

2. Phenylmercuric chloride, *o*- and *p*-tolylmercuric chlorides, 2,5-dimethylphenylmercuric chloride and α -naphthylmercuric chloride have been prepared by the above method.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

SILICA GEL AS A CATALYST IN THE PREPARATION OF NITRILES¹

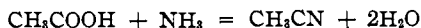
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RECEIVED NOVEMBER 14, 1930

PUBLISHED JANUARY 12, 1931

Previous investigations have shown that silica gel is an excellent catalyst for certain dehydrating reactions involving organic compounds. Milligan, Chappell and Reid³ showed it to be an extraordinarily good esterification catalyst; Brown and Reid studied its application in the alkylation of ammonia and dehydration of alcohols⁴ and also in the alkylation of aniline.⁵

The catalytic dehydration of the nascent amide formed from acetic acid and ammonia, according to the equation



in the presence of thoria and alumina, has been studied by Van Epps and Reid.⁶ They found that an 85% yield of nitrile could be obtained at 500° with the better catalyst, alumina. They reported that no nitrile was obtained by passing ethyl acetate and ammonia over alumina, while Mailhe⁷ obtained nitriles from esters and ammonia with both thoria and alumina.

This reaction has been investigated in the presence of silica gel.

Results

We have found that silica gel is a more efficient catalyst than either thoria or alumina in the preparation of nitriles from acids and ammonia. Using acetic acid and an excess of ammonia, as the temperature of operation is raised the percentage conversion to acetonitrile increases until at 500–525° a maximum is reached (practically quantitative). Increasing the temperature to 550° results in a decreased yield and increasing it to 575° lowers the yield still further. It appears that operation at tempera-

¹ This and the two following papers, presented at the Atlanta meeting of the American Chemical Society, April, 1930, are extracted from a dissertation presented by James A. Mitchell to the Faculty of the Graduate School of Johns Hopkins University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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³ Milligan, Chappell and Reid, *J. Phys. Chem.*, **28**, 872 (1924).

⁴ Brown and Reid, *ibid.*, **28**, 1067, 1077 (1924).

⁵ Brown and Reid, *THIS JOURNAL*, **46**, 1836 (1924).

⁶ Van Epps and Reid, *ibid.*, **38**, 2128 (1916).

⁷ Mailhe, *Bull. soc. chim.*, [4] **23**, 232 (1918); *Ann. chim.*, [9] **13**, 213 (1920).

tures above 500° fouls the catalyst, for after such treatment runs at lower temperatures gave low yields.

If the temperature of operation was not allowed to rise above 500° the catalyst was very slightly discolored and its activity continued unimpaired almost indefinitely, even after repeated heating and cooling in air.⁸

In every case when the temperature of operation was above 500° a noticeable quantity of a white solid formed in the condenser when distilling the lower (water) layer of the product. The higher the temperature the greater was the yield of this material. It was identified as ammonium carbonate. It is reasonable to suppose that even at temperatures of 500° or lower some ammonium carbonate is formed—which may account, in part, for the salting out of the nitrile to form the upper layer. The acetic acid not converted to nitrile or amide is, of course, in the lower layer in the form of ammonium acetate, and is also efficient as a salting out agent.

A rough calculation of the velocity of passage of the reactants through the catalyst in the case of acetonitrile shows that when the time of contact is twenty-five seconds at 500°, the percentage conversion is 95% (practically quantitative) and only 60% when the rate of flow of the reactants is twice as fast.

The results obtained show that highly purified gel and commercial gel are of the same order of activity.

All the aliphatic acids from acetic to heptonic, with an excess of ammonia, produce large yields of nitriles. The yield from lauric acid is decidedly lower and no nitrile has been obtained from palmitic acid. High yields of nitriles are also obtained from phenylacetic and hydrocinnamic acids.

With all the acids except acetic and isovaleric the catalyst blackens readily at temperatures of 500° or lower and loses its activity in most cases very gradually with use.

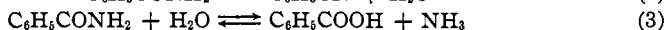
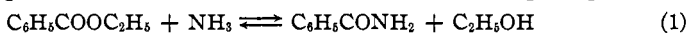
The yields of isovaleronitrile, above 90%, offer a rather surprising contrast with the yield of *n*-valeronitrile, which never exceeded 80%. The difference can hardly be ascribed to any difference in thermal stability of the two acids and, as the nitriles are relatively more stable than the acids, the results may indicate that the formation of nitrile from the isovaleric acid is much more rapid than from the normal acid.

In passing an ester with an excess of ammonia over silica gel the initial percentage conversion to nitrile is high, approximately the same as with the acid. The catalyst, however, in contrast with the acid reaction, is rapidly fouled. Aside from the greater instability of the ester as compared with the acid, the fouling of the catalyst might be partially explained by the decomposition products of the alcohol formed in the ester reaction.

⁸ With thoria and alumina the catalytic efficiency has been shown to fall off fairly rapidly with use.

Brown and Reid⁹ have shown that large amounts of aldehyde are formed in passing butyl alcohol over silica gel. Our experience indicates that silica gel is rapidly fouled in any reaction involving the presence of aldehyde, probably due to the formation of polymerization products.

In passing ethyl benzoate and ammonia over silica gel, ammonium benzoate was obtained as one of the products of the reaction. In this instance we are dealing, after the initial reaction (1), with two competing reactions



The fouling of the catalyst has been found to favor Reaction 3 (*i. e.*, more ammonium benzoate is formed) and decrease the yield of nitrile, Reaction 2. If the catalyst is effective in the establishment of both equilibria (2) and (3), it is only reasonable to expect that if it becomes less effective in one reaction it will also become less effective in the other. Two alternative explanations of the experimental result are possible: first, either the gel is *such an effective catalyst* for the establishment of equilibrium, (3) that partial fouling hardly impairs its activity, or, second, the hydration of the amide and dehydration of the ammonium salt, (3), is *independent of the catalyst* and merely involves a thermal equilibrium. As less amide is converted to the nitrile more is available for hydrolysis to the acid and ammonia.

In order to ascertain which of these two explanations is correct, benzamide was hydrolyzed in sealed tubes with and without silica gel. The gel had no effect on the rate of hydrolysis. Similar experiments using ammonium acetate showed that silica gel has no influence on the rate of formation of the amide.

It is evident, therefore, that silica gel affects only the second reaction, in the conversion of acids and ammonia to nitriles.

It is, of course, a well-known fact that ammonium salts of the aliphatic acids are easily dehydrated to the amide by the application of heat. Boehner and Andrews¹⁰ and Boehner and Ward¹¹ have shown that various large-surface catalysts are active in the dehydration of amides. In our experiments in which amides were swept over silica gel by a current of air or nitrogen at temperatures above 400° very high yields of nitriles were obtained.

Experimental

Apparatus and Procedure.—The horizontal tube furnace used was similar to that described by Kramer and Reid.¹²

⁹ Brown and Reid, *J. Phys. Chem.*, **28**, 1080 (1924).

¹⁰ Boehner and Andrews, *THIS JOURNAL*, **38**, 2503 (1916).

¹¹ Boehner and Ward, *ibid.*, **38**, 2505 (1916).

¹² Kramer and Reid, *ibid.*, **43**, 880 (1921).

The catalyst, 100 g. of silica gel, was placed in a pyrex tube approximately 56 cm. by 23 mm. and activated by heating for four or five hours at 210° in a slow current of dried air, gradually raising the temperature to that desired in the experiment, while continuing the current of dried air.

An accurately measured quantity of acid (or ester) was passed through a dropping arrangement, the flow of which could be regulated by means of a glass rod ground in the tip, and introduced directly by a capillary into an atmosphere of ammonia, over the gel. The ammonia was passed through a calibrated flowmeter and led in through a separate tube ending a little short of the end of the capillary tube. An excess of ammonia was always used.

The temperature was read from a thermometer placed between the catalyst tube and the wall of the furnace and kept constant within 1°. Temperatures above 500° were read with a thermocouple.

The gases after leaving the catalyst were led through a condenser, cooled by very cold water, and thence into a receiver, which in the case of acetonitrile was immersed in an ice-salt bath. The excess ammonia was allowed to escape.

The product invariably separated into two layers—the upper layer being practically pure nitrile and ammonia. The nitrile is salted out by ammonium acetate and ammonium carbonate. The lower layer in the case of the soluble nitriles also contained considerable nitrile.

Analysis.—Van Epps and Reid⁶ estimated acetonitrile by fractional distillation. The product obtained, however, cannot be freed completely from ammonia, even after refluxing for some time.

The following analytical method proved very satisfactory. The two layers from the run were separated and distilled separately from a Claisen flask with an extended neck and the distillates collected up to 90°. The combined distillate from both layers was weighed and entered as product. The acetonitrile present was determined as follows. An accurately weighed sample of the product (about 0.5 g.) was sealed in a glass tube with 2 cc. of 18 *N* sulfuric acid and heated at 150° for two and one-half to three hours. The tube contents, after hydrolysis, were carefully washed into a 50-cc. volumetric flask. A 5-cc. aliquot was titrated for total acidity with 0.1 *N* sodium hydroxide with phenolphthalein as an indicator, using throughout carbon dioxide-free water. A similar 5-cc. aliquot was heated in a porcelain dish on a water-bath for one and one-half hours, frequently washing down the sides of the dish with distilled water. The acetic acid formed by the hydrolysis of the nitrile was volatilized, leaving the excess sulfuric acid behind. The residue was titrated as before. The difference in the titers, of course, represents the acetic acid present—whence the acetonitrile in the product can be calculated. The estimation of propionitrile was effected in much the same manner. The two-layer product from the run was saturated with potassium carbonate. This effectively salted out the nitrile (an aqueous solution of propionitrile saturated with potassium carbonate retains in solution only about 0.02 g. per cc.). The upper layer was separated, distilled, and the fraction boiling between 90–98° analyzed as before.

Several similar analyses were run on butyronitrile, but this and the higher nitriles were easily purified and quickly freed of ammonia by distillation. Accordingly the higher nitriles were purified and estimated by fractional distillation.

Catalyst.—The catalyst used for the most part was ordinary 8–14 mesh commercial gel.¹³ A purified gel catalyst was prepared by refluxing a sample of the commercial gel for several hours with concentrated nitric acid and subsequently cleaned by continued washing with distilled water until it was snow-white and acid free. A portion of the

¹³ Kindly furnished by Professor W. A. Patrick.

gel purified in this manner was further purified by electrolysis, until entirely freed of electrolyte.¹⁴

Materials.—The acetic acid was c. p. glacial acetic acid. The propionic, butyric and caproic¹⁵ acids were technical materials carefully purified by distillation through a precision fractionating column. The isovaleric, lauric, palmitic and phenylacetic acids, butyl acetate and ethyl benzoate employed were the purest materials obtainable from the Eastman Kodak Company. The normal valeric acid used was prepared by the Grignard reaction from *n*-butyl bromide and carbon dioxide and purified by distillation through a fractionating column. Normal heptoic acid was prepared by oxidizing heptaldehyde with chromic acid mixture, separating the product formed and purifying by fractionation through a column.

Hydrocinnamic acid was prepared by completely reducing pure cinnamic acid with amalgamated zinc according to the method of Clemmensen¹⁶ and recrystallizing the product from water until an accurate, sharp melting point was obtained.

n-Butyl *n*-butyrate was prepared by the oxidation and esterification of *n*-butyl alcohol with sulfuric-chromic acid.¹⁷

TABLE I
ACETONITRILE

Temp., °C.	Acid used, g.	Time of expt. min.	Rate of flow of ammonia, cc./min.	Amount, g.	Product Purity, %	Yield, %
Effect of variation in temperature						
400	26.0	72	100	15.08	84	71
450	26.0	70	100	17.06	91	87
500	26.0	70	100	19.20	90	97
525	26.0	70	100	19.19	89	96
550	26.0	69	105	18.11	81	82
575	26.0	70	105	17.62	78	77
500	26.0	72	105	16.00	94	84
550	26.0	66	110	15.33	85	73
500	26.0	75	100	15.77	89	78
Effect of variation in rate of flow						
500	26.0	74	110	18.13	85	87
500	26.0	80	150	17.60	79	78
500	26.0	71	180	17.44	81	79
500	26.0	105	150	14.28	92	74
500	26.0	30	230	11.83	89	60
500	26.0	89	105	18.43	85	88
500	26.0	110	100	20.30	87	98
500	26.0	100	80	19.58	83	91
Gel purified by nitric acid and electrolysis						
500	31.0	77	105	21.07	92	92
500	26.0	75	110	19.37	84	91
500	26.0	75	110	17.37	89	87
500	26.0	72	105	17.27	93	90

¹⁴ Using the method described by O. G. Bennett, "Dissertation," Johns Hopkins University, 1930.

¹⁵ Kindly furnished by Sharp and Dohme, Baltimore, Md.

¹⁶ Clemmensen, *Ber.*, **46**, 1837 (1913); **47**, 51, 681 (1914).

¹⁷ "Organic Syntheses," John Wiley and Sons, Inc., New York, 1925, Vol. V, p. 23.

The Preparation of Nitriles from Acids

Acetonitrile (Methyl Cyanide).—The effect of variation of temperature on the yield of nitrile is indicated in the first section of Table I.

Variation in the rate of flow of the two reactants was studied and the results are tabulated in Section II, Table I. Keeping the temperature constant at 500° it is evident, as is to be expected, that the time of contact with the catalyst is a factor of considerable importance. Increasing the rate of flow of either the acid or ammonia results in a decreased yield.

The results obtained in using a highly purified sample of the same gel are indicated in the third section of Table I. It is evident that similar yields of nitriles are obtained.

Each section of the table represents the results from a fresh charge of catalyst.

The two-layer product from the run was always water white without the least discoloration.

Propionitrile (Ethyl Cyanide).—The product, which always separated into two layers, was almost colorless, although several times a slight yellow coloration was apparent. After salting out with potassium carbonate, the upper layer upon distillation was quickly freed of ammonia and the boiling point rose rapidly to 95°. The fraction was taken between 90–98°—the major portion distilled between 95–97°. The propionitrile occasionally smelled faintly of ammonia, generally not at all, and the analyses showed a high degree of purity (98%).

TABLE II
PROPIONITRILE

Temp., °C.	Acid used, g.	Time of expt., min.	Rate of flow of ammonia, cc./min.	Amount, g.	Product Purity, %	Yield, %
450	24.5	77	100	14.90	99	81
500	24.5	69	100	15.53	98	83
500	24.5	76	105	15.07	97	80
500	24.5	101	90	15.37	99	83
410	24.5	63	115	10.00	94	51
450	24.5	70	110	12.60	100	69
A new catalyst						
500	24.5	92	95	15.87	98	85
500	24.5	104	90	16.47	98	88
500	24.5	108	85	15.97	98	86

Lauronitrile (*n*-Undecyl Cyanide).—Ninety grams of lauric acid was passed over commercial gel at 500° with an excess of ammonia. The rate of flow was comparable with those of the other experiments. The acid was kept molten by surrounding the dropping apparatus with a "chimney," through which a current of hot air was passed. The temperature was kept constant (65°) to insure an even flow of acid.

TABLE III

Temp., °C.	Acid used, g.	HIGHER NITRILES		Product, g.	Yield, %
		Time of expt., min.	Rate of flow of ammonia, cc./min.		
<i>n</i> -Butyronitrile					
450	23.7	65	100	15.24	82
500	23.7	105	100	17.57	94
500	23.7	68	100	17.00	91
500	26.0	113	90	19.00	93
450	23.7	63	110	14.37	77
500	23.7	71	110	16.37	88
500	23.7	84	80	16.88	90
<i>n</i> -Valeronitrile					
500	44.0	134	95	27.10	76
500	22.0	92	80	14.40	80
500	22.0	105	80	14.60	81
510	22.0	80	90	13.00	73
Isovaleronitrile					
500	23.0	75	90	16.9	90
500	23.0	89	95	17.3	92
500	23.0	114	85	17.7	94
500	23.0	84	85	17.4	93
<i>n</i> -Capronitrile					
500	26.7	98	80	19.90	89
500	24.0	89	90	17.97	88
500	25.3	105	100	18.80	89
500	24.0	78	90	18.30	90
500	24.0	62	105	17.14	84
500	24.0	117	85	18.88	93
<i>n</i> -Heptonitrile					
500	22.6	90	95	17.72	92
500	22.6	73	100	18.30	94
500	22.6	54	90	17.65	91
500	45.2	141	90	36.00	93

A fair amount of solid material was obtained in the product, which seemed to consist of the amide, and the ammonium salt of the acid.

The liquid product was washed with water and distilled under 98 mm. pressure. The larger part of the material distilled at 192–195°; yield of nitrile, 46.0 g. (55%).

Palmitic acid was passed over silica gel at 500° with an excess of ammonia. The acid was kept molten and at a temperature of 90°, using the same technique as with the lauric acid. The product was distilled under diminished pressure. The major portion distilled within 1.5 of 265° under 32 mm. pressure. It appeared to be a mixture of the amide and the acid. The product after several recrystallizations was still very impure

and melted sluggishly around 40°. No noticeable amount of nitrile was obtained.

Phenylacetonitrile (Benzyl Cyanide).—One hundred and fifty grams of phenylacetic acid was passed over commercial gel at 500° with an excess of ammonia at a rate comparable to those in the previous experiments. The acid in the dropping arrangement was kept molten and at a temperature of 90° as before. The product separated into two layers. The upper (nitrile) layer was separated and distilled under vacuum. The product was almost pure nitrile. That fraction boiling between 128.5–129.5° at 31 mm. was entered as nitrile; yield, 112 g. (87%). The gel was completely blackened after use, but was still active.

Phenylpropionitrile (Phenylethyl Cyanide).—One hundred and twenty-three grams of hydrocinnamic acid was passed over commercial gel at 500° with an excess of ammonia, using the same technique as in the previous experiments with solid acids. The upper layer was distilled as before, practically all of it distilling at 141–142° at 25 mm.; yield of nitrile, 87 g. (81%).

The Preparation of Nitriles from Esters

Acetonitrile from *n*-Butyl Acetate.—The results obtained upon passing *n*-butyl acetate over commercial gel with an excess of ammonia are indicated in Table IV. Each space in the table indicates a change in catalyst.

TABLE IV
ACETONITRILE FROM *n*-BUTYL ACETATE

Temp., °C.	Ester used, g.	Time of expt., min.	Rate of flow of ammonia, cc./min.	Product Amount, g.	Purity, %	Yield, %
500	21.8	64	95	9.64	70	87
444	21.8	47	100	9.80	65	82
400	21.8	77	95	10.50	59	80
400	21.8	81	90	10.22	46	61
370	45.3	129	90	11.17	59	41
404	43.6	112	90	12.17	47	37
370	43.6	120	90	12.00	52	40
400	43.6	120	85	14.57	52	49
455	43.6	112	95	15.82	61	63
455	43.6	123	105	14.60	55	52

The two layers of the product, highly colored and fluorescent, were separated and each distilled up to 85°. The material was analyzed for nitrile in the same manner as was the product obtained from acetic acid. At 500° the efficiency of the catalyst decreased rapidly. At lower temperatures the life of the catalyst was longer, but its decline was still marked.

***n*-Butyronitrile from *n*-Butyl *n*-Butyrate.**—Here again it is evident that good yields of nitrile are obtainable with a fresh catalyst, but the efficiency drops off rapidly with use (Table V, Section I).

Benzonitrile from Ethyl Benzoate.—As the use of benzoic acid was precluded by the type of apparatus employed, ethyl benzoate was passed over silica gel with an excess of ammonia gas. The formation of nitrile from the ester may be taken as sufficient indication that it is also obtainable from the acid. The results of experiments with ethyl benzoate are noted in Table V, Section II. It is apparent that favorable yields may be obtained. The catalyst, as with the other esters, is rapidly fouled.

The product invariably separated into two layers. The lower (nitrile) layer was distilled. The boiling point rapidly rose to 190° and practically all of the layer boiled between 190–195°. This fraction was taken as nitrile.

It was observed that during the experiments a considerable quantity of white solid collected in the condenser. As the catalyst was used and its efficiency decreased, the yield of this material increased. These crystals, upon examination, proved to be ammonium benzoate.

TABLE V
EXPERIMENTAL DATA

Temp., °C.	Ester used, g.	Time of expt., min.	Rate of flow of ammonia, cc./min.	Product, g.	Yield, %
<i>n</i> -Butyronitrile from <i>n</i> -Butyl <i>n</i> -Butyrate					
380	43.4	96	90	11.00	53
410	45.1	122	85	12.50	58
450	43.4	123	80	13.51	65
500	43.4	102	95	15.49	75
450	43.4	113	80	11.70	56
Benzonitrile from Ethyl Benzoate					
500	26.3		90	12.0	66
440	52.6	125	70	24.0	66
420	26.3	60	70	10.8	60
455	26.3	70	65	14.0	77
410	26.3	60	90	7.4	41
455	26.3	65	80	8.1	45

The Influence of Silica Gel on the Amide-Ammonium Salt Equilibrium.—Exactly weighed quantities of purified benzamide (0.3–0.4 g.) and a weighed quantity of water (about 1.1 g.—a large excess of water was used to force the hydrolysis of the amide) were sealed in pyrex tubes, half of the tubes containing about 0.5 g. of activated silica gel. Pairs of tubes with and without gel were heated at varying periods at 300°. The mixture of benzamide and ammonium benzoate was analyzed by the method outlined by Reid.¹⁸ No difference was observed in the rate of hydrolysis of the amide, with or without gel.

Similar experiments were performed using ammonium acetate (at 150°). The rate of formation of acetamide was the same, with and without the gel.

¹⁸ Reid, *Am. Chem. J.*, **44**, 76 (1910).

A solution of 100 g. of ammonium carbonate in 200 cc. of glacial acetic acid was divided into two equal portions, 5 g. of activated silica gel being added to one of them. These were refluxed side by side and at suitable intervals exact portions drawn off from each and analyzed. The rate of formation of amide was the same in both cases.

Summary

The formation of nitriles from acid or ester vapors mixed with an excess of ammonia in the presence of silica gel has been studied.

From the acids the following yields were obtained: methyl cyanide, 95%; ethyl cyanide, 85%; *n*-propyl cyanide, 90%; *n*-butyl cyanide, 80%; isobutyl cyanide, 94%; *n*-pentyl cyanide, 90%; *n*-hexyl cyanide, 93%; *n*-undecyl cyanide, 55%; benzyl cyanide, 87%; phenylethyl cyanide, 81%. No cyanide was obtained from palmitic acid.

From the esters the following yields were obtained: methyl cyanide, 87%; *n*-propyl cyanide, 75%; phenyl cyanide, 77%.

The life of the catalyst is long in the case of the acids and short in the case of the esters.

The optimum operating temperature for the reaction is 500°.

The catalyst is only active in dehydrating amides, and is not effective in the establishment of the ammonia-acid, amide-water equilibrium.

Silica gel is by far the best catalyst for the reaction that has, as yet, been studied.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

THE DECOMPOSITION OF KETONES IN THE PRESENCE OF SILICA GEL

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RECEIVED NOVEMBER 14, 1930

PUBLISHED JANUARY 12, 1931

The decomposition of ketones in the presence of various dehydrating catalysts has been rather widely studied. Acetone has received the most attention, the condensation products being particularly well investigated.

Acetone kept for a long time over lime or aluminum chloride is transformed into mesityl oxide and phorone.¹ By passing acetone vapors over catalysts heated at a suitable temperature, thoria and alumina usually being employed, mesityl oxide, phorone, etc., have been obtained.² Ipatiew

¹ Sabatier-Reid, "Catalysis in Organic Chemistry," D. Van Nostrand Co., New York, 1923, p. 287.

² (a) Fittig, *Ann.*, **110**, 23 (1859); (b) Bellstein and Reith, *ibid.*, **126**, 245 (1863); (c) Paulow, *ibid.*, **188**, 128 (1877); (d) Louise, *Bull. soc. chim.*, [2] **39**, 522 (1883); (e) Senderens, *ibid.*, [4] **3**, 824 (1908); *Compt. rend.*, **146**, 1212 (1908); (f) Mallhe and de Godon, *Bull. soc. chim.*, [4] **21**, 63 (1917).