(Communicated at the meeting of February 29, 1936).

§ 1. For the purpose of continuing our investigations [1]) about the influence which the introduction of bivalent and optically-active diamines into the complex ions of bi- and polyvalent metals has on the molecular rotations and rotatory dispersion of the antipodes, it was necessary to prepare a number of cyclic diamino-compounds suited for this kind of research. As the formation of complex ions of this type occurs more easily with 1-2-, than with 1-3- or 1-4-diamines, it was beforehand indicated to limit our tentatives to the preparation of *ortho*-substituted *diamino*-derivatives of *cyclohexane*. For this reason we started the synthesis of 1-2-*Diaminocyclohexane*, 1-*Methyl*-2-3- and 1-*Methyl*-3-4-*diamino-cyclohexanes* and of 3-4-*Diamino-p-menthane* (= 1-*Methyl*-4-*isopropyl*-3-4-*diamino-cyclohexane*. In this paper some data about the results obtained and of some of the properties of the bases mentioned are given; later on their full description and that of the complex salts derived from them will be published in detail.

The general way followed in the synthesis of the bases of the first group mentioned was: *Cyclohexanone* → *Cyclohexanone-oxalylic ester* → *Cyclohexanone-carboxylic-ester* → *Cyclohexanone-isonitroscompound* (= *-monoxime*) → *Cyclohexane-dioxime* → *Diamino-cyclohexane*. The last mentioned base of the series was prepared, starting from *Menthone* → *Nitro-menthone* → *Aminomenthone* → *Aminomenthone-oxime* → *Diamino-menthane*, in the way followed by KONOWALOW and ISCHEWSKI [2]) but somewhat modified, so as to ascertain a better yield of the product.

§ 2. As an example of the general way of preparation of the three bases first mentioned, the synthesis of 1-*methyl*-2-3-*diaminocyclohexane* will here be described more particularly; the preparation of the other bases of this series occurs in a completely analogous way.

200 Grammes of 1-*methyl*-2-*cyclohexanone* (boilingpoint: 164°—165° C.) and 300 grammes of *diethyloxalate* (boilingpoint: 186° C.) are mixed and thoroughly cooled at —15° C. The mixed liquids are, under perpetual stirring, slowly added to an equally cooled, freshly prepared

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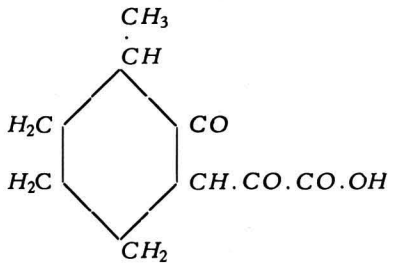
[1]) F. M. JAEGER and H. BLUMENDAL, Zeitschr. f. anorg. Chem., **175**, 161 (1928).

[2]) M. KONOWALOW and W. ISCHEWSKI, Ber. d. d. chem. Ges., **31**, 1478 (1898); cf also: *ibidem*, **28**, 1054 (1895).

solution of 40 grammes sodium in 650 grammes of absolute ethylalcohol [1]), which is contained in a reservoir of about 4 liters volume. Under continuous stirring the whole quantity is added in 1 or 2 hours; the contents of the vessel now were changed into a thick, pale yellow mass, which still for some time afterwards is stirred under cooling and then is left standing at room-temperature for 24 hours. The yellow mass now is poured into about 4.5 liters of a cooled 30 % solution of somewhat more than the calculated quantity of sulphuric acid. A reddish or yellow oily liquid is separated from the acid solution, collected, washed and treated with a solution of sodium bicarbonate, whilst the aqueous solution is three or four times extracted with ether, the latter destilled off and the residue added to the first mass; then so much ether is added to it, that a clear reddish solution is obtained. This is dried with anhydrous sodium sulphate and the dried ethereal solution left standing at room-temperature till all ether is evaporated. Besides the liquid condensation product, ordinarily some solid substance is obtained, which proves to be the free *oxalylic* acid:



which crystallizes from water in beautiful, colourless, monoclinic crystals with the axial ratio: $a : b : c = 1.712 : 1 : 1.724$; $\beta = 73° 26'$ and the forms: $r = \{\bar{1}01\}$, often predominant; $c = \{001\}$ broad, sometimes predominant; $m = \{110\}$, well developed; $s = \{201\}$, narrow, like $b = \{010\}$; sometimes $\omega = \{\bar{2}11\}$ as a very narrow truncation of the edges $r : m$. (Fig. 1).

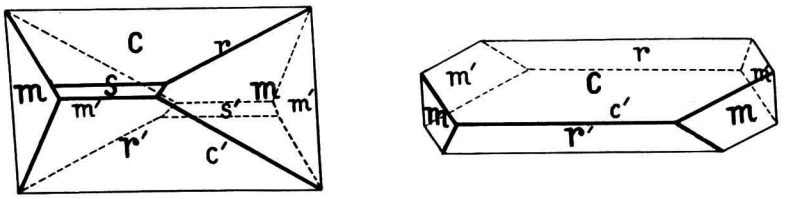


Fig. 1. 1-Methyl- 2-Cyclohexanone- 3-Oxalylic Acid.

Often the edges of the crystals are rounded; *s* and *b* usually yield only weak reflections, the other faces very good ones. The habitus of the crystals is represented in Fig. 1.

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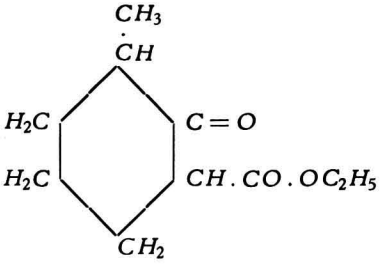
[1]) A. KÖTZ and L. HESSE, Ann. d. Chemie, **342**, 315 (1905).

Angular Values:	*Observed:*	*Calculated:*
$c : m = (001) : (110) =$	* 81° 28′	—
$m : r = (110) : (10\bar{1}) =$	* 63 43	—
$c : r = (001) : (\bar{1}01) =$	* 74 50	—
$c : s = (001) : (201) =$	50 39	50° 48′
$s : r = (201) : (10\bar{1}) =$	54 31	54 22
$b : m = (010) : (110) =$	31 28	31 22
$m : m = (110) : (1\bar{1}0) =$	62 56	62 44

No distinct cleavability was observed.

The impure condensation product is subjected to a vacuum distillation and the fraction boiling under a pressure of 12—13 mm at 97° C. or lower, — which chiefly consists of water, unchanged methylcyclohexanone and diethyloxalate, — separately collected. During this distillation a partial decomposition of the oxalylic ester formed already takes place under development of carbon monoxide; the remaining liquid is, in order to complete this decomposition, during a sufficiently long time heated on a sand-bath in a flask with reflux-cooler at 210°—220° C., till no carbon monoxide is any longer set free. The *carboxylic ester* thus generated:



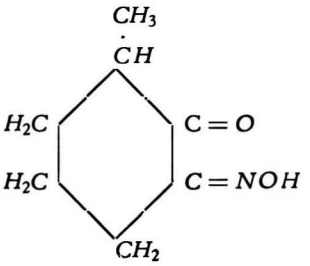
is now subjected to a vacuum distillation and the fraction boiling under 12—13 mm at 115°—116°.5 C. collected. The yield of this pure ester never exceeds 62 % of the calculated quantity, but occasionally is less than this (42 %): from 1530 grammes methylcyclohexanone we obtained about 1050 grammes of the carboxylic ester (45 %—46 %); in the vessel remains a dark, resinous mass, whilst a small quantity of oxalylic acid and a good deal of unchanged diethyloxalate, some water, alcohol and other by-products are simultaneously obtained. It proved advisable to subject no more than about 200 grammes of methylcyclohexanone at the same time to this condensation, as with greater quantities the final yield seems to decrease.

§ 3. The pure carboxylic ester thus obtained now is mixed with somewhat more than the calculated quantity of a 6 % solution of potassium hydroxide and the theoretical quantity of sodium nitrite and during 48 hours shaken at room-temperature in a hermetically closed bottle[1].

[1]) E. TAKENS, Diss. Göttingen, 30 (1910).

After the liquid is poured into a cooled 30 %-solution of sulphuric acid, the solid white *isonitroso*-compound is precipitated, which is filtered off, whilst from the solution, when extracted with ether, still somewhat of another monoxime, besides a coloured liquid, is obtained; the latter is a mixture of both isonitroso-compounds. The first mentioned monoxime readily crystallizes from methyl- or ethylalcohol, still better from ethylacetate, in beautiful, colourless flat crystals, which, under decomposition, melt at 167° C. From 1050 grammes of the carboxylic ester we, in this way, obtained 500 grammes of the solid monoxime, 14 grammes of the other monoxime melting at 65° C. and 140 grammes of the liquid mixture of the two compounds.

1-*Methyl-2-Oxo-3-Isonitroso-cyclohexane* (mpt. : 167° C.) of the composition:



crystallizes from alcohol or ethylacetate in parallelogram-shaped, colourless, monoclinic tables. They are monoclinic-prismatic, with the axial ratio: $a : b : c = 1.933 : 1 : 1.223$ and $\beta = 73° 16'$. The perfectly transparent crystals (Fig. 2) show the following forms: $c = \{001\}$, very lustrous and predominant; $m = \{110\}$, $o = \{111\}$ and $\omega = \{111\}$ about equally broad and all yielding very good reflections. Sometimes o is absent. The form $b = \{010\}$ is only small, giving weak images. The crystals are flat tables parallel to $\{001\}$.

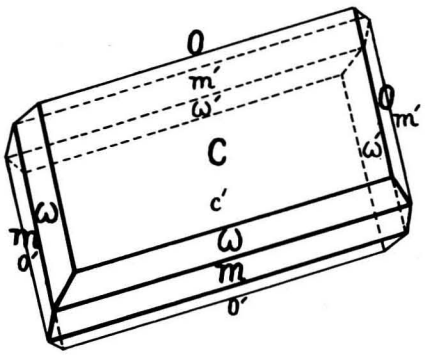


Fig. 2. 1-Methyl- 2-Oxo-3-Isonitroso-Cyclohexane

Angular Values:	*Observed*:	*Calculated*:
$c : \omega = (001) : (111) =$*	48° 7′	—
$\omega : m = (111) : (110) =$*	34 1	—
$m : m = (110) : (1\bar{1}0) =$*	123 14	—
$c : m = (001) : (110) =$	82 8	82° 8′
$c : o = (00\bar{1}) : (11\bar{1}) =$	57 51	58 11

Angular Values:	*Observed*:		*Calculated*:	
$m : b = (110) : (010) =$	28	23	28	23
$\omega : \omega = (111) : (1\bar{1}1) =$	83	4	82	48
$\omega : b = (111) : (010) =$	48	33	48	36
$m : o = (110) : (1\bar{1}1) =$	40	1	39	42

Cleavable parallel to {001}.

The plane of the optical axes is {010}. The apparent axial angle on {001} is fairly great.

Reactions of the Monoxime. An alcoholic solution of this compound, if added to aqueous solutions of the following salts, yields:

1) with *ferrous sulphate* a beautifully reddish-violet solution.
2) with *ferric chloride* a dark violet, almost black solution; on heating, its colour changes into a reddish-brown.
3) with *copper sulphate* a yellowish-green solution, the colour turning to a brownish-green on heating the liquid.
4) with *nickel sulphate* no change of the colour of the solution occurs, but on heating it turns to a more yellowish-green, and finally a dull red, complex nickel salt is precipitated.
5) with *cobaltous chloride* a brick-red solution is obtained, its colour getting darker on heating the liquid.
6) with *sodium rhodium chloride* no appreciable change of colour; but on heating the latter turns to a yellow-orange.

§ 4. As to the isomeric monoxime formed in small quantity and melting at 65° C., it can be remarked that its reactions with the reagents mentioned above differ only slightly, but yet distinctly, from those of the monoxime of meltingpoint 167° C.: thus *ferrous sulphate* in the cold yields about the same violet colour, which on heating, however, gets much darker; *ferric chloride* gives a violet-blue solution which on heating turns to a pale brown colour; *copper sulphate* gives about the same coloration as before, but on heating this turns to a dark emerald-green. The principal difference, however, between the two monoximes manifests itself by the different colours of the precipitate formed, if an aqueous solution of a *nickel* salt and some hydroxylamine is heated with them: the thus formed *dioxime* in the first case yields a clear *red*, in the second case an *orange*-coloured internally complex *nickel* salt, proving that the two dioximes formed are distinctly different from each other. To this difference we will return later on in describing the dioximes themselves.

Finally the viscous liquid extracted from the aqueous solution by means of ether (see above), evidently being a mixture of the two monoximes, — as is proved by the fact that, on standing, the monoxime of meltingpoint 167° C. is gradually crystallizing from it, — yields reactions which are

intermediate between those described in the two cases, besides those of the *dioxime*, as is proved by the *orange-red* precipitate with *nickel sulphate* and the colorations with *ferric chloride* and *copper sulphate*. Evidently a minute quantity of the corresponding dioximes is also present in it, although it is not clear, how they can have been formed in the process. Tentatives made with the purpose of distilling the liquid in vacuo remained without result, as the substance evidently decomposes. On treating it with hydroxylamine (see § 5), *no* crystallized product could be obtained, although, on reduction, it chiefly gave the same *diamino-cyclohexane* as the pure dioxime derived from the monoxime of meltingpoint 167° C., — besides a monobasic substance, which most probably is an amino-methyl-cyclohexane (see § 6).

§ 5. The solid monoxime of meltingpoint 167° C., after careful purification by recrystallizing it from ethylacetate, was transformed into the corresponding *dioxime* in the following way[1]): 10 grammes of the monoxime were dissolved in methylalcohol and then added to a methylalcoholic solution of 6 grammes hydroxylamine-hydrochloride + of 1.98 grammes sodium dissolved in 25 cm^3 methylalcohol. The mixture was left standing for 24 hours at room-temperature, the sodiumchloride filtered off and the alcohol distilled off in vacuo at 40° C. The *dioxime* which was obtained in a yield of 96 %—100 % of the calculated quantity was repeatedly recrystallized from alcohol or ethylacetate or from a mixture of hot water and alcohol: it crystallizes in colourless small needles with the same meltingpoint as the monoxime, i.e. 167° C. Although it seems to be identical with the dioxime obtained by WALLACH and WEISSENBORN[2]) in quite another way, there are some striking discrepancies between their description of the compound and ours: not only did we never meet with the difficulties in reducing the substance to the diamino-compound mentioned by them, but most remarkable is that, notwithstanding the identity of the meltingpoint with that of our preparation, they describe the colour of the complex *nickel salt* as being *orange-red,* whilst we always found a *pure red* colour and an *orange* colour only with the nickel salt of the isomeric dioxime of meltingpoint 65° C., which in our synthesis was obtained as a by-product only in a small amount. The *dioxime* obtained from this monoxime of meltingpoint 65° C. crystallizes from alcohol in yellowish, not perfectly pure crystals which melt at 140° C. It is possible that the two monoximes (65° and 167° C.), as well as the two corresponding dioximes (140° and 167° C.) are related to each other as *syn-* and *anti-*isomerides. Most probably the preparation of the German authors has been a mixture of the two dioximes, as may be deduced from their indication of the colour of their complex *nickel* salt.

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[1]) E. TAKENS, loco cit., 45.

[2]) O. WALLACH and A. WEISSENBORN, Lieb. Ann. **437**, 148 (1924).

The *dioxime* obtained yielded the following reactions:

1) with *ferrous sulphate* it gave an orange-brown solution and finally a precipitate, getting darker on heating.
2) with *ferric chloride* a brown solution was obtained, which, on heating, became darker brown.
3) with *copper sulphate* the solution got an olive-green colour.
4) with *nickel sulphate* immediately an insoluble, *red* precipitate of the internal complex nickel salt is produced, which is decomposed by hydrochloric acid, so that the solution again turns green.
5) with *cobaltous chloride* an insoluble, dark red precipitate is formed, which dissolves in hydrochloric acid to a blue solution.
6) with *sodium rhodium chloride* an orange-red solution is obtained, which does not change on heating.

§ 6. The *dioxime* can be quantitatively reduced to the *diamino-compound* in portions of 10 grammes by means of an excess of sodium in boiling absolute alcohol. To this end the fivefold of the calculated quantity of sodium is given into a wide, round-bottom flask provided with a reflux-cooler and then a small quantity of ethylalcohol is added. The alcoholic solution of the dioxime now is rapidly added from a dropping funnel, whilst the content of the flask is continuously stirred; successively more alcohol is then added. When all dioxime and the necessary quantity of alcohol is added, the mixture is for some hours heated on the water bath, till all the sodium is completely dissolved. Then the reaction product is distilled with water vapour and the volatile base caught in dilute hydrochloric acid; it is advisable to avoid a great excess of the acid. The solution is finally evaporated on the water bath to a small volume, the liquid discoloured with coal, filtered and left to crystallization over sulphuric acid in an exsiceator. The *hydrochloride* crystallizes as a mass of fine, colourless needles, which contain 13.28 H_2O and on analysis yield: 12.12 % N and 30.71 % Cl; so that its constitution is: $C_7H_{16}N_2$, $HCl + 2H_2O$.

For the isolation of the free base a concentrated solution of this salt, from a dropping bottle, is slowly added to an excess of solid potassium hydroxide, contained in a vessel provided with a cooler; the flask is continuously cooled by means of ice and salt. The liquid base thus obtained is preserved for a long time over solid potassium hydroxide, then equally over metallic sodium and finally distilled in vacuo over fresh sodium in an apparatus provided with glass-joints; as the base rapidly attracts water vapour and carbon dioxide, it is necessary to provide all recipients with tubes filled with sodium hydroxide and calcium chloride. The pure base boils at 84° C. under 12 mm pressure; it is a colourless, strongly alkaline liquid, which has an odour reminding of ethylenediamine, and like this, attracts the carbon dioxide of the air with great avidity and readily condenses water vapours on it.

On reducing the dioxime obtained from the oily monoxime, the same bivalent base was obtained; but besides it another colourless and much more volatile basic liquid, which constantly boiled at 41° C. under 12 mm pressure. It has a penetrating amine-like odour, is only *mono*basic, precipitates the hydroxides of iron and nickel from the aqueous solutions of their salts and most probably is an *amino-methyl-cyclohexane*. Its tendency to form complex metallic salts is much less than that of the diamines. The base contains 12.25 % *N*; calculated for *amino-methylcyclohexane*: 12.39 % *N*.

Its *benzoyl*-derivative had a meltingpoint of 106° C.; so that the base must be the *1-methyl-3-amino-cyclohexane*, as the *benzoyl*-derivatives of the 1-2-, and of the 1-4-isomerides melt at 147° and 180° C. respectively. The amino-compound is only sparely soluble in water; its hydrochloride melts under decomposition at 260°—265° C.

Of the dioxime of meltingpoint 65° C. finally too little was left for reduction-experiments, so that it is not yet possible to say, what is the corresponding diamine in this case. In the distillation of the bulk of the crude base we got, however, a small fraction which constantly distilled between 79° and 80° C. under 12 mm pressure, i.e. 4° lower than the base already described.

1-Methyl-2-3-diamino-cyclohexane forms with a number of metallic salts complex compounds of various types, which also will be described in detail in a later publication.

§ 7. In the same way the correspondent bivalent bases derived from *cyclohexanone* and from *1-Methyl-3-* and *1-Methyl-4-cyclohexanone* were prepared and some of their properties studied.

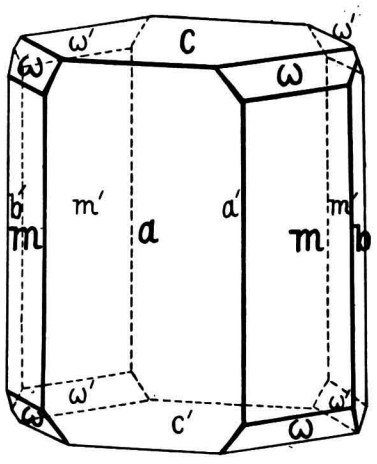

Fig. 3. Cyclohexanone-oxalylic Acid.

Cyclohexanone (boilingpoint: 155° C.) yielded a *carboxylic ester* which under 14 mm pressure boils at 111°—112° C., under 11—12 mm at 106°—107° C. As a by-product in its synthesis a little of the corresponding *oxalylic acid*[1]) (meltingpoint: 122° C.) was obtained in well measurable crystals (Fig. 3), which are rhombic-bipyramidal with the axial ratio: $a : b : c = 1.402 : 1 : 1.553$ and the forms: $a = \{100\}$, predominant; $c = \{001\}$, well developed, like $m = \{110\}$; $r = \{201\}$ and $b = \{010\}$, narrow; $\omega = \{111\}$, small, but very lustrous. The crystals are tabular parallel to $\{100\}$.

[1]) A. KÖTZ and A: MICHELS. Lieb. Ann. d. Chem., **350**, 211 (1906).

Angular Values:	*Observed*:	*Calculated*:
$a : m = (100) : (110) =$*	54° 30′	—
$c : \omega = (001) : (111) =$*	62 20	—
$m : b = (110) : (010) =$	35 30	35° 30′
$\omega : m = (111) : (110) =$	27 40	27 40
$a : \omega = (100) : (111) =$	58 58	59 3
$\omega : m = (111) : (\bar{1}10) =$	73 3	73 15
$\omega : b = (111) : (010) =$	43 53	43 51
$c : r = (001) : (201) =$	65 30	65 42
$r : a = (201) : (100) =$	24 30	24 18

No distinct cleavability was observed.

The optical extinction on *a* is normal; most probably the *a*-axis is the second bissectrix, but the axial image was not very distinct.

From the carboxylic ester mentioned the *isonitroso*-compound was prepared in the way described: it is a non-crystallizable, oily liquid. The *dioxime*, however, is well crystallized and melts at 187°—189° C. On reduction with sodium and alcohol, the *diamino-cyclohexane* is obtained, besides a lower boiling monobasic substance. *Diamino-cyclohexane* boils at 79°—81° C. under a pressure of 15 mm. It is a colourless, strongly alkaline liquid, which readily absorbs the carbon dioxide of the air and condenses water-vapours upon itself. It possesses the *trans*-configuration, as is proved by its *resolvability into optical antipodes*. The base forms typical complex salts; thus, with *cobaltous chloride* and after oxidation with hydrogen peroxide, a green *praseo-* and an orange-brown *triammino*-salt.

As already mentioned, also in this case a fraction was obtained of the lower boilingpoint 37°—39° C. under 16 mm pressure. It is a colourless, alkaline liquid, which proved to be *mono*basic and the nitrogen-content of which was found at 13.86 %; evidently it is, therefore, the *amino-cyclohexane* (14.1 % *N*). This was finally proved [1]) (BIJKERK) by means of its boilingpoint at ordinary pressure: 134°—135° C. and by the meltingpoint of its pure hydrochloride, which was determined to be 206°—207° C.

1-Methyl-3-cyclohexanone (boilingpoint: 169° C.) gives a *carboxylic ester*, — in a yield of 60—62 % of the calculated quantity, — which under 13 mm pressure boils at 118°—120° C. Its *monoxime* is a colourless, crystallized substance (meltingpoint: 159° C.), which can readily be transformed into the crystallized *dioxime* (meltingpoint: 180°—181° C.); the latter is identical with the dioxime finally obtained from *1-methyl-4-cyclohexanone*. With *nickel* salts it forms a beautifully red complex salt.

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[1]) A. BAEYER, Ann. d. Chem., **278**, 103 (1894); W. MARKOWNIKOFF, ibid., **302**, 22 (1898).

The dioxime was reduced to the *diamino-cyclohexane* in the way previously mentioned; *1-methyl-3-4-diamino-cyclohexane* is a colourless, strong alkaline liquid, which under a pressure of 13 mm boils at 81°.5 C.

It readily combines with the carbon dioxide of the air and condenses water vapours upon itself.

1-Methyl-4-cyclohexanone (boilingpoint: 169° C.) gives a *carboxylic ester,* in a yield of 55—60 % of the calculated quantity; the ester boils at 113°—115° C. under a pressure of 13 mm. The corresponding *isonitroso-*compound (*monoxime*) is a non-crystallizable liquid; the *dioxime* (melting-point: 180°—181° C.), however, is solid and identical with that obtained from *1-methyl-3-cyclohexanone.* Both dioximes in consequence on reduction yield *the same* diamino-compound of boilingpoint: 81°.5 C. under 13 mm pressure.

With *cobaltous chloride* this *diamino-cyclohexane,* on simultaneous oxidation with hydrogen peroxide, furnishes a beautiful, green *praseo-*salt; with *nickel-* and *copper sulphate* violet complex salts are formed.

§ 8. Finally *3-4-diamino-menthane* was prepared, starting from *menthone.* This compound was first transformed into the liquid *nitro-menthone;* the crude substance ordinarily still contains 30 % *menthone.* It was reduced to *amino-menthone* (boilingpoint: 215° C. under 16 mm pressure) by heating it with tin and hydrochloric acid on the water-bath. The yield is appreciably improved *by the addition of alcohol* to the reduction-mixture and boiling at a reflux-cooler for a considerable time: if the unchanged *menthone* present is accounted for, a yield of 70 % in this reaction may be attained. This *amino-menthone* then was transformed into the corresponding *oxime* by means of hydroxylamine; *amino-menthone-oxime* is a liquid boiling at 182° C. under 16 mm pressure. By reduction with sodium and boiling alcohol in the way described, the compound was transformed into the theoretical quantity of *diamino-menthane,* a colourless, strongly alkaline base, which under 12 mm pressure boils at 110°—113° C. It readily combines with water vapours and carbon dioxide of the air; with metal salts it forms complex compounds; i.e. with *cobaltous chloride,* — on simultaneous oxidation with H_2O_2, — a beautiful, green *praseo-*salt and also typical complex *nickel-* and *copper* salts.

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