fractions were collected, all of essentially the same density, but increasing in refractive index as b.p. rose. A fraction (no. 8) boiling at 185–187° (40 mm.) was representative of the majority of the distillate; $d^{20}{}_4$ 1.0365; n^{20}D 1.5356; ΣMR 55.21; MR calcd. 57.20.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.73; H, 7.42. Found: C, 75.95; H, 7.43.

The material reacted with semicarbazide hydrochloride to form a semicarbazone which, after two recrystallizations from dilute alcohol, melted at 151–152°.

Anal. Calcd. for $C_{13}H_{17}N_3O_2$ (semicarbazone of 4-methyl-1-phenoxy-4(or 3)-penten-2-one): C, 63.14; H, 6.93; N, 16.99. Found: C, 63.41; H, 7.05; N, 17.36.

Fraction No. 3 had $d^{20}{}_4$ 1.0391; n^{20}D 1.5187; ΣMR 55.21; MR calcd. 55.66; but b.p. 120–132° (40 mm.).

Interaction of β-(2-Ethoxyethoxy)-propionitrile with Allylmagnesium Bromide.—The Grignard reagent was prepared from 121 g. (1 mole) of allyl bromide and 73 g. (3 gram-atoms) of magnesium under 770 ml. of anhydrous ether. The excess magnesium was removed by rapid filtration through a Buchner funnel, and the filtrate was treated with 106 g. (0.5 mole) of β-(2-ethoxyethoxy)-propionitrile[21] in 750 ml. of dry ether. The mixture was stirred during 24 hours and then was hydrolyzed with ice and water. The ether layer was extracted with two 300-ml. portions of 3%

(21) H. A. Bruson, U. S. Patent 2,280,792; through *C. A.*, **36**, 5590 (1942).

hydrochloric acid. These extracts were made alkaline with 10% sodium hydroxide solution and extracted with ether. The ether extracts of[13] acid-soluble and of acid-insoluble materials were separately dried over anhydrous sodium sulfate. Concentration of the acid-insoluble extract yielded 35 g. of orange-red resinous material. Distillation of the acid-soluble extract produced 14 g. (12% yield) of amine boiling at 117–120° (3 mm.); $d^{20}{}_4$ 0.9220; n^{20}D 1.4649; ΣMR 68.02; MR calcd. 68.15.

Anal. Calcd. for $C_{13}H_{25}NO_2$: C, 68.83; H, 11.08. Found: C, 68.15; H, 11.10.

Although this product, 1-allyl-1-[2-(2-ethoxyethoxy)-ethyl]-3-butenylamine, reacted readily with acetic anhydride, benzoyl chloride and picric acid, no crystalline product resulted.

Seven grams of this substituted butenylamine was dissolved in 50 ml. of absolute alcohol and shaken under an atmosphere of hydrogen with 0.1 g. of reduced Adams catalyst. After filtration from the catalyst, the solvent was removed and the product fractionated; 4 g.; b.p. 114–115° (1 mm.); $d^{20}{}_4$ 0.8937; n^{20}D 1.4450; ΣMR 68.96; MR calcd. 69.13.

Anal. Calcd. for $C_{13}H_{29}NO_2$: C, 67.48; H, 12.63. Found: C, 66.73; H, 12.94.

Although this carbinamine, 1-[2-(2-ethoxyethoxy)-ethyl]-1-propylbutylamine, reacted readily with picric acid, the product did not solidify.

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The Interaction of Certain Grignard Reagents with Cinnamonitrile[1]

By Henry R. Henze and Leo R. Swett

Cinnamonitrile reacted readily with ethylmagnesium bromide, benzylmagnesium chloride, allylmagnesium bromide and phenylmagnesium bromide, respectively; the subsequent behavior of each adduct upon hydrolysis established the fact that these addition products resulted from 1,2-addition to the nitrile group. However, the hydrolysis products varied according to the specific agent used. Thus, upon hydrolysis of the adducts derived from the ethyl, benzyl and phenyl reagents by means of dilute hydrochloric acid, the corresponding styryl ketones were obtained. But when an ice-cold solution of ammonium chloride was used for hydrolysis, nitrogenous products, having the analytical compositions corresponding to ketimines, resulted. However, molecular weight determinations established these products to be dimers, in this respect confirming the very recent findings of Piper and Wright. Depending upon the ratio in which allylmagnesium bromide reacted with cinnamonitrile, the product was either a ketine dimer or a carbinamine.

It is well established that alkyl- or arylmagnesium halides react with nitriles in a 1:1 molecular ratio to yield addition products; the latter are ketimine derivatives. Although hydrolysis, especially by means of acids, usually yields ketones, occasionally hydrolysis produces ketimines sufficiently stable to permit of their isolation.

In 1939, there was reported[2] the first instance in which two equivalents of a Grignard reagent added to one of an alkoxynitrile, subsequent hydrolysis of the adduct yielded a tertiary alkyl primary amine (termed a carbinamine) of the type $ROCH_2$-$(CH_2{=}CHCH_2)_2C$—NH_2. Later studies have shown that this behavior is characteristic of nitriles in general. Allylmagnesium bromide also reacts with the addition product resulting from interaction of an alkylmagnesium halide and a nitrile; here, too, hydrolysis of this adduct yields a carbinamine. This greater activity of the unsaturated Grignard reagent has been shown also by methallylmagnesium chloride[3]; however, in this case, upon hydrolysis of the adduct, some

isomeric, unsaturated ketones were isolated in addition to a carbinamine.

Some attention had previously been paid elsewhere to the interaction of Grignard reagents and *unsaturated* nitriles.[4] Since the latter may contain conjugated double-bond systems, 1,4-addition, as well as 1,2-addition to the nitrile is conceivable. The 1,4-addition in 1:1 ratio of reactants, might be expected to produce an adduct from which, upon hydrolysis, a saturated nitrile would result

$$RCH{=}CH—C{\equiv}N + R'MgX \longrightarrow$$
$$RR'CH—CH{=}C{=}N—MgX \longrightarrow$$
$$RR'CH—CH{=}C{=}NH \rightleftarrows RR'CHCH_2CN$$
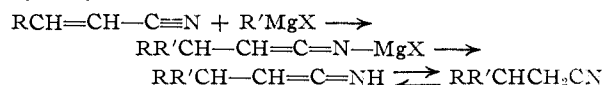
Thus, Kohler[5] observed that although cinnamonitrile and methylmagnesium iodide interacted through 1,2-addition and ultimately yielded benzalacetone, α-phenylcinnamonitrile reacted with ethylmagnesium bromide as a result of 1,4-addition to produce β-ethyl-α-phenylhydrocinnamonitrile. However, in the interaction of α-phenylcinnamonitrile and phenylmagnesium bromide, both ω-

(1) Abstracted from the M.A. thesis of Leo R. Swett, January, 1950.

(2) Allen and Henze, This Journal, **61**, 1790 (1939).

(3) Henze, Sutherland and Edwards, *ibid.*, **73**, 4915 (1951).

(4) Runge, "Die organische Synthese mit Hilfe von Organometall-verbindungen," Wissenschaftliche Verlagsgesellschaft m. b. H., Stuttgart, 1944, pp. 431–432.

(5) Kohler, *Am. Chem. J.*, **35**, 386 (1905).

benzalacetophenone (because of 1,2-addition) and α,β-diphenylhydrocinnamonitrile (due to 1,4-addition) were obtained.

From such scanty data, it is not possible to predict with confidence and accuracy what will be the products of hydrolysis of the adducts produced by interaction of unsaturated nitriles and Grignard reagents. This is particularly true if allylmagnesium bromide is involved. Hence, the behavior has been investigated of alkyl-, aryl-, aralkyl- and alkenylmagnesium halides on a nitrile possessing conjugated unsaturation, namely, cinnamonitrile.

Cinnamonitrile was treated, in turn, with an excess of an ethyl-, benzyl- or phenylmagnesium halide to form adducts. When the latter were hydrolyzed by treatment with dilute **hydrochloric acid, styryl ketones resulted** indicating that the adduct had been formed as a result of 1,2-addition to the nitrile group. The ketones were converted into the corresponding 5-styryl-5-substituted-hydantoins. However, the adduct from interaction of cinnamonitrile and *excess* of allylmagnesium bromide upon hydrolysis with acid yielded diallylstyrylcarbinamine.

Hydrolysis of the first three adducts by means of saturated **ammonium chloride solution produced nitrogenous compounds,** rather than the styryl ketones. It was to be anticipated that these compounds were ketimines, and this assumption was supported by the analytical composition of these products. However, the nitrogenous compounds could not be converted into ketones, even upon treatment with concd. hydrochloric acid.

About this time, Piper and Wright[6] reported the results of their similar study involving interaction of phenylmagnesium bromide and "styryl cyanide" (cinnamonitrile). They had demonstrated that the adduct yielded on hydrolysis with ammonium chloride solution, a ketimine **dimer**; to the latter was assigned the structure of a bridged pyrimidine. A molecular weight determination for our supposed ketimine confirmed its dimeric composition. Likewise, the melting point of the dimer, and that of the product into which it is converted by treatment with hydrochloric acid, agreed exactly with those recorded by Piper and Wright.[7]

It was of immediate interest to determine the molecular weight of the nitrogenous products resulting from the hydrolysis of the 1:1 addition products of the ethyl-, benzyl- and allylmagnesium halides. These compounds, too, appear to be dimeric. However, these alkyl, aralkyl and alkenyl derivatives are insoluble in and stable toward concd. hydrochloric acid, being in this respect wholly unlike the phenyl ketimine dimer which Piper and Wright[6] have shown to be converted by such treatment into 3-benzoyl-2,4,6-triphenyl-2,3,4,5-tetrahydropyridine. A comparison of the ultraviolet absorption spectra of the four dimeric

(6) Piper and Wright, 116th Meeting of the American Chemical Society, September, 1949; subsequently published in THIS JOURNAL, **72**, 1669 (1950).

(7) Professor George F. Wright, Department of Chemistry, University of Toronto, made available a copy of this paper to us. The writers wish to express their appreciation of his courtesy and their indebtedness for a knowledge of the data and experimental details included in their earlier investigation.

compounds, Fig. 1, reveals a high degree of similarity between the ethyl, benzyl and allyl derivatives, but seems to indicate a definite difference in structure of these three from that of the tetraphenyl derivative. Nevertheless, an "active hydrogen" determination on the ethyl styryl ketimine dimer showed that there was one "active hydrogen" present in this compound, which in this respect is thus similar to the phenyl dimer.
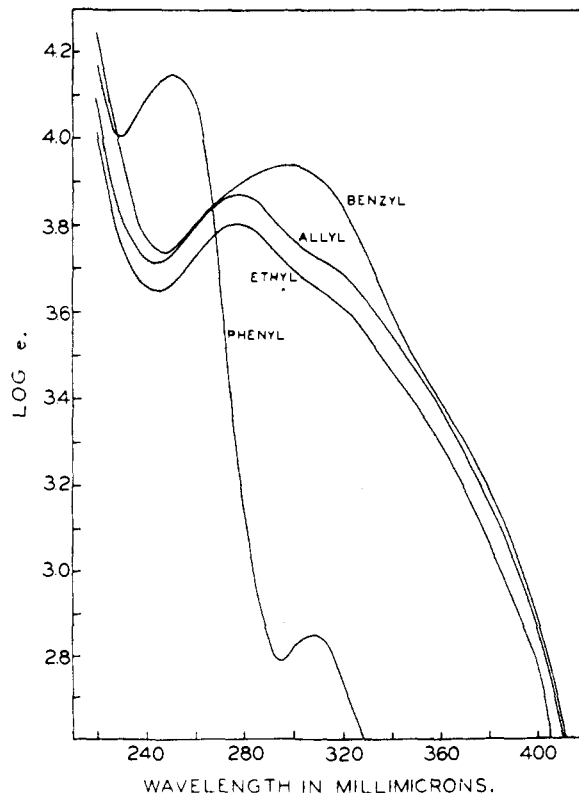

WAVELENGTH IN MILLIMICRONS.

Fig. 1.

Experimental

Interaction of Grignard Reagents with Cinnamonitrile.— A dilute solution of the ethyl-, benzyl, phenyl- or allylmagnesium halide in absolute ether was prepared and added usually to one-fourth mole-equivalent of cinnamonitrile in six volumes of dry ether. The adducts were hydrolyzed by being poured into a mixture of cracked ice and a concd. solution of ammonium chloride. The layers were separated, the ether extract dried over anhydrous sodium sulfate, and saturated with dry hydrogen chloride causing immediate precipitation of the hydrochloride salt. The latter was purified by crystallization from a chloroform–ether mixture. Concentrated ammonium hydroxide was added to liberate the base from the hydrochloride; the ketimine dimer was crystallized from a benzene–petroleum ether mixture.

A.—From 0.4 mole of ethylmagnesium bromide and 0.1 mole of cinnamonitrile was obtained 14.2 g. (72.8% yield) of **ethyl styryl ketimine dimer hydrochloride**, m.p. 148–150°.

Anal. Calcd. for $C_{22}H_{26}N_2 \cdot 2HCl$: mol. wt., 391.3; C, 67.51; H, 7.21; N, 7.16. Found: mol. wt. (ebullioscopic in ethanol), 383; C, 67.68; H, 7.30; N, 7.11.

The dihydrochloride yielded 11.3 g. (98%) of **ethyl styryl ketimine dimer** as a pale yellow powder; m.p. 98–99° (dec.).

Anal. Calcd. for $C_{22}H_{28}N_2$: mol. wt., 318.4; C, 82.97; H, 8.22; N, 8.79. Found: mol. wt. (ebullioscopic in acetone), 320; C, 82.65; H, 8.01; N, 8.61.

The dimer could be recovered unchanged from treatment with cold, concd. hydrochloric acid for three to four hours. "Active hydrogen" determination, using a half-mole excess

of methylmagnesium iodide, showed the presence of one "active hydrogen" per molecule.

Another portion of the ethylmagnesium bromide–cinnamonitrile adduct was hydrolyzed with cold, dilute hydrochloric acid to give the known ethyl styryl ketone,[8] melting at 38–39°.

B.—To prepare this ketimine, 0.4 mole of phenylmagnesium bromide and 0.1 mole of cinnamonitrile was used. The product of hydrolysis of the adduct with ammonium chloride solution was a brown, sticky mass; an ethanol solution of the latter, after standing for several days, deposited pale brown crystalline material weighing 7.3 g. (36% yield) of **phenyl styryl ketimine dimer**; m.p. 179–180°. Recrystallization from ether gave a white crystalline product melting at 183–184° (dec.).[9]

Anal. Calcd. for $C_{30}H_{26}N_2$: mol. wt., 414.5; C, 86.92; H, 6.32; N, 6.76. Found: mol. wt. (ebullioscopic in acetone), 428; C, 86.86; H, 6.25; N, 6.80.

The ketimine dimer formed a picrate melting at 175–176°.

Anal. Calcd. for $C_{36}H_{29}N_5O_4$: N, 10.88. Found: N, 10.97.

The ketimine dimer in ether formed a very hygroscopic hydrochloride melting at 85–89°. The dimer was treated with concd. hydrochloric acid and, after stirring for approximately one hour, a white precipitate was formed. This material was removed, dissolved in methanol, and treated with a calculated quantity of sodium methoxide. Again, white crystalline material separated and was recrystallized from ethanol to melt at 156–158°.[6]

Another portion of this adduct between phenylmagnesium bromide and cinnamonitrile was hydrolyzed with dilute hydrochloric acid to yield the known **phenyl styryl ketone**[10] melting at 56°.

C.—To prepare the benzyl analog, 0.8 mole of benzylmagnesium chloride and 0.2 mole of cinnamonitrile yielded an adduct which, subsequently, was hydrolyzed with ammonium chloride solution to produce 41.7 g. (81% yield) of the dihydrochloride, a yellow powder melting at 145–146° (dec.).

Anal. Calcd. for $C_{32}H_{30}N_2 \cdot 2HCl$: mol. wt., 515.5; C, 74.17; H, 6.25; N, 5.43. Found: mol. wt. (ebullioscopic in ethanol), 530; C, 74.28; H, 6.23; N, 5.51.

Neutralization of this salt with ammonium hydroxide liberated **benzyl styryl ketimine dimer**, which, after recrystallization from benzene–petroleum ether, gave 34.5 g. (95% yield) of a yellow powder melting at 105–106° (dec.).

Anal. Calcd. for $C_{32}H_{30}N_2$: mol. wt., 442.6; C, 86.84; H, 6.83; N, 6.33. Found: mol. wt. (ebullioscopic in acetone), 451; C, 86.62; H, 6.69; N, 6.28.

This dimer was recovered unchanged upon treatment with cold, concd. hydrochloric acid for three to four hours.

A portion of the adduct formed from benzylmagnesium chloride and cinnamonitrile was hydrolyzed with dilute hydrochloric acid to give the known **benzyl styryl ketone**,[11] melting at 71°.

D_1.—In this experiment, 12.9 g. (0.1 mole) of cinnamonitrile was added to 0.1 mole of allylmagnesium bromide to form an adduct that, after hydrolysis with ammonium chloride solution, yielded an ether extract from which dry hydrogen chloride precipitated a dihydrochloride; 18.2 g., 88% yield; m.p. 172–173° (dec.).

Anal. Calcd. for $C_{24}H_{28}N_2 \cdot 2HCl$: mol. wt., 417.4; C, 69.39; H, 6.79; N, 6.74. Found: mol. wt. (ebullioscopic in ethanol), 420; C, 69.71; H, 6.73; N, 6.82.

Neutralization of this dihydrochloride liberated **allyl styryl ketimine dimer**; 14.5 g. (96% yield); m.p. 135–136°.

Anal. Calcd. for $C_{24}H_{26}N_2$: mol. wt., 344.5; C, 84.17; H, 7.65; N, 8.18. Found: mol. wt. (ebullioscopic in acetone), 340; C, 84.02; H, 7.55; N, 8.10.

This ketimine dimer was recovered unchanged upon treatment with cold, concd. hydrochloric acid for three to four hours.

D_2.—In another experiment, 25.9 g. (0.2 mole) of cinna-

monitrile was added to 0.8 mole of allylmagnesium bromide to give an addition product which was hydrolyzed with ammonium chloride solution; the ether layer was dried and saturated with hydrogen chloride to precipitate 42.3 g. (85% yield) of a very pale brown hydrochloride of the carbinamine; m.p. 95–97°.

Anal. Calcd. for $C_{15}H_{19}N \cdot HCl$: C, 72.12; H, 8.07; N, 5.61. Found: C, 72.18; H, 8.13; N, 5.70.

Freed from its hydrochloride, **diallylstyrylcarbinamine** formed as a pale yellow liquid, which distilled at 138–139° (5 mm.); $n^{25}D$ 1.5408; d^{25}_4 0.9566; MR 70.05, MR calcd. 69.89.

Anal. Calcd. for $C_{15}H_{19}N$: C, 84.44; H, 8.97. Found: C, 84.45; H, 8.88.

Confirmation of Identity of the Styryl Ketones through Hydantoin Formation (A).—A mixture of 16 g. of ethyl styryl ketone, 8.8 g. of potassium cyanide and 29 g. of ammonium carbonate in 80 ml. of alcohol and 56 ml. of water was warmed for 24 hours at 60°. After concentration to one-half volume, acidification caused precipitation of a brown, solid mass. Treatment with 5% sodium hydroxide solution left some unreacted ketone; the hydantoin was reprecipitated upon acidification. Ten grams of crude material, melting at 210–211°, was obtained. After recrystallization from diluted alcohol, the hydantoin[12] weighed 9.5 g. (41.3% yield) and melted at 213°.

Anal. Calcd. for $C_{13}H_{14}N_2O_2$: C, 67.82; H, 6.12; N, 12.16. Found: C, 68.09; H, 6.23; N, 12.11.

B.—Sixteen grams of benzyl styryl ketone, 8 g. of potassium cyanide, 25.8 g. of ammonium carbonate and 195 ml. of 50% alcohol were heated for 24 hours at 60°. The yield of crude product, melting at 205–206°, was 13 g. After recrystallization from diluted alcohol, there remained 12.6 g. (59.9% yield), of **5-benzyl-5-styrylhydantoin**, m.p. 211°.

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.51; N, 9.58. Found: C, 73.82; H, 5.50; N, 9.43.

C_1.—In this attempt, 10.4 g. of phenyl styryl ketone, 3.5 g. of potassium cyanide and 14.4 g. of ammonium carbonate were dissolved in 80% alcohol and heated for 24 hours at 60°. The mixture was purple-colored; upon acidification, there formed a bluish-green precipitate. The latter was insoluble in 5% sodium hydroxide solution, so was crystallized from diluted alcohol to leave 8 g. of fluffy, white crystals melting at 124–125°.

Anal. Calcd. for (anticipated hydantoin) $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.06; calcd. for (ketone cyanohydrin) $C_{16}H_{13}NO$: C, 81.60; H, 5.52; N, 5.91. Found: C, 82.04; H, 5.55; N, 6.03.

C_2.—A second attempt to obtain the hydantoin was made following the procedure of Henze and Long[13]; 100 g. of acetamide was fused and used to dissolve 10.4 g. of phenyl styryl ketone and 4.5 g. of potassium cyanide, then 14.4 g. of ammonium carbonate was added and the mixture was placed in a sealed container and the latter heated at 130° for 18 hours. The reaction mixture was poured onto 500 ml. of water and acidified, whereupon an orange solid separated. The solid was dissolved in 5% sodium hydroxide solution, the mixture was filtered to remove some unaltered ketone, and the filtrate acidified to reprecipitate the product which separated as 0.9 g. of amorphous solid; m.p. 180–185°. Further purification gave 0.75 g. (5.6% yield) of **5-phenyl-5-styrylhydantoin**, m.p. 189–190°.

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.06. Found: C, 73.28; H, 5.10; N, 10.15.

Study of Ultraviolet Absorption of the Ketimine Dimers.—All measurements of the absorption in the ultraviolet of solutions of the four ketimine dimers were made using a Beckmann quartz spectrophotometer, model DU, equipped with cells 1.006 cm. in width.

A comparison of the absorption spectra, in Fig. 1, of the ketimine dimers shows a high degree of similarity between the ethyl, benzyl and allyl compounds, but appears to indicate a fundamental difference in structure of three examples from that of the phenyl derivative.

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(8) Harries and Muller, *Ber.*, **35**, 968 (1902), reported m.p. 38–39°.

(9) Piper and Wright, ref. 6, using larger quantities of reactants, obtained in 40% yield material melting at 180–182° (out of ethanol).

(10) "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 78, records m.p. 55–57°.

(11) Knopfer, *Monatsh.*, **18**, 438 (1897), reported m.p. 71°.

(12) Henze and Long, THIS JOURNAL, **63**, 1941· (1941), reported m.p. 213–214° for 5-ethyl-5-styrylhydantoin.

(13) Henze and Long, *ibid.*, **63**, 1941 (1941).