

They are easily benzoylated and acetylated, and form condensation products with benzaldehyde. They react with nitrous acid and with benzene diazonium chloride.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TEXAS]

ISOPROPYL, MENTHYL AND BORNYL SEMICARBAZIDES. REDUCTION OF PHENYLHYDRAZONES

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Isopropyl Semicarbazide¹

Introduction

Lochte and Bailey by employing the Skita method of reduction with colloidal platinum as catalyst succeeded in preparing 2,2'-hydrazobispropane, $(\text{CH}_3)_2\text{CHNHNHCH}(\text{CH}_3)_2$, from dimethyl-ketazine, $(\text{CH}_3)_2\text{C}=\text{NN}=\text{C}(\text{CH}_3)_2$. This reaction with the use of other reducing agents had been previously attempted by other investigators with negative results.² It is evident that a successful extension of this kind of reduction will be of great preparative value, more especially in the aliphatic and hydroaromatic series, in obtaining hydrazine derivatives, since it will make available as intermediates the numerous hydrazones and azines which are easily obtained from the corresponding aldehydes and ketones. The work on hydrazopropane, azopropane, and isopropylhydrazine is being continued by Lochte in the University of Illinois as a thesis problem with Professor W. A. Noyes.³

In the Texas laboratory several lines of investigation, involving the reduction of the $\text{C}=\text{N}$ complex, are under way. In the present paper it is shown that acetone semicarbazone, $(\text{CH}_3)_2\text{C}=\text{NNHCONH}_2$, yields isopropyl semicarbazide, and a preliminary report is submitted on the reduction of camphor and menthone semicarbazones, and acetaldehyde phenylhydrazone.

An extensive investigation on the reduction of semicarbazones with sodium amalgam has recently been carried out by Rupe and Oestreicher⁴ with the purpose of preparing the corresponding semicarbazides. It developed in this work that the reduction by the method they employed takes place only in such cases where the $\text{N}=\text{C}$ complex is joined through its carbon atom to an aryl or other electronegative radical. The result

¹ By De Witt Neighbors and J. R. Bailey.

² Curtius, *J. prakt. Chem.*, [2] **44**, 163 (1891). Thiele, *Ann.*, **376**, 262 (1910). Maible, *Compt. rend.*, **170**, 1265 (1920).

³ Noyes, Lochte and Bailey, *THIS JOURNAL*, **43**, 2603 (1921). Ref. 24.

⁴ Rupe and Oestreicher, *Ber.*, **45**, 30 (1912).

of their work is summed up in the following statement translated from the German:

"It is shown that the reaction takes place only within narrow limits, since the reduction of semicarbazones depends in large degree on the constitution of these substances. There must be in direct connection with the $N=C$ complex a phenyl group, which fact excludes semicarbazones of aliphatic aldehydes and ketones. These cannot be reduced by the method employed by us. That the phenyl group must be in direct union with the $N=C$ complex is indicated by the fact that, while benzophenone semicarbazone is readily converted to diphenylmethyl semicarbazide, dibenzyl-ketone semicarbazone is not reduced under the same conditions, because there exists here a methylene group between the phenyls and the $N=C$."

Rupe and Oestreicher in the paper referred to above state that menthone semicarbazone is not reducible with sodium amalgam, whereas Clark and Bailey, as shown further on, find that by catalytic reduction it yields smoothly menthyl semicarbazide. Miller and Bailey likewise experience no difficulty in reducing camphor semicarbazone to bornyl semicarbazide. This work is referred to at this time in order to direct attention to the importance of catalytic reduction to hydrazino chemistry in the terpene series. Work is also under way in connection with the reduction of the azines and hydrazones of menthone and camphor.

Emil Fischer first called attention to the difficulty that has often been encountered later in reduction of the $C=N$ complex to $CHNH$. He states,⁵

"Toward sodium amalgam acetaldehyde phenylhydrazone is surprisingly stable. Even after shaking its solution in dilute alcohol for 24 hours with an excess of sodium amalgam, it is in great part unchanged."

Foster and Bailey now find that catalytic reduction offers a very simple method of preparation of phenyl-hydrazo-ethyl, $C_6H_5NHNHC_2H_5$, from the above mentioned hydrazone in a yield of over 90%, whereas Fischer obtained this hydrazo body in a long series of reactions with a yield of only a few per cent. of the theoretical.⁵ Oskar Schlenk⁶ later also attempted the reduction of phenylhydrazones with sodium amalgam and reported as follows: "This reaction is not capable of extensive employment. . . . ; it succeeds only in the case of phenylhydrazones from aromatic aldehydes, not, however, in the case of ketone hydrazones or aliphatic aldehyde hydrazones. The reaction goes especially smoothly in the case of benzal-phenylhydrazone, $C_6H_5NHN=CHC_6H_5$, which is thereby converted to benzyl-hydrazo-phenyl, $C_6H_5NHNHCH_2C_6H_5$." The success obtained in reducing acetaldehyde phenylhydrazone lends encouragement to the contemplated investigation of numerous other phenylhydrazones in this direction.

As is well known, the reduction of hydrazones, hydrazo compounds and azo compounds can be readily effected with cleavage of the molecule, and this affords a valuable method of preparing primary and secondary

⁵ Fischer, *Ber.*, 29, 797 (1896).

⁶ Schlenk, *J. prakt. Chem.*, [2] 78, 49 (1908).

amines.⁷ It is interesting to note that in addition to simple hydrogenation the catalytic process also effects cleavage of the N—N complex in certain instances; *e. g.*, it is shown in the present paper that, along with isopropyl semicarbazide, isopropylamine is formed at least in a small amount in the catalytic reduction of acetone semicarbazone.

Experimental Part

Reduction of Acetone Semicarbazone.—To 45 cc. of 10% chloroplatinic acid are added 0.5 g. of gum arabic in 10 cc. of water and a small amount of seeding colloid, and the mixture shaken in a pressure flask with hydrogen under 3 atmospheres pressure until all the platinum is reduced. Fifteen g. of acetone semicarbazone⁸ and 6.7 cc. of hydrochloric acid (s. g. 1.2) are now introduced and the reduction is carried on in the usual way until the calculated amount of hydrogen is absorbed. In reducing hydrazine derivatives it will often be found advisable to follow the procedure recommended above of preparing the colloidal solution before introducing the substance to be reduced, because these nitrogen compounds sometimes form insoluble salts with platinum chloride which are difficult to bring into reaction. The reduction of acetone semicarbazone requires about 8 hours. The platinum is precipitated with acetone, the filtered solution evaporated *in vacuo*, the residue extracted with alcohol, and the isopropyl semicarbazide hydrochloride precipitated with ether. If it be desired to obtain the base, the alcoholic solution from the platinum obtained above is concentrated *in vacuo* to a small volume and then precipitated in great part by neutralizing the solution with caustic alkali. Any dissolved base can be extracted with chloroform.

It is advisable to use a considerable excess of caustic alkali and to heat the solution to boiling before extracting the base. A small amount of the original semicarbazone is hydrolyzed and thus escapes reduction. The presence of semicarbazide can be shown by the formation of benzal semicarbazone on treating the mother liquor from the chloroform extraction with benzaldehyde. Furthermore, a small amount of the isopropyl semicarbazide is reduced to isopropylamine, evidenced by the strong amine odor on making the reduction mixture alkaline. On extraction of the semicarbazide from the alkaline solution there is a strong carbylamine odor. However, this is due in part at least to the fact that isopropyl semicarbazide itself even at room temperature produces isonitrile in the presence of chloroform and alkali.⁹

The yield of isopropyl semicarbazide in this preparation is about 70% of the calculated. The hydrochloride is conveniently purified by recrystallization from 95% alcohol, from which it separates in short, thick prisms, melting at 186.5°. This salt is very soluble in water, less soluble in alcohol, and practically insoluble in the other common solvents.

Analysis. Calc. for $C_4H_{12}ON_3Cl$: N, 27.36. Found: 27.51.

For purification, isopropyl semicarbazide is treated in water solution in the usual way with benzaldehyde to remove traces of semicarbazide, resulting from hydrolysis of the acetone semicarbazone in the reduction, and after extraction with chloroform recrystallized from acetic ether. It is readily soluble in water, alcohol, chloroform and benzene, and difficultly soluble in the other common solvents. It crystallizes in plates, rhombic in appearance, and melting at 128°, undecomposed.

⁷ Tafel, *Ber.*, **19**, 1924 (1886).

⁸ Thiele and Stange, *ibid.*, **27**, 32 (1894).

⁹ Cf. H. Meyer, "Konstitutionsermittlung organischer Verbindungen," 2nd. Ed., p. 879.

Analyses. Calc. for $C_4H_{11}ON_3$: C, 41.00; H, 9.40; N, 35.89. Found: C, 40.90; H, 9.30; N, 35.74.

Isopropyl Semicarbazide Oxalate may be prepared by adding anhydrous oxalic acid in ether solution to an ether-alcohol solution of the semicarbazide, whereupon the salt separates. Recrystallized from water, it is obtained in large prisms, melting at 172° .

Analysis. Calc. for $C_6H_{13}O_5N_3$: N, 20.29. Found: 20.54.

The Nitroso Derivative of Isopropyl Semicarbazide separates on the addition of the calculated amount of sodium nitrite to a solution of isopropyl semicarbazide hydrochloride. It crystallizes from ethyl acetate in short prisms of a light yellow color, which decompose with gas evolution at 128° . It is very readily soluble in alcohol and water, and difficultly soluble in benzene, ether, and chloroform. The nitroso-amine gives the Liebermann reaction, and in aqueous solution, heated to boiling, gives off a gas reacting alkaline to turmeric paper. The alkalinity is probably due to a hydrolysis of the nitroso-semicarbazide, in accordance with the equation,¹⁰ $C_3H_7N(NO)NHCONH_2 + H_2O = (CH_3)_2CHNH_2 + N_2O + NH_3 + CO_2$.

Conversion of Isopropyl Semicarbazide to Isopropylhydrazine.— $2(CH_3)_2CHNH-NHCONH_2 + 2H_2SO_4 + 2H_2O = ((CH_3)_2CHNHNH_2)_2 \cdot H_2SO_4 + (NH_4)_2SO_4 + 2CO_2$. One g. of isopropyl semicarbazide is heated on a boiling water bath with 1.5 cc. of 80% sulfuric acid as long as carbon dioxide is evolved. The solution diluted to 15 cc. is now digested on the water bath with barium carbonate until all the sulfuric acid is precipitated and the ammonia driven off. On adding solid caustic to the filtered solution, the isopropylhydrazine separates as an oil. For identification it was extracted with ether and converted to the dibenzoyl derivative by adding the calculated amount of benzoyl chloride and a slight excess of sodium carbonate. The reaction proceeds in the cold with the separation of the difficultly soluble dibenzoyl compound. After being filtered off, it was washed with ether to remove any benzoyl chloride and finally with water. For analysis it was recrystallized from dil. alcohol, and was then obtained in clusters of radiating needles melting at 161.5° .¹¹

Analysis. Calc. for $C_{17}H_{18}O_2N_2$: N, 9.93. Found: 10.02.

Benzoyl Isopropyl Semicarbazide.—To isopropyl semicarbazide dissolved in benzene are added molecular quantities of benzoyl chloride and sodium hydrogen carbonate. The benzoyl derivative is readily formed on warming the mixture and crystallizes on cooling. Recrystallized from 95% alcohol, it is obtained in needles melting at 228° . It is quite soluble in hot water, but difficultly soluble in organic solvents other than alcohol.

Analysis. Calc. for $C_{11}H_{13}O_2N_3$: N, 19.00. Found: 18.82.

3-Hydroxy-1-Isopropyl-5-phenyltriazole.—The above benzoyl isopropyl semicarbazide illustrates the general reaction of acyl semicarbazides which under the influence of alkalis condense to triazoles.¹² The benzoyl semicarbazide, heated with 20 times its weight of 30% sodium hydroxide solution at 80° for $1/2$ hour, loses a molecule of water and, on cooling, the sodium salt of the hydroxy-isopropyl-phenyltriazole separates in hair-like needles. From an aqueous solution of this salt, acidified with hydrochloric acid, the triazole is obtained in prisms, melting at 185.5° . It is only slightly soluble in

¹⁰ Cf. Bailey and Snyder, *THIS JOURNAL*, **37**, 942 (1915).

¹¹ This dibenzoyl-isopropylhydrazine was compared with a sample of the same material furnished us by Mr. Lochte. His product, which was made from isopropylhydrazine, prepared by the catalytic reduction of acetone hydrazone, $(CH_3)_2C=N-NH_2$, proved identical with ours.

¹² Cf. Bailey and Acree, *Ber.*, **33**, 1520 (1900).

water, practically insoluble in ether, and readily soluble in alcohol, chloroform and acetic ether.

Analyses. Calc. for $C_{11}H_{13}ON_3$: C, 65.02; H, 6.40; N, 20.69. Found: C, 65.04; H, 6.72; N, 20.77.

Oxidation of Isopropyl Semicarbazide in Alkaline Solution.—The semicarbazide in aqueous solution, treated with the calculated amount of potassium permanganate, is converted to acetone semicarbazone, which can be isolated by evaporating the filtered, alkaline oxidation mixture *in vacuo* to a small volume, when the semicarbazone precipitates. For analysis it was crystallized from alcohol and then from water. A comparison with a stock sample of acetone semicarbazone proved the identity of the two products.

Analysis. Calc. for $C_4H_9ON_3$: N, 36.52. Found: 36.71.

Oxidation of Isopropyl Semicarbazide in Acid Solution. Preparation of 2-Carbonamido-azopropane, $(CH_3)_2CHN=NCONH_2$.—To 3 g. of isopropyl semicarbazide, dissolved in 20 cc. of water containing 1 cc. of conc. sulfuric acid, is added with cooling and stirring a solution of 0.81 g. of potassium permanganate in 15 cc. of water. The oxidation proceeds with very little gas evolution. As soon as all the permanganate has been introduced, the solution is repeatedly extracted with ether and, after drying with sodium sulfate, the ether is distilled, leaving a residue weighing about 1 g. The original aqueous solution soon develops a strong smell of acetone, indicating that along with the azo body there is formed a large amount of the isomeric acetone semicarbazone, which undergoes hydrolysis in the acid medium. Both semicarbazide and acetone semicarbazone here react on the addition of sodium acetate and benzaldehyde to form the difficultly-soluble benzaldehyde semicarbazone, melting at 214° . 2-Carbonamido-azopropane, which has a deep yellow color, is readily soluble in the common solvents and crystallizes from a mixture of benzene and petroleum ether in slender prisms, melting at $65.5\text{--}66^\circ$. The azo structure is indicated by the fact that the substance, apart from being strongly colored, does not form salts with acids. A very interesting property of the azo compound is the ease with which it transforms to acetone semicarbazone. On the addition of a trace of caustic potash to an aqueous solution of the azo body, the deep yellow color quickly fades with a separation of the more insoluble, colorless semicarbazone. The same rearrangement takes place but more slowly in acid solution.¹³ The following analytical results were obtained on the azo compound.

Analyses. Calc. for $C_4H_9ON_3$: C, 41.74; H, 7.83; N, 36.52. Found: C, 41.48; H, 7.81; N, 36.53.

It is probable that the azo compound is formed as an intermediary product, when isopropyl semicarbazide is oxidized with permanganate in alkaline solution; at least it can be isolated in small amount, if the permanganate solution strongly cooled is added to an aqueous solution of the semicarbazide containing pieces of ice. The mixture assumes a decided yellow color and, if it be immediately extracted with ether, the yellow color is imparted to the ether layer. In this way a small amount of the azo compound was isolated and identified. Oxidation with bromine water also produces the azo compound, but hydrogen peroxide, which Thiele found effective in oxidizing hydrazophenylmethane and phenylhydrazobenzyl to the corresponding azo compounds¹⁴ gives only the semicarbazone from isopropyl semicarbazide.

¹³ A carefully purified sample of the azo compound, after standing for several weeks exposed to the air, became colorless, and the resulting substance was identified as acetone semicarbazone. A similar transformation of phenylazobenzyl to the corresponding hydrazone in the absence of a solvent was observed by Thiele (Ref. 1, p. 268).

¹⁴ Thiele, Ref. 1, p. 267.

The Reduction of Phenylhydrazones¹⁵

Three methods of preparing phenyl-hydrazo-ethyl, $\text{C}_6\text{H}_5\text{NHNHC}_2\text{H}_5$, have been published. Emil Fischer¹⁶ obtained the substance in poor yield along with 1,1-ethyl-phenyl-hydrazine, $\text{C}_2\text{H}_5(\text{C}_6\text{H}_5)\text{NNH}_2$, and the quaternary ammonium salt, $\text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2\text{NBrNH}_2$, by the action of ethyl bromide on phenylhydrazine. Knorr and Weidel¹⁷ later obtained it by modifying the process employed by Knorr and Köhler in the discovery of hydrazomethane.¹⁸ Their method consisted of splitting 1-phenylpyrazole-iodoethylate with caustic potash. Third, there is a patented process for the preparation of this and homologous hydrazo compounds¹⁹ from the sodium salt of formyl-phenylhydrazine, $\text{C}_6\text{H}_5\text{NHN}(\text{Na})\text{CHO}$, and alkyl halides as intermediates.

The following method of reducing acetaldehyde phenylhydrazone, $\text{C}_6\text{H}_5\text{NHN}=\text{CHCH}_3$, which gives the corresponding hydrazo compound in a yield of about 95%, offers a very convenient method of preparation.

Fifty cc. of 10% chloroplatinic acid, mixed with 20 cc. of water, 24 cc. of hydrochloric acid (s. g. 1.19), and 2 cc. of seeding colloid are reduced in the usual way with hydrogen under a pressure of 3 atmospheres. About 20 minutes is required in this step. Twenty-five g. of the hydrazone,²⁰ partly dissolved in 200 cc. of 50% ethyl alcohol, is now added to the colloidal solution, when, after 3 hours of hydrogenation, the calculated amount of gas is absorbed. After breaking the colloid and filtering off the precipitated platinum, the alcohol and acetone are removed *in vacuo* with a stream of nitrogen passing through the apparatus. The method of Knorr and Weidel is used in liberating the hydrazo base. A steam-distillation apparatus, from which oxygen is eliminated by passing a current of nitrogen through the system, is provided with a dropping funnel, through which conc. caustic soda can be introduced into the solution of the hydrochloride of the hydrazo compound in such a way as to liberate the base at about the rate that it distills over. The distillation is continued until the milky emulsion coming over clears, and a drop treated with Fehling solution no longer yields the very characteristic yellow azo compound which is very insoluble and has an unpleasant, penetrating odor. The distillate is extracted with ether, and dried with potassium carbonate, after which the base is precipitated as oxalate with an ether solution of anhydrous oxalic acid. For purification, the salt is first recrystallized from water with the addition of a little Filtchar and then from alcohol. It is thus obtained in long prismatic plates, melting, as reported by Knorr and Weidel, at 166–167°. For further confirmation, the oxalate was analyzed.

Analyses. Calc. for $\text{C}_{10}\text{H}_{14}\text{O}_4\text{N}_2$: C, 53.10; H, 6.19; N, 12.39. Found: C, 53.42; H, 6.19; N, 12.50.

Phenylethyl Semicarbazide.—This substance, prepared by dissolving the oxalate of phenyl-hydrazo-ethyl in glacial acetic acid²¹ with a slight excess of potassium cyanate,

¹⁵ A preliminary report on an extension of the Lochte-Bailey method of preparing hydrazine derivatives by A. L. Foster and J. R. Bailey.

¹⁶ Fischer, *Ann.*, **190**, 102 (1877); **199**, 325 (1879).

¹⁷ Knorr, *Ber.*, **39**, 3265 (1906). Knorr and Weidel, *ibid.*, **42**, 3523 (1909).

¹⁸ Knorr and Köhler, *ibid.*, **39**, 3257 (1906).

¹⁹ Ger. pat., 57,944; Friedländer, III, 23 1890–1894.

²⁰ Lockemann and Liesche, *Ann.*, **342**, 25 (1905).

²¹ Cf. Bailey and Read, *This Journal*, **37**, 1884 (1915).

is purified by crystallization once from alcohol and twice from benzene. It is readily soluble in ether, chloroform and acetic ether, and difficultly soluble in cold, readily in hot, water. This ureide crystallizes in microscopic needles, melting at 138°. It remains to be determined to which nitrogen the carbonamido group is attached.

Analyses. Calc. for $C_9H_{13}ON_3$: C, 60.34; H, 7.26; N, 23.46. Found: C, 60.37; H, 7.16; N, 23.51.

In this research, which deals with the reduction of phenylhydrazones, it has been found that acetone phenylhydrazone can be reduced catalytically with the same ease as the acetaldehyde compound.

Preparation of Menthyl Semicarbazide,²²



A mixture of 21.1 g. of menthone semicarbazone,²³ 175 cc. of 50% methyl alcohol, 57 cc. of 10% chloroplatinic acid, 5 cc. of 10% gum arabic solution, and 8.1 cc. of hydrochloric acid (s. g. 1.19) are reduced under 4 atmospheres pressure. In the beginning, a considerable portion of the semicarbazone is undissolved but, as the formation of the basic semicarbazide proceeds, the semicarbazone gradually dissolves until at the end of about 2½ hours there is a clear solution. Under the conditions employed here, the hydrogen is absorbed at the rate of from 700 to 1100 cc. per hour for the first 2 hours after the colloid has formed, and then the rate decreases gradually until finally with the theoretical amount of gas absorbed the reaction stops. The process requires 6 to 9 hours for completion, depending on the condition of the catalyst. The usual procedure of removing the platinum and organic solvents is now followed, and the menthyl semicarbazide precipitated from the aqueous solution of its hydrochloride with caustic soda. It crystallizes from ethyl acetate in colorless, acicular needles melting at 179–180° (apparently undecomposed), and gives in methyl alcoholic solution a rotation of $[\alpha]_D^{20} = -43.8$. The base is practically insoluble in water and is soluble in the common organic solvents. Menthyl semicarbazide shows strong reducing action. Certain derivatives have been prepared which are being further investigated.

Analyses. Calc. for $C_{11}H_{23}ON_3$: C, 61.97; H, 10.80; N, 19.72. Found: C, 61.67; H, 10.69; N, 20.00.

Bornyl Semicarbazide,²⁴



Camphor semicarbazone²⁵ is reduced under conditions similar to those employed with menthone semicarbazone. After removal of the platinum and organic solvents in the usual way, the bornyl semicarbazide is precipitated from its solution with caustic soda, taken up in chloroform, and the residue, obtained on evaporation of the chloroform solution, recrystallized from dil. alcohol. It is readily soluble in alcohol, acetic ether, and chloroform and difficultly soluble in ether, benzene, and water. It crystallizes in prisms melting at 192.5°. This semicarbazide shows the characteristic strong reducing action of this class of substances and reacts with acid chlorides and nitrous acid. An attempt to prepare bornylhydrazine from the semicarbazide by the action of 80% sulfuric acid under conditions similar to those described above in the case of *isopropyl*-semicarbazide was unsuccessful. Among the reaction products there is formed hydrazine sulfate, which was converted to benzalazine for further identification.

²² By S. M. Clark and J. R. Bailey.

²³ Flatau and Labbé, *Bull. soc. chim.*, [3] 19, 788 (1898).

²⁴ By J. E. Miller and J. R. Bailey.

²⁵ Wallach, *Ann.*, 353, 214 (1907).

Analyses. Calc. for $C_{11}H_{21}ON_3$: C, 62.56; H, 9.95; N, 19.91. Found: C, 62.89; H, 10.03; N, 19.87.

Summary

It has long been recognized that a method of reducing aliphatic hydrazones, azines and semicarbazones would be of great preparative value in the case of hydrazino-, hydrazo-, and azo paraffins. Wieland in "Die Hydrazine," p. 94, sums up the efforts of chemists in this direction as follows: "The unsaturated complex $C=N$ shows no great tendency to take up hydrogen. No positive results have been accomplished in the hydrogenation of aliphatic hydrazones, and Thiele only a short time ago showed in the case of the azines their incapability of reduction to hydrazoparaffins." Lochte and Bailey by applying catalytic reduction to the problem found that the reaction unsuccessfully attempted by Thiele can be effected with the greatest ease, and in the present paper it is shown that the same method of attack leads to the reduction of certain semicarbazones and hydrazones where other investigators have obtained only negative results.

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AMIDE FORMATION FROM ESTERS OF SECONDARY ALKYL MALONIC ACIDS

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The striking difference in behavior of the ethyl esters of mono-alkyl- and di-alkyl-malonic acids was pointed out by Fischer and Dilthey.¹ According to their experiments the ethyl esters of methyl-, ethyl- and propylmalonic acids react readily with alcoholic and with liquid ammonia, giving good yields of the corresponding di-amides, together with small amounts of the intermediate ester-amides. On the other hand, the ethyl esters of dimethyl-, diethyl- and dipropylmalonic acids give under the same conditions no amide at all, or else the merest traces. The reaction obtained with the mono-alkyl derivatives was attributed by Fischer and Dilthey to the unsubstituted hydrogen which confers acidic properties upon the substance and makes possible the formation of an intermediate addition product with ammonia. This explanation was shown by Meyer² to be inadequate. Meyer found that the methyl esters of dimethyl- and methylethyl-malonic acids readily formed amides when treated with aqueous ammonia. With the methyl ester of diethyl-malonic acid, however, no amide was formed. The presence of 2 ethyl groups, whether in the side chains or in the nucleus, apparently brings about a condition of

¹ Fischer and Dilthey, *ibid.*, **35**, 844 (1902).

² Meyer, *ibid.*, **39**, 198 (1906).