

2,3,5,6-Tetraphenylbenzene-1,4-dicarboxylic Acid.—The reaction mixture was carbonated with gaseous carbon dioxide at 0°. After decomposition of the reaction mixture the acidic material was extracted with alkali and precipitated with dilute hydrochloric acid. The resulting solid was boiled with several portions of water to remove benzoic acid and finally crystallized from acetic acid. The acid formed tiny white needles which did not melt up to 320° (bloc Maquenne).

Anal. Calcd. for $C_{32}H_{20}O_4$: C, 81.70; H, 4.70; neut. equiv., 235. Found: C, 81.01; H, 4.71; neut. equiv., 232.

Methyl 2,3,5,6-Tetraphenylbenzene-1,4-dicarboxylate.—The acid was esterified with diazomethane in the usual way. The product crystallized from acetic acid as tiny white prisms, m. p. 280°.

Anal. Calcd. for $C_{34}H_{26}O_4$: C, 81.90; H, 5.40. Found: C, 81.50; H, 5.26.

Phenylmagnesium Iodide and Hexabromobenzene.—To the Grignard reagent prepared from 59.2 g. of iodobenzene and 7.05 g. of magnesium in ether was added 20 g. of

hexabromobenzene. After refluxing for twenty-four hours the reaction mixture was hydrolyzed with ice-hydrochloric acid and steam distilled. Extraction of the distillate with ether followed by distillation yielded 3.20 g. of bromobenzene, identified by its boiling point and by the preparation of *p*-nitrobromobenzene, m. p. 127–128°; mixed with an authentic sample, m. p. 126–128°. The residue from the steam distillation yielded 0.90 g. (7.9%) of 1,2,4,5-tetraphenylbenzene, m. p. 260–262°.

Summary

1. The reaction between hexabromobenzene and phenylmagnesium bromide has been reinvestigated, and the intermediate formation of 2,3,5,6-tetraphenylbenzene-1,4-dimagnesium bromide has been established.

2. An explanation of the course of the reaction has been suggested.

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RECEIVED MAY 5, 1939

[CONTRIBUTION NO. 160 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Tertiary Alkyl Primary Amines, $RR'R''CNH_2$. I. Ethoxymethyldiallylcarbinamine and Some Analogs^{1,2}

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There has been in progress in this Laboratory for some years an extensive study of substituted ketones of the alkoxy, aryloxy, and halogenoalkoxy alkyl (and aryl) types. Such ketones have been and are being synthesized from the appropriate substituted nitriles by means of Béhal and Sommelet's³ modification of the Grignard reaction; with the exception of the tertiary butyl analogs, relatively little difficulty has been experienced in obtaining, for almost every series, both the straight and branched chain alkyl derivatives through the amyls. Since these numerous ketones have been synthesized with the view to their further use in the preparation of compounds having physiological activity, it became desirable to have examples in which the alkoxy alkenyl grouping was represented. Hence, an attempt was made to prepare ethoxymethyl allyl ketone from ethoxyacetonitrile and allylmagnesium bromide.

It was noted with considerable surprise, then, that when equimolecular quantities of allylmagnesium bromide, prepared independently accord-

ing to Gilman,⁴ and ethoxyacetonitrile were brought together, apparently only one-half of the nitrile reacted, and although a constant boiling product was obtained, no ketonic material was formed. Moreover, this product, while possessing physical constants which made impossible its being unreacted nitrile, contained nitrogen, was basic in character, formed solid derivatives with such common amine reagents as picric acid and phenyl isocyanate, but failed to undergo the typical primary amine reaction of isonitrile formation. In a subsequent preparation it was found that by increasing the ratio of Grignard reagent to nitrile from 1:1 to 2:1 no unreacted nitrile was recovered and a correspondingly greater yield of basic product was formed.

Analyses of the purified, basic substance established $C_{10}H_{19}NO$ as its empirical formula. It was possible to conceive of the addition of two molecules of allylmagnesium bromide to one of ethoxyacetonitrile and of subsequent hydrolysis of the addition product to yield a compound of molecular formula $C_{10}H_{19}NO$. Analysis of the picrate of the basic compound obtained verified this formulation.

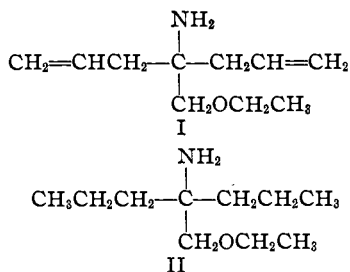
(1) Presented before the Division of Organic Chemistry at the 97th meeting of the American Chemical Society at Baltimore, Maryland, April 3–7, 1939.

(2) From the Ph. D. dissertation of B. B. Allen, June, 1938.

(3) Béhal and Sommelet, *Compt. rend.*, **138**, 89 (1904).

(4) Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1322 (1928).

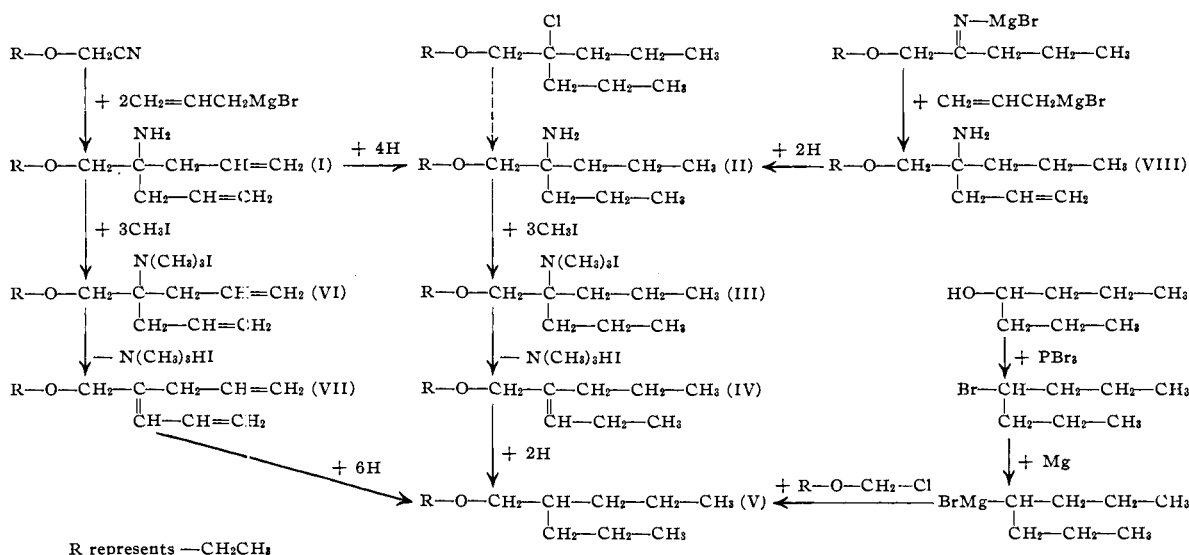
Although the structure visualized for the compound (I), one which was substantiated by molecu-



lar refraction values, required that the substance be a primary amine, actual proof that an amine of this class had been formed was not ob-

statement that "methods apparently are not available for the preparation in quantity of the aliphatic amines which bear the same relationship to primary amines that tertiary alcohols bear to primary alcohols."

The amino ether (I) was reduced with hydrogen catalytically to produce $\text{C}_{10}\text{H}_{23}\text{NO}$ (II); the introduction of four hydrogen atoms excluded the possibility of (I) having a ring structure. The methiodide of (II) was heated above its melting point to yield an unsaturated ether (IV) of the formula $\text{C}_{10}\text{H}_{20}\text{O}$, which was reduced to form the corresponding saturated ether (V) formulated as being 4-ethoxymethylheptane.



tained until the methiodide, prepared from (I) with ease and in good yield, was analyzed. The data from these analyses indicated that one molecular weight of the amine had reacted with three of methyl iodide; only primary amines react in this proportion. Final proof of the structure of the primary amino ether (I) was obtained through degradation and through conversion into a substance of established structure. Synthesis of the amino ether by known procedures was made highly improbable, and unsuccessful attempts to do so are recorded in the experimental portion of this report, since reference to the literature indicated that simpler amines of a type in which the primary amino group is attached to a tertiary aliphatic carbon have been prepared in a very limited number of cases and usually in poor yield. Recently Adkins⁵ has reported the attempt to synthesize an amine of this type and made the

Synthesis of (V) was visualized in the reaction of the Grignard reagent from 4-bromoheptane with chloromethyl ethyl ether. The physical properties and analytical data for the product resulting from such a reaction indicated it to be 4-ethoxymethylheptane and identical with (V). For the sake of completeness, the methiodide of (I) was decomposed in the formation of the corresponding ether containing three double linkages, and then this compound was hydrogenated to form (V). The physical constants for the three samples of 4-ethoxymethylheptane have been collected in Table I.

Additional proof of the structure of the amine (I) was obtained when equivalent amounts of allylmagnesium bromide and the addition product resulting from interaction of ethoxyacetonitrile and propylmagnesium bromide reacted to form compound (VIII), an amine of structure intermediate between that of (I) and (II) in that of the

(5) Smith and Adkins, *THIS JOURNAL*, **60**, 407 (1938).

TABLE I
PHYSICAL CONSTANTS AND ANALYTICAL DATA FOR 4-ETHOXYMETHYLHEPTANE

Prepared from	B. P.		d_{20}^4	n_D^{20}	n_D^{20}	γ_D^{20}	MR		Carbon, %		Hydrogen, %		
	°C.	Mm.					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
Methiodide of I	170-171	740	0.7884	1.4131	22.95	50.02	50.07	444.2	439.4	75.88	76.19	14.01	14.06
Methiodide of II	170-171	740	.7881	1.4139	22.95	50.02	50.13	444.2	439.6	75.88	75.71	14.01	13.90
(C ₂ H ₅) ₂ CHMgBr + C ₂ H ₅ OCH ₂ Cl	169.5-171	740	.7879	1.4129	22.89	50.02	50.08	444.2	439.4	75.88	75.96	14.01	14.12

TABLE II



CERTAIN PHYSICAL CONSTANTS AND ANALYTICAL DATA FOR AMINES DERIVED FROM ALLYLMAGNESIUM BROMIDE R-O-CH₂-C-NH₂

R	R'	R''	B. P. (corr.)	Mm.	Yield, %	d_{20}^4	n_D^{20}	γ_D^{20}	MR	Parachor	Carbon, %	Hydrogen, %	Nitrogen, %					
			°C.					dynes/cm.	Calcd.	Found	Calcd.	Found	Calcd.	Found				
Methyl	Allyl	Allyl	187.5-188.0	753	65.6	0.8829	1.4571	27.41	47.89	47.89	412.8	402.3	69.63	69.51	11.04	11.09	9.02	8.84
Ethyl	Allyl	Allyl	196.0-197.0	755	78.7	.8690	1.4526	28.37	52.51	52.60	451.8	449.5	70.96	70.55	11.32	11.41	8.28	8.26
Ethyl	Allyl	Propyl	197.0-198.0	753	60.7	.8580	1.4420	25.87	52.98	52.82	462.8	450.2	70.12	70.10	12.36	12.20	8.18	7.96
Ethyl	Propyl	Propyl	198	754	98.9	.8381	1.4304	24.85	53.45	53.45	473.8	461.6	69.31	69.24	13.38	13.41	8.08	7.96
<i>i</i> -Propyl	Allyl	Allyl	203.0-204.5	753	66.3	.8611	1.4490	26.70	57.13	57.10	490.8	483.9	72.07	72.04	11.55	11.45	7.64	7.46

groups attached to the tertiary carbon, one was propyl and another allyl. Hydrogenation of (VIII) resulted, as did reduction of (I), in the formation of (II).

Finally, the synthesis of the methoxy and isopropoxy analogs of (I) from allylmagnesium bromide and the appropriate nitriles proves definitely that this reaction is not confined to the formation of only one amine and requires qualification of the statement that there is no method for the preparation of quantities of primary amines in which the amino group is attached to a tertiary aliphatic carbon.

Experimental

Preparation of Alkoxyalkyl-dialkylcarbinamines.—In each instance wherein an amine was obtained from a nitrile and allylmagnesium bromide, the Grignard reagent was prepared independently, using essentially those proportions of magnesium, ether, and allyl bromide as suggested by Gilman⁴: to three gram atoms of magnesium turnings, suspended by very rapid stirring in 200 cc. of anhydrous ether, was added the solution of one mole of allyl bromide in approximately 570 cc. of dry ether, the addition being at such a rate that from five to six hours were required. Following the introduction of the last of the bromide, the mixture was stirred for an additional hour while the flask was warmed over a hot-plate. While still slightly warm, the gray-colored ether solution of the Grignard reagent was decanted rapidly from the flask into another of the same size through a 3-inch (8-cm.) Witte plate supported in a large funnel; the funnel, Witte plate, and second flask were at 35-40° so that a fairly rapid evaporation of the solvent would occur during the transfer and thereby tend to minimize contact between moist air and the reagent.

The resulting solution of allylmagnesium bromide was then treated with such an amount of the solution of the appropriate alkoxy nitrile⁶ as would represent a ratio of two parts of allylmagnesium bromide to one part of nitrile in an equal volume of dry ether; a considerable heat effect was noted during the nitrile addition; hence, the rate of this introduction was moderated until the solvent just refluxed. During the latter half of the reaction period, the addition product generally began to separate as a gummy, grayish-colored solid. Reaction was completed either by allowing the mixture to stand without stirring for from eight to twelve hours or by heating gently over the hot-plate with stirring for from four to six hours.

Hydrolysis of the addition product was accomplished by adding a chilled, saturated aqueous solution of ammonium chloride until all of the solid had dissolved and two clear, liquid layers resulted. These were separated; the lower aqueous layer was extracted twice with ether, and the ether solutions of the amine were combined and

(6) The alkoxy nitriles employed in this study were synthesized from the corresponding alpha chloro ethers and cuprous cyanides by following the modification of Gauthier's procedure [Gauthier, *Compt. rend.*, **143**, 831 (1906)] discussed by us previously [Allen with Henze, *This Journal*, **59**, 540 (1937)].

dried over anhydrous sodium sulfate. After the ether had been removed by evaporation under reduced pressure, the amine was purified by distillation, also *in vacuo*. After two such fractionations, the amines could be distilled under atmospheric pressure with no apparent decomposition.

From a typical preparation was obtained 156.6 g. (78.7% yield) of ethoxymethyldiallylcarbinamine when 100 g. (1.18 mole) of ethoxyacetonitrile, 200 g. (8.23 g. atoms) of magnesium, 370 g. (3.06 moles) of allyl bromide, and 2400 cc. of anhydrous ether were combined in the manner described.

The amines, the physical constants, yields, and analytical data for which are summarized in Table II, are colorless oils of not unpleasant, quite characteristic odor which somewhat resembles that of molding wood.

Crystalline picrates could be prepared for all of the amines synthesized by merely dissolving the base in sulfuric acid solution and then adding a saturated aqueous solution of picric acid. The picrates were recrystallized from either water or aqueous alcohol.

Preparation of Ethoxymethylpropylallylcarbinamine.—To the ether solution of propylmagnesium bromide, prepared under the usual anhydrous conditions from 15.6 g. (0.64 atom) of magnesium, 86.3 g. (0.7 mole) of *n*-propyl bromide, and a total of 400 cc. of anhydrous ether, was added 49.5 g. (0.58 mole) of ethoxyacetonitrile dissolved in 100 cc. of ether. After approximately one-third of the nitrile solution had been introduced, separation of a white solid was noted; in order that this solid might not settle to the bottom of the flask and subsequently form the customary gummy mass, the rate of stirring was increased to the maximum possible with the mechanical device employed and kept thus throughout the remainder of the nitrile addition. This vigorous agitation resulted in maintaining the addition product in the form of a finely divided, gray-white, semi-crystalline precipitate.

Approximately thirty minutes after completion of the nitrile-propylmagnesium bromide reaction, the filtered ether solution of allylmagnesium bromide, prepared in the manner previously described from 100 g. (0.83 mole) of allyl bromide, 61 g. (2.5 atoms) of magnesium, and 500 cc. of dry ether, was run into this suspension during thirty minutes. Signs of reaction throughout this addition were feeble refluxing of the ether and, more important, a change in the color and character of the ether-insoluble addition product from the gray-white semi-solid previously described to a heavy, green-brown oil which settled to the bottom of the vessel despite the rapid stirring.

Agitation of the mixture was continued, with the latter at room temperature for one hour after the addition of the allyl compound, and then at such a temperature that the ether refluxed vigorously for two hours; during the last hour of this period the large excess of ether was reduced to a volume which permitted more ease in manipulation. Hydrolysis was accomplished by pouring the ether and viscous material into a mixture of crushed ice and saturated ammonium chloride solution which was stirred rapidly during the reaction.

After separation of the two layers resulting from hydrolysis, the ether solution of the amine was dried over sodium sulfate, the ether removed by the usual evapora-

tion under reduced pressure, and the crude amine purified by two fractionations under the pressure of the water pump. The observed physical constants and analytical data for this compound have been included in Table II.

Preparation of Ethoxymethyldipropylcarbinamine.—This amine was prepared in two separate instances from different starting materials but by the same method, namely, by the catalytic hydrogenation of both ethoxymethyldiallylcarbinamine and ethoxymethylpropylallylcarbinamine. The reduction was accomplished in each case by shaking the solution of 0.1 mole of the unsaturated amine in 40–50 cc. of acetone in the presence of the Adams platinum catalyst and hydrogen under approximately one atmosphere pressure. After hydrogenation was complete, usually in two to six hours, the catalyst was removed by filtration, the solvent by distillation, and the saturated amine purified by fractionation under reduced pressure. The two samples of the amine thus obtained had identical physical constants. These constants, as well as certain analytical data for the amine, have been included in Table II.

Picrates were prepared from both samples of the amine, and the individual melting points and mixed melting point were determined. Both picrates melted at 123.5–124.5° (corr.) and the mixing occasioned no depression of this value.

Exhaustive Methylation of Diallyl- and Dipropyl-ethoxymethylcarbinamines.—Into a 250-cc. Erlenmeyer flask fitted with reflux condenser was introduced in the order named, 0.14 mole of the amine, 75 cc. of 40% aqueous potassium hydroxide solution, and 0.49 mole of methyl iodide. When the flask was rotated gently, vigorous reaction commenced so that cooling with an ice-bath was required to prevent loss of material through the condenser. After reaction had subsided, a change in the density of the organic material was noted; *i. e.*, it constituted the lower layer before, and the upper after, reaction. The mixture was then refluxed gently for one hour, cooled, and transferred to a separatory funnel where it was shaken with 50 cc. of ether to remove any unreacted methyl iodide. The three layers were separated, the uppermost (ether) and the lowest (aqueous) being discarded and the middle layer shaken with an additional 100-cc. portion of ether. After several minutes the viscous quaternary ammonium iodide solidified and could then be filtered from the ether and dried. In both methylations the crude material represented about 94% of that theoretically possible.

The methiodides were recrystallized from anhydrous benzene; after three such treatments the following melting points and analytical data for the solids were obtained:

The product from ethoxymethyldiallylcarbinamine melted at 100.5–101.5° (corr.) and decomposed with effervescence above this temperature. *Anal.* Calcd. for $C_{13}H_{25}INO$: C, 46.02; H, 7.73; N, 4.14. Found: C, 46.32; H, 7.76; N, 4.27.

The product from ethoxymethyldipropylcarbinamine decomposed with effervescence at 132.5–133.5° (corr.). *Anal.* Calcd. for $C_{18}H_{30}INO$: C, 45.48; H, 8.81; N, 4.08. Found: C, 45.55; H, 8.77; N, 3.98.

Pyrolysis of the Quaternary Ammonium Iodides.—When 0.12 mole of either of the two methiodides was

packed into a 50-cc. distilling flask, which was set up as for distillation under diminished pressure, the pressure reduced to that of the water-pump (25–27 mm.), and the flask heated to 150–180° by means of an oil-bath, some effervescence occurred and a colorless liquid began to distill. Heating was continued until no more liquid was produced, at which time 16–21 cc. of crude ether (73–78%) had been collected and a white solid residue remained in the flask. The ethers were purified by distillation under reduced pressure.

In this manner, then, 4-ethoxymethyl-3-heptene was obtained from the methiodide of ethoxymethyldipropylcarbinamine, and 4-ethoxymethyl-1,3,6-heptatriene from that of ethoxymethyldiallylcarbinamine. The following physical constants were determined and analytical results obtained for these two unsaturated ethers:

For 4-ethoxymethyl-3-heptene: yield, 77.8%; b. p. 72.0–73.0° (17 mm.), 173.5–175.0° (corr.) (740 mm.); d^{20}_4 0.8059; n^{20}_D 1.4298; MR calcd., 49.56; MR found, 50.07; γ^{20} 25.08 dynes/cm.; P calcd., 433.2; P found, 433.9. *Anal.* Calcd. for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 77.02; H, 12.91.

For 4-ethoxymethyl-1,3,6-heptatriene: yield, 73.0%; b. p. 71–72° (16–17 mm.); d^{20}_4 0.8484; n^{20}_D 1.4701; MR calcd., 50.07; MR found, 48.627; γ^{20} 25.79 dynes/cm.; P calcd., 411.2; P found, 404.4. *Anal.* Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.89; H, 10.43.

Preparation of 4-Ethoxymethylheptane.—Three different specimens of this compound were prepared from separate and different starting materials. The physical properties, yields, and analytical data for these three specimens have been referred to previously in Table I.

Two of the three samples were obtained through catalytic hydrogenation of 4-ethoxymethyl-3-heptene and 4-ethoxymethyl-1,3,6-heptatriene using platinum black as a catalyst, acetone as a solvent, and hydrogen under one atmosphere pressure.

The third sample of this ether was obtained as the product of the interaction of chloromethyl ethyl ether and the appropriate heptylmagnesium bromide: to the ether solution of heptylmagnesium bromide, prepared from 8.1 g. (0.33 atom) of magnesium, 67.0 g. (0.38 mole) of 4-bromoheptane,⁸ and 260 cc. of anhydrous ether, was added the solution of 31 g. (0.33 mole) of freshly distilled chloromethyl ethyl ether⁹ in an equal volume of dry ether.

The pure product from this reaction was obtained after the reaction mixture had been treated with crushed ice and dilute acid (in this case to neutralize the basic salt

(7) The specific exaltation, obtained from the difference between calculated and observed molecular refractivity, is, in this case, 0.96. This value compares favorably with an average value for specific exaltation determined by Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **84**, 1 (1911), as equal to 1.10.

(8) Heptanol-4 was prepared in 53% yield by the action of propylmagnesium bromide upon butyraldehyde: b. p. 71.5–72.5° (25.5–26 mm.); d^{20}_4 0.8183; n^{20}_D 1.4205. From this alcohol, a 78.6% yield of 4-bromoheptane was obtained by treatment with phosphorus tribromide: b. p. 64–65° (21–22 mm.); d^{20}_4 1.1373; n^{20}_D 1.4498; MR calcd., 42.29; MR found, 42.31. *Cf.* Sherrill, *THIS JOURNAL*, **52**, 1982 (1930).

(9) This alpha chloro ether was synthesized after the manner of Henry, *Bull. Acad. Roy. Belg.*, [3] **25**, 439 (1893); and was collected during distillation at 79–80° (748 mm.).

from any unreacted Grignard reagent) and the ether solution of the product processed in the customary manner.

The analytical data and observed physical properties for this compound likewise appear in Table I.

Attempted Preparation of Ethoxymethyldiallylcarbinamine (4-Amino-4-ethoxymethylheptane).—The methods employed in attempts to synthesize this amine (other than the method described previously) all required the use of the appropriate alkyl halide, namely, 4-chloro-4-ethoxymethylheptane. This halide in turn required the preparation of the tertiary alcohol, 4-hydroxy-4-ethoxymethylheptane. The latter was obtained in 94.6% yield from the interaction of two moles of propylmagnesium bromide and one of *n*-propyl ethoxyacetate¹⁰; the following constants and analytical data were observed: b. p. 200.0–201.0° (corr.) (752 mm.); d^{20}_4 0.8706; n^{20}_D 1.4286; γ^{20} 26.24 dynes/cm.; MR calcd., 51.55; MR found, 51.57; P calcd., 464.2; P found, 453.1. *Anal.* Calcd. for $C_{10}H_{22}O_2$: C, 68.91; H, 12.72. Found: C, 69.01; H, 12.67.

This alcohol was converted in 40.7% yield into the desired 4-chloro-4-ethoxymethylheptane merely by shaking it with concentrated hydrochloric acid. The following data were collected concerning this halide: b. p. 94–95° (25 mm.); d^{20}_4 0.9115; n^{20}_D 1.4344; γ^{20} 26.33 dynes/cm.; MR calcd., 54.89; MR found, 55.11; P calcd., 481.4; P found, 479.0. *Anal.* Calcd. for $C_{10}H_{21}ClO$: Cl, 18.40. Found: Cl, 18.10.

All attempts to convert this chloride into the desired amine were unsuccessful. The methods employed were the Grignard reagent-chloroamine reaction of Coleman, Gabriel's primary amine synthesis, and both liquid ammonia and sodium amide in liquid ammonia treatment. In all instances the chloride was recovered, and no basic material was obtained. The Coleman reaction failed primarily because the halide did not react with magnesium to form the desired Grignard reagent.

Summary

1. An abnormal reaction has been noted between allylmagnesium bromide and ethoxyacetonitrile as a result of which, instead of the anticipated ketone, was produced ethoxymethyldiallylcarbinamine, an amine of unusual type, namely, one in which the primary amino group is attached to a tertiary carbon.

2. The reaction has been shown to be of application more general than to this one isolated case through its utilization in the synthesis of two analogous alkoxyalkyldiallylcarbinamines.

3. Allylmagnesium bromide has been shown to be capable of reaction with a typical Grignard reaction product, namely, that resulting from interaction of *n*-propylmagnesium bromide and ethoxyacetonitrile.

AUSTIN, TEXAS

RECEIVED MARCH 30, 1939

(10) Obtained by passing hydrogen chloride through a solution of ethoxyacetonitrile in *n*-propyl alcohol: yield, 83.4%; b. p. 173.5° (corr.) (748 mm.); d^{20}_4 0.9594; n^{20}_D 1.4083; γ^{20} 28.34 dynes/cm.