6.5 ml. of a 50% potassium hydroxide solution was refluxed for 6 hr. The solution was then acidified with dilute sulfuric acid, diluted with water to 100 ml., and distilled. When two thirds of the liquid had distilled, 50 ml. of water was added and the distillation was resumed. The combined distillates were titrated with N sodium hydroxide solution.

Anal. Calcd. for $C_8H_{13}NO_4$: Acetyl, 45.9. Found: Acetyl, 45.3.

(*B*) *Phosphorus pentachloride.* Addition of 4.16 g. (0.02 mole) of phosphorus pentachloride to 3.74 g. (0.02 mole) caused an exothermic reaction to take place, with evolution of a gas. Further heating up to 150° produced 2.45 g. (0.031 mole) of acetyl chloride, b.p. 50–53°, which gave acetanilide, m.p. 115–116°, on reaction with aniline.

Ethyl dipropionimidoacetate. A mixture of 6.45 g. (0.05 mole) of ethyl isocyanatoacetate and 5.62 g. (0.043 mole) of propionic anhydride was heated in a bath at 200° for 6 hr. Carbon dioxide was evolved. The mixture was distilled and a fraction weighing 6.0 g., b.p. 125–150° (2 mm.), was separated and distilled again. The middle fraction was ethyl dipropionimidoacetate, b.p. 109° (0.2 mm.); n_D^{25} 1.4512; weight, 4.0 g.

Anal. Calcd. for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 54.42; H, 7.87; N, 7.08.

The discrepancy in the analysis suggests the presence of small amounts of ethyl 1-propionyl-3-hydantoinacetate, and some was actually isolated from the main fraction.

Ethyl 1-propionyl-3-hydantoinacetate. A total of 2.5 g. of this ester was extracted from the above distillation residue with boiling ligroin (86–100°). It melted at 117–118°.

Anal. Calcd. for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.83; N, 11.57; neut. equiv., 242.2. Found: C, 50.03; H, 6.00; N, 11.77; neut. equiv., 242.

Ethyl dioctanimidoacetate. (A) A mixture of 10.3 g. (0.038 mole) of octanoic anhydride and 4.90 g. (0.038 mole) of ethyl isocyanatoacetate was heated in a bath at 175° for 10 hr. Distillation of the mixture yielded crude ethyl dioctanimidoacetate, which was purified by two redistillations. The final product weighed 9.5 g. (70% yield); b.p. 177–179° (0.9 mm.).

Anal. Calcd. for $C_{20}H_{37}NO_4$: C, 67.57; H, 10.49. Found: C, 67.36; H, 10.19.

Ethyl 1-octanoyl-3-hydantoinacetate. Repetition of the above experiment at 197° and with a 10% excess of the isocyanate, followed by prolonged chilling at 0° of the crude fraction of ethyl dioctanimidoacetate produced 0.3 g. of ethyl 1-octanoyl-3-hydantoinacetate, m.p. 93.5–94.5° (acetone-water).

Anal. Calcd. for $C_{15}H_{24}N_2O_5$: C, 57.67; H, 7.74; N, 8.97. Found: C, 57.84; H, 7.62; N, 9.33.

Ethyl dibenzimidoacetate. A mixture of 6.78 g. (0.03 mole) of benzoic anhydride and 3.87 g. (0.03 mole) of ethyl isocyanatoacetate was heated in a bath kept at 200° for 8.5 hr., and then distilled. The fraction distilling at 160–190° (0.15 mm.) was a very viscous liquid, which by repeated alternate chilling to 0°, and thawing, was made to crystallize in part. The crystalline material weighed 6.5 g., and melted at 96–99°. Three recrystallizations from methanol produced pure ethyl dibenzimidoacetate, m.p. 103.5–104°.

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50. Found: C, 69.10; H, 5.50.

In another experiment with the same reagents it was observed that when the bath temperature was below 195° there was no evolution of carbon dioxide from the mixture. The evolution would start again as soon as the bath temperature was over 195°. From a reaction mixture kept at 177° for 6 hr., 98.7% of the benzoic anhydride, and 83% of the isocyanate were recovered.

Ethyl phenaceturate. A mixture of 9.7 g. (0.038 mole) of phenylacetic anhydride and 4.9 g. (0.038 mole) of ethyl isocyanatoacetate was heated in a bath at 175° for 9 hr. Carbon dioxide evolution was observed at temperatures over 160°. Distillation of the mixture at 1.5-mm. pressure yielded 10 g. of a fraction distilling at 170–195°, and 2.4 g. of a residue. The main fraction was ethyl phenaceturate, m.p. 77–78° (ether), mixed melting point with pure ethyl phenaceturate of m.p. 80–81.5° was 78–80°. Its nitrogen content by analysis was 6.35% (theory, 6.33). Extraction of the residue with various solvents failed to yield any other material.

EVANSTON, ILL.

The Grignard Reaction with 2-(β-Cyanoethyl)-2-ethylhexanal and Further Conversions of the Reaction Products. Limitations of Anisole as Solvent for the Grignard Reaction

JAMES CASON, KENNETH W. KRAUS, AND WM. D. MacLEOD, JR.

Reaction of *n*-butylmagnesium bromide with an approximately equimolar amount of 2-(β-cyanoethyl)-2-ethylhexanal at 0° in diethyl ether as solvent yields about equal amounts of the reduction product, 2-(β-cyanoethyl)-2-ethyl-1-hexanol (II), and the addition product, 6-(β-cyanoethyl)-6-ethyl-5-decanol (III). There could be detected no product resulting from reaction of the nitrile grouping. Yields were similar, whether normal addition or inverse addition was used in the reaction. In anisole as solvent, considerable quantities of two unidentified by-products could be detected by gas phase chromatography, and the yield of the addition product, III, was somewhat lower. With inverse addition in anisole, the amount of reduction was much greater than observed when diethyl ether was the solvent. The addition product, the cyano alcohol III, was hydrolyzed to a lactone which was transesterified with methanol to yield a mixture of unsaturated esters. Ozonolysis of these esters indicates the mixture expected from rearrangement of the carbonium ion resulting from alkyl-oxygen fission of the lactone, and development of the double bond at less substituted positions as well as the most substituted position.

The reaction of *n*-butylmagnesium bromide with an equimolar amount of 2-(β-cyanoethyl)-2-ethyl-hexanal (I) has been examined, partly in order to evaluate the relative reactivities of the nitrile and the highly hindered aldehyde, and partly to supply for futher study compounds containing the highly

hindered quaternary carbon atom. There have already been reported[1] reactions of this cyano aldehyde with excess of Grignard reagent. The observed products were hydroxy nitriles (homologous to III) and dihydropyrans resulting from cyclization and dehydration of hydroxy ketones resulting from further reaction of the hydroxy nitriles with Grignard reagent.

The Grignard reaction in diethyl ether with an equimolar amount of cyano aldehyde I, at 0°, whether by normal addition of the cyano aldehyde to the Grignard reagent or inversely, gave no significant amount of product resulting from reaction with the nitrile. Further, the yields of products resulting from reaction with the aldehyde were similar for the two methods of addition. The only identified reaction products were the primary alcohol (II), resulting from reduction of the starting material, and the secondary alcohol (III), resulting from addition of the Grignard reagent to the aldehyde. Average yields are recorded in Table I.
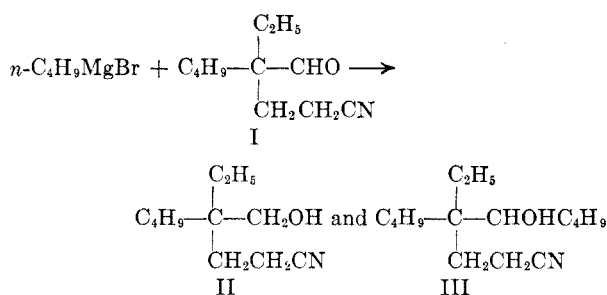
$$n\text{-}C_4H_9MgBr + C_4H_9-\overset{\overset{\displaystyle C_2H_5}{|}}{\underset{\underset{\displaystyle CH_2CH_2CN}{|}}{C}}-CHO \longrightarrow$$
$$I$$

$$C_4H_9-\overset{\overset{\displaystyle C_2H_5}{|}}{\underset{\underset{\displaystyle CH_2CH_2CN}{|}}{C}}-CH_2OH \text{ and } C_4H_9-\overset{\overset{\displaystyle C_2H_5}{|}}{\underset{\underset{\displaystyle CH_2CH_2CN}{|}}{C}}-CHOHC_4H_9$$
$$II \hspace{3cm} III$$

TABLE I

REACTION OF n-BUTYLMAGNESIUM BROMIDE WITH 2-(β-CYANOETHYL)-2-ETHYLHEXANAL

Solvent	Mode of Addition	Yields, % Pri. alc. II	Yields, % Sec. alc. III
Diethyl ether	Normal	30	33
Diethyl ether	Inverse	26	33
Anisole	Normal[a]	21	25
Anisole	Inverse[b]	42	23

[a] In this run there was also observed a 17% yield of product of slightly shorter retention time in gas chromatography than II, and an 11% yield of product with retention time between II and III; cf. Table II. [b] In this run, yields of products mentioned in Note a were respectively 10% and 7%.

It has been reported[2] that the reducing action of a Grignard reagent is less favored when a less basic ether is used as solvent for the reaction. Specifically, less reduction was found when anisole was the solvent than was the case when diethyl ether was the solvent. Although the yield of Grignard reagent is poor in anisole, this is a rather minor disadvantage when the other component of the

(1) N. Rabjohn, M. J. Latina, and L. V. Phillips, J. Org. Chem., **21**, 285 (1956).

(2) R. N. Lewis and J. R. Wright, J. Am. Chem. Soc., **74**, 1253 (1952).

reaction is relatively expensive; therefore, the effect of anisole was examined in the Grignard reaction with 2-(β-cyanoethyl)-2-ethylhexanal. When the products of the reaction in anisole were isolated by fractional distillation, there appeared to be an increase in the yield of product III resulting from addition to the carbonyl group, as would be expected from the previous work[2]; however, the intermediate fraction between the primary and secondary alcohols seemed rather large, and isolation of pure products was difficult. When the reaction mixture was subjected to gas phase chromatography, nine bands appeared in the recorder tracing, and two of these were almost as large as the bands for alcohols II and III. In runs carried out in diethyl ether, these large by-product bands were entirely absent, or barely visible; indeed, for runs in diethyl ether, the two alcohols accounted for about 90% of the total area under all bands. There are recorded in Table II representative results of the chromatography of runs in which normal addition was used. From the data in Tables I and II, it may be noted that use of anisole as solvent reduces the yield of addition product, results in large amounts of by-products, and with inverse addition increases the yield of reduction product. The by-products may have resulted in part from the small excess of Grignard reagent used in the runs in anisole, but it seems improbable that this is a major factor.

TABLE II

GAS CHROMATOGRAPHY OF PRODUCTS OF GRIGNARD REACTIONS IN DIETHYL ETHER AND IN ANISOLE[a]

Diethyl Ether Solvent Retention time[b] (min., sec.)	% of total area under bands	Anisole Solvent Retention time[b] (min., sec.)	% of total area under bands
1′ 45″	0.2	1′ 45″	0.1
		3′ 10″	5.5
6′ 15″	4.6	6′ 32″	2.2
		7′ 40″	0.6
10′ 06″	0.4	10′ 10″	2.2
12′ 27″[c]	4.4		
		15′ 25″	17.8
20′ 07″[d]	34.4	19′ 30″	20.0
32′ 32″	0.7	33′ 50″	15.1
49′ 52″[e]	55.3	48′ 25″	36.5

[a] A solution in the appropriate ether of n-butylmagnesium bromide, assayed by titration, was treated at −5 to 0° with a solution of an approximately equimolar amount of 2-(β-cyanoethyl)-2-ethylhexanal. [b] Retention time was taken as time elapsing between injection of sample and the peak of the band. A smaller area under the band gives a slightly shorter retention time; for a similar size of band, reproducibility of retention time is about 0.5 min. for a time of 30 min. Values in this table were determined by injection of 70–80 λ of the reaction product into a 3 m. × 15 mm. O.D. column, at 226°, with helium flow of 145 ml./min. [c] Retention time of 2-(β-cyanoethyl)-2-ethylhexanal. [d] Retention time of primary alcohol II. [e] Retention time of secondary alcohol III. Injection of smaller amounts resolved this band into two overlapping bands with peaks at 44 min., 00 sec. and 45 min., 55 sec. These are believed to represent diastereoisomers.

The significant by-products observed in the runs in anisole have not been identified; in fact, re-chromatography of the material from the band appearing between the alcohols gave several new bands, so cracking at the chromatography temperature of 226° (or on passing the heated detector) is indicated. The byproduct with shorter retention time than the primary alcohol (II) showed a single sharp band in the same position on rechromatography. Analysis indicated a ratio of one oxygen to about fifteen carbons, consistent with a dihydropyran as reported by Rabjohn and co-workers[1]; however, the infrared spectrum exhibited a significant carbonyl band, so it is presumed that this fraction is not a single compound, and its investigation has not been pursued further.

Evidence has been presented that the Grignard reaction with the carbonyl group is second order with respect to Grignard reagent,[3] while the reaction with a nitrile is first order[4] with respect to Grignard reagent. If this be the case, inverse addition of the Grignard reagent should favor reaction with the nitrile, since the lower concentration of this reagent would enter the rate equation only once for the nitrile reaction. Failure to isolate or detect any product from reaction with the nitrile for either method of addition, however, prevents utilization of the present data for a test of the validity of these reaction mechanisms. It is possible that nitrile is too unreactive to compete significantly with aldehyde, even when favored by a low concentration. On the other hand, failure of inverse addition in diethyl ether to favor reduction is surprising if, indeed, the reduction is first order in respect to Grignard reagent,[5] and the addition reaction is second order.[3] It is the case that twice as much reduction was obtained with inverse addition in anisole; however, this increased reduction was at the expense of the uncharacterized side products observed in anisole. The yield of addition product in anisole was the same for normal or inverse addition (cf. Table I).

The primary alcohol, 2-(β-cyanoethyl)-2-ethylhexanol, II, was characterized by hydrolysis to γ-butyl-γ-ethyl-δ-valerolactone, IV, previously pre-


IV

V
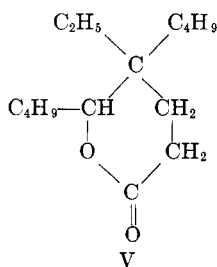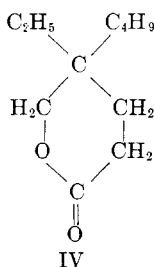
(3) C. G. Swain and H. B. Boyles, J. Am. Chem. Soc., 73, 870 (1951).

(4) C. G. Swain, J. Am. Chem. Soc., 69, 2307 (1947).

(5) H. S. Mosher and E. La Combe, J. Am. Chem. Soc., 72, 3994 (1950).

pared by Bruson and Riener.[6] The liquid lactone was further characterized by oxidation with permanganate in alkaline solution to yield the known[6] α-butyl-α-ethylglutaric acid of melting point 78–80°.

The secondary alcohol, 6-(β-cyanoethyl)-6-ethyl-5-decanol, III, was similarly characterized by hydrolysis to lactone V. When this lactone was transesterified with methanol in presence of hydrogen chloride, the product was not the ester of a hydroxy acid but the ester of an unsaturated acid containing the same number of carbons as the starting lactone. The presence of the double bond was established by the ultraviolet spectrum, hydrogenation, bromination, and oxidation. Molecular weight was established by quantitative hydrogenation and equivalent weight of the corresponding acid. The most plausible route to an unsaturated ester would probably involve[7] attack of a proton on the ring oxygen of the lactone, followed by opening of the ring to give the carbonium ion, VI. Although this ion might go directly to alkene by loss of a proton from the carbon adjacent to the charge, such an ion would be expected to rearrange

VI

VII

VIII
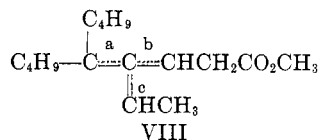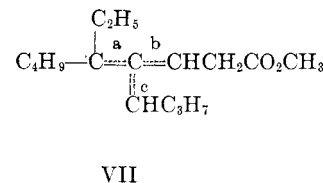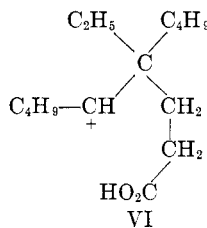
rapidly by migration of one of the groups on the quaternary carbon adjacent to the charge. Indeed, rearrangement and ring opening may be concerted. Since a butyl group is present on each of the adjacent carbons involved in the rearrangement, there would result the two carbon skeletons shown in formulas VII and VIII after rearrangement, loss of a proton, and esterification. Since it has been well demonstrated[8] that steric strain resulting from substitution of large groups on a double bond can render the more substituted position for the double bond the position of higher energy, generation of structures VII and VIII by the route proposed

(6) H. A. Bruson and T. W. Riener, J. Am. Chem. Soc., 66, 56 (1944).

(7) For a discussion of unimolecular acid-catalyzed ester hydrolysis involving alkyl-oxygen fission, reference may be made to E. R. Alexander, Principles of Ionic Organic Reactions, John Wiley and Sons, Inc., New York, 1950, pp. 226, 230; or to J. Hine, Physical Organic Chemistry, McGraw-Hill Book Co., Inc., New York, 1956, pp. 270-272.

(8) H. C. Brown and I. Moritani, J. Am. Chem. Soc., 77, 3607 (1955); R. B. Turner, D. E. Nettleton, Jr., and M. Perelman, J. Am. Chem. Soc., 80, 1430 (1958).

would be expected to give compounds with unsaturation in each of the positions a, b, and c.

Since gas phase chromatography of the unsaturated ester gave a single symmetrical band, separation of a mixture of the six compounds represented by formulas VII and VIII would appear to be impractical or impossible; however, partial separation of the products of ozonolysis of the mixture has proved possible. The appearance of eight major bands in the chromatogram of the
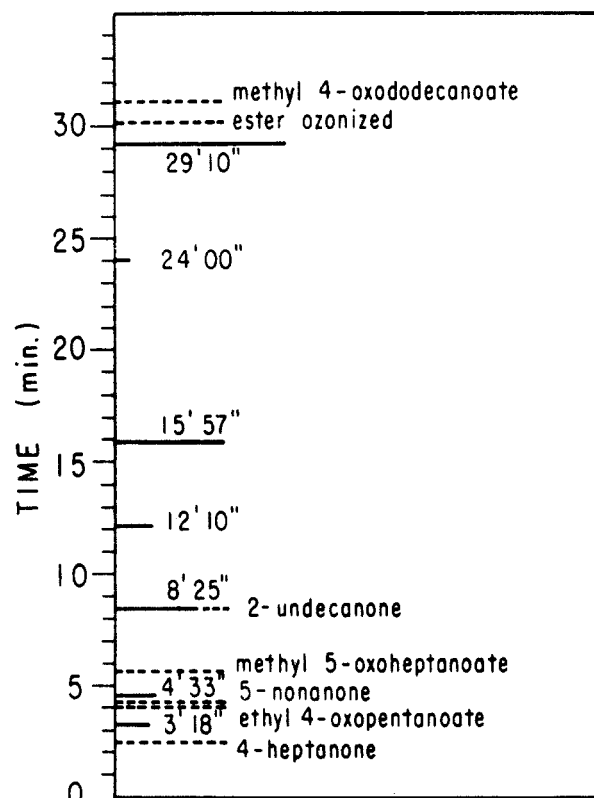

Fig. 1. Gas chromatography of ozonolysis products of the mixed unsaturated esters (Formulas VII and VIII). Chromatography was at 200° in the 3 meter × 15 mm. O.D. column with high vacuum silicone grease as partitioning agent; helium pressure of 16.4 cm. of mercury gave a flow rate of approximately 180 ml./min. The dotted lines indicate the positions observed for known compounds. The solid lines indicate the positions of bands in the chromatogram of the ozonolysis mixture, and the lengths of the lines are proportional to the areas under the bands. Ozonolysis products whose retention times would correspond to those of the observed bands are as follows:

3' 18" band: 3-heptanone from VIIa; in chromatography of the series of octadecanones, retention time became shorter as the keto approached the center of the chain

4' 33" band: 5-nonanone and methyl 4-oxohexanoate from VIIIa

8' 25" band: methyl 4-oxooctanoate from VIIa and the branched C₁₂ ketones from VIIb and VIIIb. Chromatography at 190° gave resolution of this band into two overlapping bands with peaks at 15' 18" and 17' 10", and 2-undecanone appeared at 16' 55"

12' 10" and 15' 57" bands: possibly condensation products of methyl formylacetate from VIIb and VIIIb

24' 00" band: methyl 4-oxo-5-ethylnonanoate from VIIc

29' 10" band: methyl 4-oxo-5-butylnonanoate from VIIIc
Any of the starting ester not ozonized would also appear in this band.

ozonolysis product attests to the complexity of the mixture ozonized. Several known compounds were chromatographed in order to locate the approximate positions of the expected degradation products. In Fig. 1 are tabulated the bands observed in the chromatography carried out at 200°, and the positions on the scale of the known compounds are indicated. As noted in the legend to this figure, bands are observed at the positions expected for all of the keto esters and ketones. If any unsaturated ester should have been formed directly from ion VI, without rearrangement, an ozonolysis product would be methyl 4-ethyl-4-formyloctanoate whose retention time in gas chromatography would be expected to be similar to that of the keto ester from VIIc. The small size of the band at 24 min. in Fig. 1 suggests no more than traces of unrearranged ester. No effort was made to recover the low molecular weight aldehydes that would result from VIIc and VIIIc, and the methyl formylacetate from VIIb and VIIIb would be expected to condense with itself or an aldehyde. The unidentified bands at about 12 min. and 16 min. may be due to these condensation products.

When the unsaturated ester was formed by methanolysis of lactone V, lactone recovered from the reaction amounted to about 25% of the starting material. This recovered lactone had an index of refraction differing somewhat from that of lactone V, showed infrared bands characteristic of a γ-lactone (5.66 μ) as well as a δ-lactone (5.76 μ), and in gas chromatography showed a band at the correct position for starting lactone as well as one at a somewhat shorter retention time. Further, heating with 2N sulfuric acid of the unsaturated acid, obtained by saponification of the ester from methanolysis, converted about 10% of it to neutral material with infrared absorption at 5.66 and 5.76 μ. Thus, all the characteristics of the unsaturated ester and its formation are consistent with conversion of lactone V via the carbonium ion VI (or a concerted reaction) to a mixture of unsaturated esters of structures indicated in formulas VII and VIII.

Reaction of n-butylmagnesium bromide with 2-(β-cyanoethyl)-2-ethylhexanal. Average yields under the several conditions are recorded in Table I. These data were determined by quantitative gas phase chromatography of the total reaction product distilled from a Claisen flask at about 0.5 mm. pressure and a bath temperature up to about 200°. Direct comparisons of area were made for alcohols II and III by injection of 0.06-ml. volumes of 2.5% benzene solutions of pure samples of the alcohols separated by fractional distillation. Known samples were run on each occasion that quantitative work was done, and the unknowns were run without any alteration of the bridge current. Precision of the data is regarded as approximately ± 3%. Yields of the unidentified compounds giving major bands were calculated on the assumptions that they have molecular weights similar to alcohols II and III, which occur near them in the chromatograph, and that area under the tracings is related to

molecular weight as reported by Eastman.[10] Results obtained on fractional distillation of one run gave excellent agreement with the chromatography data; however, the distillation data are subject to the uncertainty of estimating composition of intermediate fractions. In the gas chromatography, the tracing went to baseline between the major bands.

A. *Normal addition in diethyl ether solvent.* A Grignard reagent was prepared in 75 ml. of anhydrous ether from 13.7 g. (0.1 mole) of *n*-butyl bromide (b.p. 100-101°, n_D^{22} 1.4389) and 2.43 g. (0.1 g.-atom) of magnesium turnings. Titration of aliquots of several runs indicated yields of 80-83% of Grignard reagent. The stirred solution of Grignard reagent was cooled to −5°, then there was added as rapidly as consistent with keeping the temperature of the reaction mixture in the range −5° to 0° a solution in 50 ml. of benzene of 14.5 g. (0.08 mole) of 2-(β-cyanoethyl)-2-ethylhexanal[6] (b.p. 125-128°/4 mm., n_D^{22} 1.4528). After addition had been completed (about 15 min.), stirring was continued at about 0° until a negative Gilman test for Grignard reagent had been obtained (45-90 min.). The reaction mixture was finally treated with ice and 50 ml. of 6N sulfuric acid, most of the ether was distilled with stirring, and the mixture was heated under reflux with stirring for an additional hour in order to ensure hydrolysis of any imine that may have been formed by reaction of the nitrile grouping. The organic phase was separated, the aqueous phase was extracted with two portions of ether, and the organic phase and extracts were washed in sequence with two portions of water. After solvent had been distilled the product was distilled from a Claisen flask and the total distillate collected up to a b.p. of 170°/0.5 mm., weight 13.1 g.

By quantitative gas chromatography and comparison with known quantities of the primary and secondary alcohols, this distillate was determined to contain, in addition to 5.5% of the starting cyano aldehyde (I), 31% of primary alcohol II and 44% of secondary alcohol III. Thus, the yield of primary alcohol was 4.1 g. (28%) and that of secondary alcohol was 5.8 g. (30%). In the 2 m. × 9 mm. O.D. gas chromatography column, at 200°, helium flow rate of 145 ml./min., retention times for compounds I, II, and III were respectively 2′ 35″ (min., sec.), 3′ 45″ and 9′ 10″.

As a check on the results of gas chromatography, 13.0 g. of the above run was fractionated through the 60-cm. column at 3.4 mm. pressure, to yield the following fractions: (1) b.p. 77-140°, wt. 1.0 g.; (2) b.p. 140-147°, wt. 0.5 g.; (3) alcohol II, b.p. 147-151°, wt. 3.7 g.; (4) b.p. 151-165°, wt. 1.5 g.; (5) alcohol III, b.p. 165-167°, wt. 4.5 g. If it be assumed that the intermediate fraction is one third the lower-boiling primary alcohol and two thirds the higher-boiling secondary alcohol, the mixture distilled is calculated to have contained about 32% primary alcohol and 42% secondary alcohol.

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(9) Gas phase chromatography was carried out on a 3 m. × 15 mm. O.D. column except for a part of the quantitative work recorded in Table I, which utilized a 2 m. × 9 mm. O.D. column. The packing material was Chromosorb, 30-60 mesh, impregnated with 4 parts of high vacuum silicone grease for 10 parts of Chromosorb. Carrier gas was helium, and detection was by a thermistor in a bridge circuit. Rate of gas flow and temperature are indicated in each instance where data are cited.

Distillations, unless otherwise specified, were carried out in a 60-cm. Podbielniak type column with simple tantalum wire spiral, heated jacket, and partial reflux head. Boiling points are uncorrected and melting points are corrected. Ultraviolet spectra were determined with a Beckman DU spectrophotometer, and infrared spectra were recorded on a Baird spectrophotometer. Microanalyses were by the Microanalytical Division, Department of Chemistry, University of California, Berkeley.

(10) R. H. Eastman, *J. Am. Chem. Soc.*, **79**, 4243 (1957).

An analytical sample of *2-(β-cyanoethyl)-2-ethyl-1-hexanol*, II, was collected as a center cut in a fractional distillation, b.p. 143.7°/3 mm., n_D^{28} 1.4608.

Anal. Calcd. for $C_{11}H_{21}ON$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.68; H, 11.66; N, 7.66.

An analytical sample of *6-(β-cyanoethyl)-6-ethyl-5-decanol*, III, was collected as a center cut in a fractional distillation, b.p. 171.5°/4 mm., n_D^{28} 1.4641.

Anal. Calcd. for $C_{15}H_{29}ON$: C, 75.25; H, 12.21; N, 5.85. Found: C, 75.19; H, 12.14; N, 6.06.

B. *Inverse addition in diethyl ether solvent.* The procedure was the same as described for normal addition, except that the solution of Grignard reagent was forced under nitrogen pressure into a separatory funnel, and the solution of cyano aldehyde I was placed in the flask and stirred as the Grignard solution was added during 30-45 min. After completion of addition, stirring at −5 to 0° was continued until a negative Gilman test was obtained. Work-up and assay of the yields by gas chromatography was as described for normal addition.

C. *Reactions in anisole as solvent.* For preparation of the Grignard reagent from 0.2 mole of butyl bromide, the magnesium was placed in 25 ml. of anisole (dried over sodium, distilled; n_D^{20} 1.5170), and this mixture was stirred at 75-80° as the bromide solution in 75 ml. of anisole was added during 30-45 min. After addition was complete, stirring was continued at 75-80° for 3 hr. Titration indicated yields of Grignard reagent of about 50%. There was used 0.08 mole of cyano aldehyde I dissolved in 50 ml. of anisole. Other details of procedure were the same as described for the diethyl ether runs, except for omission of the period of heating with sulfuric acid after decomposition of the Grignard complex with water. It was found that omission of this step did not result in any product with the properties of an imine sulfate.

γ-Butyl-γ-ethyl-δ-valerolactone (IV) was obtained by hydrolysis of an 11.7-g. sample of alcohol II by heating under reflux with stirring for 5 hr. with a solution of 4.25 g. of potassium hydroxide in 45 ml. of water. On acidification of the reaction mixture and extraction, the lactone was obtained in a yield of 73.5%, b.p. 145-147°/7 mm., n_D^{26} 1.4634. Bruson and Riener[6] reported for this lactone b.p. 124°/3.5 mm., n_D^{25} 1.4635.

For more positive identification of the lactone by oxidation, an 8.4-g. sample was dissolved by warming to 50° in a solution of 3.6 g. of potassium hydroxide in 125 ml. of water. During 15 min., there was added 10.5 g. of solid potassium permanganate at such a rate as to keep the temperature of the reaction mixture at 50-55°. Stirring was continued at 55-60° for 1.75 hr., at which time the permanganate color had disappeared. After the manganese dioxide had been removed by suction filtration, it was extracted with 25 ml. of boiling water, and the total aqueous filtrate was clarified with Supercel. Acidification of the clear solution gave a heavy oil, which slowly crystallized to give 7.9 g. (80.5%) of slightly waxy *α-butyl-α-ethylglutaric acid*. After one crystallization from nitromethane, hard white crystals were obtained, m.p. 78-80°, no depression on mixing with an authentic sample.[11]

γ-Ethyl-γ,δ-dibutyl-δ-valerolactone (V) was obtained by hydrolysis of the secondary alcohol, III, in the manner described for hydrolysis of alcohol II to lactone IV. The yield of product of b.p. 142-143°/1.5 mm. was 83.5%. For analysis there was used a center cut, b.p. 142.7°/1.5 mm., n_D^{26} 1.4681. Infrared absorption was at 5.76 μ, and gas phase chromatography gave a single symmetrical band.

Anal. Calcd. for $C_{15}H_{28}O_2$: C, 74.94; H, 11.74. Found: C, 75.06; H, 11.60.

Methanolysis of lactone V. There was heated under reflux for 5 hr. a solution of 6.0 g. (0.025 mole) of lactone V in 8.0 g. of methanol which had been saturated with hydrogen chloride gas at 0°. The cooled reaction mixture was added to 100 ml. of water, and the product was extracted with three portions of ether. The extracts were washed in sequence

(11) J. Cason, *J. Org. Chem.*, **13**, 227 (1948).

with water, sodium carbonate solution, water, and saturated sodium chloride solution, then dried by filtering through a layer of anhydrous sodium sulfate. The product recovered from the extracts was fractionated at 4 mm. pressure to yield: (1) 0.9 g., b.p. 126–130°, n_D^{25} 1.4508; (2) 2.5 g., b.p. 130°, n_D^{25} 1.4508; (3) 1.6 g., b.p. 159–163°, n_D^{25} 1.4610.

Fractions 1 and 2 were taken as the yield of unsaturated esters (VII and VIII), wt. 3.4 g. (55%). For analysis, there was used a center cut, b.p. 130°/4 mm., n_D^{25} 1.4508.

Anal. Calcd. for $C_{16}H_{30}O_2$: C, 75.33; H, 11.89. Found: C, 75.64; H, 11.78.

On quantitative hydrogenation in acetic acid, with platinum oxide catalyst, consumption of hydrogen was one millimole per 254 mg. of ester (calcd. mol. wt. is 254). The ultraviolet spectrum showed a rapidly rising absorption as the wave length was decreased below 220 mμ until at 200 mμ, ϵ was 6280. Carbonyl absorption in the infrared was at 5.75 μ. In gas chromatography, a single symmetrical peak was observed (*cf.* data below on recovered lactone).

The principal constituent of Fraction 3 in the above distillation was starting lactone, but there was also present some unsaturated ester and a third component which appears to have the γ-lactone structure. Infrared absorption was at 5.66 μ and at 5.76 μ. In gas phase chromatography in the 2 m. × 9 mm. column at 226°, helium flow of 145 ml./min., three bands with the following retention times and per cents of total area were observed: 10′ 00″ (18.5%), 14′ 04″ (18.0%), 17′ 51″ (63.5%). For the unsaturated ester, retention time was 9′ 50″, and for the starting lactone retention time was 17′ 50″; so the intermediate band presumably represents γ-lactones.

Ozonolysis of unsaturated ester mixture. Ozone, flowing at the rate of 0.29 mmole/min., was passed for 4.2 min. into a dichloroethylene solution of 305 mg. (1.2 mmole) of the unsaturated ester mixture. Temperature of the reaction was

−20°. After the reaction had stood for about 20 min., water was added, and the mixture was heated at 80° with stirring for 30 min.[12] The organic phase was separated, solvent was distilled, and the residue was used for gas phase chromatography in the 3 m. × 15 mm. column. Chromatograms were recorded at 190°, 200°, and 227°, but results at 200° recorded in Fig. 1 were most informative.

Saponification of the unsaturated ester mixture. A 2.0-g. sample of the unsaturated ester mixture was saponified by heating under reflux for 2.5 hr. with 3M equivalents of potassium hydroxide in 10% solution in ethanol. The reaction mixture was diluted with water, acidified and extracted. Distillation of the product at 4-mm. pressure yielded 0.3 g., b.p. 156–161.5°, n_D^{25} 1.4591, and 0.9 g., b.p. 161.5–163.5°, n_D^{25} 1.4592. Both fractions absorbed bromine in carbon tetrachloride solution and showed infrared absorption at 5.86 μ. Titration gave an equivalent weight of 240, which is the calculated value for the unsaturated acid.

A mixture of 0.5 g. of the unsaturated acid and 60 ml. of 2N sulfuric acid was heated to boiling for 2 min. The cooled solution was extracted with three portions of ether, and the extracts were washed with water and sodium carbonate solution. Material recovered from the ether after carbonate extraction amounted to 50 mg. and showed infrared absorption at 5.66 μ, 5.77 μ, and 5.86 μ. Acid recovered from the sodium carbonate extract showed an infrared spectrum identical with that of the starting material.

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(12) Experiments in these laboratories on methyl oleate by Dr. Peter Tavs have shown that this procedure gives a high yield of carbonyl compounds from the ozonide, with 5% or less of acids.
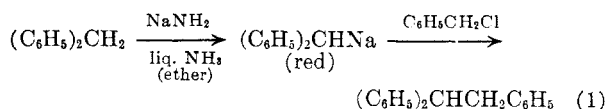

Twofold Alkylations of Sodium Diphenylmethide with Methylene Halides to Form Bisbenzhydrylmethylene Hydrocarbons. Alkylations of Sodium Triphenylmethide[1]

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Sodium diphenylmethide in liquid ammonia entered into a twofold type of alkylation with methylene chloride and certain higher methylene halides to form the corresponding bisbenzhydrylmethylene hydrocarbons in good yields. These results are of both theoretical and practical interest. Similar results were obtained with sodium triphenylmethide and certain methylene halides.

It has recently been shown[2] that sodium diphenylmethide, prepared from diphenylmethane and sodium amide in liquid ammonia and ether, can be alkylated in excellent yields with various alkyl halides in this medium. The reaction may be illustrated with benzyl chloride, which rapidly discharged the red color of the reagent (Equation 1).

$$(C_6H_5)_2CH_2 \xrightarrow[\substack{\text{liq. NH}_3 \\ \text{(ether)}}]{NaNH_2} (C_6H_5)_2CHNa \xrightarrow{C_6H_5CH_2Cl} (\text{red})$$

$$(C_6H_5)_2CHCH_2C_6H_5 \quad (1)$$

It has now been found that sodium diphenylmethide can enter into a twofold alkylation with certain methylene halides to form the corresponding bisbenzhydrylmethylene derivatives in good yields. For example, treatment of this reagent with half of a molecular equivalent of methylene chloride produced hydrocarbon I in 72% yield. This reaction presumably involves the intermediate formation of the corresponding monohaloalkyl derivative (Equation 2).

(1) Supported by the Office of Ordnance Research, U. S. Army.

(2) C. R. Hauser and P. J. Hamrick, Jr., *J. Am. Chem. Soc.*, **79**, 3142 (1957). Also see C. B. Wooster and N. W. Mitchell, *J. Am. Chem. Soc.*, **52**, 688 (1930); C. B. Wooster and J. F. Ryan, *J. Am. Chem. Soc.*, **54**, 2419 (1932).