is seen to esterify slower and to reach a lower limit than the primary, as has been found to be the case with alcohols.

The stability of the esters, as was shown by the work of Pratt and Reid, decreases with increasing melocular weight and it was found that in nearly all the tubes there were at least traces of hydrogen sulfide after heating to 200°. The decomposition of the esters seems to take place more readily when little water is present and to give rise to the formation of an acid, since in tubes where there is an excess of ester over water the amount saponified as determined by titration goes below the limit.

It is also seen that the percentage saponification varies greatly with the relative amounts of water present, relatively less saponification taking place in cases with relatively large amounts of water. This is no doubt due to the immiscibility of the ester and water at the temperature employed.

Conclusions.

1. The rates and limits of esterification of benzoic acid by isomeric butyl mercaptans have been studied and the limits determined at 200°.
2. The rates and limits for normal and iso-mercaptans were found to be nearly the same, but those for the secondary mercaptan much lower.
3. The limits found were much lower than those for the corresponding alcohols.
4. The saponification of the esters was found to be very irregular and unreliable on account of the immiscibility of the ester and water and the decomposition of the esters.
5. The limits were fouud to be independent of the relative amounts of acid and mercaptan present.

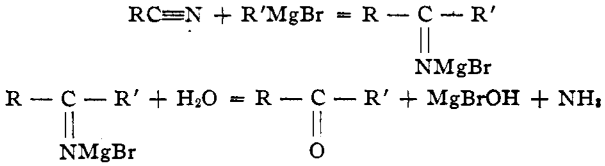
BALTIMORE, MD.

ACTION OF THE GRIGNARD REAGENT ON CN COMPOUNDS. SYNTHESIS OF AMIDINES FROM CYANAMIDES.

BY ROGER ADAMS AND C. H. BEEBE.

Received August 26, 1916.

Although the reactions of the Grignard reagent with different types of carbonyl containing compounds have been carefully and exhaustively studied, the same cannot be said concerning the reactions of the Grignard reagent with organic substances containing the cyan radical —C≡N. Blaise[1] treated cyanogen and certain aliphatic and aromatic nitriles with alkyl and aryl magnesium halides, and found he obtained ketones according to the following equations:



$$RC\equiv N + R'MgBr = R-\underset{\underset{NMgBr}{\|}}{C}-R'$$

$$R-\underset{\underset{NMgBr}{\|}}{C}-R' + H_2O = R-\underset{\underset{O}{\|}}{C}-R' + MgBrOH + NH_3$$

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[1] *Compt. rend.*, 132, 38 (1901); 133, 1217 (1901).

In only a very few instances, however, were good yields obtained. Somewhat later Gautier[1] applied this same reaction to cyanhydrines and alkoxy-nitriles, and produced in each case the corresponding ketones.

Grignard[2] allowed a molecule of alkyl or aryl magnesium halide to drop into a molecule of chlorocyan, and was able to obtain fair yields of nitriles, as follows:

$$RMgBr + ClCN = RCN + MgBrCl$$

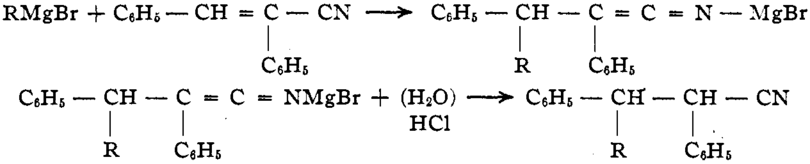
The bromocyan and iodocyan, however, yielded chiefly alkyl or aryl halides

$$RMgBr + ICN = RI + MgBrCN.$$

By the same method of procedure with cyanogen, Grignard[3] was able to produce nitriles instead of ketones, which Blaise obtained when he treated the Grignard reagent with cyanogen.

$$RMgBr + CNCN = RCN + MgBrCN.$$

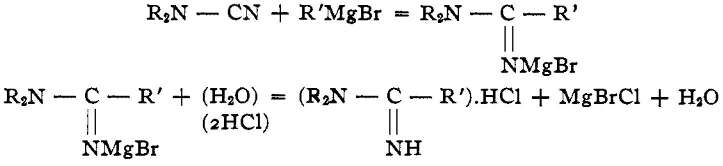
Kohler[4] tried the action of alkyl and aryl magnesium halides on α,β-unsaturated nitriles; 1,4-addition took place, and saturated nitriles were subsequently formed.



$$RMgBr + C_6H_5-CH=\underset{\underset{C_6H_5}{|}}{C}-CN \longrightarrow C_6H_5-\underset{\underset{R}{|}}{CH}-\underset{\underset{C_6H_5}{|}}{C}=C=N-MgBr$$

$$C_6H_5-\underset{\underset{R}{|}}{CH}-\underset{\underset{C_6H_5}{|}}{C}=C=NMgBr + \underset{HCl}{(H_2O)} \longrightarrow C_6H_5-\underset{\underset{R}{|}}{CH}-\underset{\underset{C_6H_5}{|}}{CH}-CN$$

Several other types of organic substances exist holding a —CN group and these have not been studied; thus cyanamides and their substitution products NH_2CN, $NHRCN$, or NR_2CN, acid nitriles $R-\underset{\underset{O}{\|}}{C}-CN$, and finally the esters of cyanic and thiocyanic acid ROCN, RSCN. It seemed to us of scientific interest to know how these substances react with the Grignard reagent, and at the same time it was possible that certain useful synthetic processes might be discovered. As yet we have studied simply the reactions of dibenzyl cyanamide. They ran, as might be predicted, to give first a magnesium halide addition compound, which on decomposition with dilute acid, yielded the salts of substituted amidines.



$$R_2N-CN + R'MgBr = R_2N-\underset{\underset{NMgBr}{\|}}{C}-R'$$

$$R_2N-\underset{\underset{NMgBr}{\|}}{C}-R' + \underset{(2HCl)}{(H_2O)} = (R_2N-\underset{\underset{NH}{\|}}{C}-R').HCl + MgBrCl + H_2O$$

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[1] *Compt. rend.*, **152**, 1100, 1259; *Ann. chim. phys.*, [8] **16**, 289 (1909).

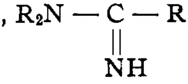
[2] *Ibid.*, **152**, 388 (1910); *Ann. chim.*, [9] **4**, 28 (1915).

[3] *Compt. rend.*, **155**, 44 (1912).

[4] *Am. Chem. J.*, **35**, 386 (1905).

In the laboratory, we treated in ether solution ethyl, phenyl, and tolyl magnesium halides with dibenzyl cyanamide. In each case, when we acidified the reaction mixture, white solids separated between the ether and dilute acid. The substances proved to be the amidine salts, and corresponded in amount to 75% or more of the theoretical yield. Some difficulty was experienced, however, in the purification of these salts for analysis, as they were soluble only in alcohol, water or dilute hydrochloric acid and tended to turn colored during crystallization. In the case of the tolyl we had so much trouble in getting the salt pure enough for analysis that we found it advisable to decompose the salt with sodium hydroxide, extract the free amidine with ether, and treat with phenyl isocyanate, in order to form the urea derivative which crystallized very nicely and was readily purified. The amidines themselves are not easy substances to work with, as most of them are oils or low melting, very soluble solids. Therefore, only in one case, the phenyl dibenzyl amidine, have we isolated and purified the free compound.

Another difficulty which we have just found when using dimethyl cyanamide, and which may be true in other cases, is that the amidine salt is very soluble in water or dilute acid, and so does not separate on acidification of the reaction mixture. This reaction we are studying further, as well as the action of alkyl and aryl magnesium halides on other disubstituted cyanamides, monosubstituted cyanamides, and on cyanamide itself. We expect to study also the action of the Grignard reagent on acid cyanamides, and on the esters of cyanic and thiocyanic acids.

Heretofore substituted amidines and their salts belonging to the type just described, namely,  $R_2N - \underset{\underset{NH}{\|}}{C} - R$, have been prepared by one method only, the action of secondary amines on imido-ethers, the other methods available for the amidines in general not being applicable to this particular type of substitution product.

$$R' - C \begin{smallmatrix} = NH \\ - OC_2H_5 \end{smallmatrix} + R_2NH = R' - C \begin{smallmatrix} = NH \\ - NR_2 \end{smallmatrix} + C_2H_5OH.$$

Experimental.

Dibenzylpropionamidine Hydrochloride, $(C_6H_5CH_2)_2NC(NH)C_2H_5HCl$.—Dissolve 2 g. of magnesium in 10 g. of ethyl bromide and dry ether. Cool in ice and allow a dry ether solution of 12 g. of dibenzylcyanamide[1] to flow in drop by drop. The mixture becomes milky in appearance, and solid matter separates. Decompose this directly with hydrochloric acid and ice, thus producing a yellowish solid which floats between the ether and water layers. This, when filtered and dried, weighs 15 g. The ether layer holds a small amount of unchanged dibenzylcyanamide, and

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[1] Prepared according to the directions of Diels and Gollmann, *Ber.*, 44, 3164 (1911).

the acid layer nothing but magnesium salts. The solid obtained is soluble in alcohol and acetone, but does not crystallize well from either. From water alone or from water containing a little alcohol, the material forms beautiful rhombohedral crystals, but the yellow color does not disappear, and the m. p. in four recrystallizations does not become constant. Dilute hydrochloric acid and a little alcohol is the best combination, thus it is possible to obtain a constant melting point of 204–204.5°. During the crystallization, a very small amount of a second substance, less soluble than the main product and crystallizing in long, fibrous, white needles, is generally obtained, but this was not investigated further.

Calc. for $C_{17}H_{11}N_2Cl$: N, 9.69%; Cl, 12.29%. Found: N, 9.65, 9.63; Cl, 12.76, 13.06.

Dibenzylbenzamidine Hydrochloride, $(C_6H_5CH_2)_2NC(NH)C_6H_5HCl$.—Prepare phenyl magnesium bromide from 15 g. of magnesium, 10.2 g. of phenyl bromide and dry ether. Cool with ice and allow 13.9 g. of dibenzylcyanamide in dry ether to drop slowly in. Treat the mixture with ice and hydrochloric acid, and a solid separates between the ether and acid layers. The material on filtering and drying weighs 14 g. Trituration with ether before crystallization served to remove most of the yellowish impurity. The hydrochloride is soluble in acetone, alcohol and chloroform, but on evaporation deposits a glassy mass. The best solvent proved to be a 5% hydrochloric acid containing a little alcohol when large rhombohedra form with a m. p. 211.5°.

Calc. for $C_{21}H_{11}N_2Cl$: N, 8.35%; Cl, 10.57%. Found: I, N, 8.52, 8.24; Cl, 10.26, 10.38, 10.66.

Dibenzylbenzamidine, $(C_6H_5CH_2)_2NC(NH)C_6H_5$.—Grind crystals of dibenzylbenzamidine hydrochloride to a fine powder, make it into a paste with water, and add strong ammonium hydroxide until excess is present. The solid material changes its appearance under this treatment, and forms pasty-like bunches. Extract with ether. This extract holds all the solid, and after drying it with anhydrous calcium chloride and spontaneous evaporation, a transparent, sticky material deposits which gradually solidifies to hard, white nodules. Yield quantitative. This substance is very soluble in water and all the ordinary organic solvents, and so difficult to purify. From ether it was possible to obtain a constant melting point of 70–71°.

Calc. for $C_{21}H_{20}N_2$: N, 9.3%; C, 84.0%; H, 6.66%. Found: N, 9.2; C, 83.3, 84.8; H, 5.6, 7.27.

Dibenzyltoluenylamidine Hydrochloride, $(C_6H_5CH_2)_2NC(NH)C_6H_4$-$CH_3(p)$.HCl.—Treat the Grignard reagent made from 2.1 g. magnesium, 14.5 g. of *p*-bromotoluene and dry ether, after cooling, with 10 g. of dibenzylcyanamide dissolved in ether. Allow the mixture to stand at room temperature a few hours, then decompose with ice and hydrochloric acid. Filter and dry the solid which separates between the ether and acid layers. A quantitative yield results. This substance proved a very difficult one to purify. Although we tried different combinations of hydrochloric acid, alcohol and water, we were unable to remove the small amount of yellowish impurity, and the analyses for chlorine did not give constant values. We found it advisable, therefore, to make the free amidine and then the phenyl isocyanate derivative.

Dibenzyltoluenylamidinemonophenyl Ureide, $(C_6H_5CH_2)_2NC(NCONHC_6H_5)C_6H_4CH_3(p)$.—Moisten 3 g. of the amidine hydrochloride with water and add a slight excess of concentrated potassium hydroxide solution. Extract with ether, and dry the solution obtained with calcium chloride. On evaporation the free amidine, a yellowish crystalline solid melting at about 80°, and very soluble in all organic solvents, results. Dissolve a known weight of this material in absolute alcohol, and add the theoretical amount of phenyl isocyanate. On evaporation of this solution, fine white needles in a quantitative yield deposit, which crystallize very readily from alcohol to a constant melting point of 158°.

Calc. for $C_{29}H_{27}N_3$: N, 10.0%; C, 80.36%; H, 6.23%. Found: N, 9.75; C, 80.38; H, 6.56.

CAMBRIDGE, MASS.

ON THE SULFONPHTHALEIN SERIES OF INDICATORS AND THE QUINONE-PHENOLATE THEORY.[1]

BY H. A. LUBS AND S. F. ACREE.

Received June 15, 1916.

In developing a method for the colorimetric determination of the hydrogen-ion concentration of bacteriological cultures and culture media, one of us and Clark[2] found that many of the available indicators were unsatisfactory for reasons previously described. On this account a number of new indicators of the methyl red and sulfonphthalein types were synthesized. The phenolsulfonphthaleins had appeared especially promising from the work of White[3] and one of us on this group, not only because the compounds show brilliant color changes but also because their chemical constitution is of such a nature that the substitution of suitable groups should cause their affinity constants to vary to almost any desired degree and give a series of indicators which can be used to measure a wide range of hydrogen-ion concentrations; furthermore, the new compounds ob-

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[1] Published by permission of the Secretary of Agriculture as a joint article from the Research Laboratories of the Dairy Division, Bureau of Animal Industry, United States Department of Agriculture, Washington, D. C., and the Forest Products Laboratory, Madison, Wisconsin.

[2] Lubs and Clark, *J. Wash. Acad. Sci.*, **5**, 609.

[3] *Science*, **42**, 101; address at New Orleans Meeting of Am. Chem. Soc., and unpublished dissertation, 1915, Univ. of Wisconsin.