chloride) was then added. The reaction mixtures were sealed in Pyrex tubes and heated in an oil bath at 80° for about 8 hr. The amounts of the hydrocarbons that had reacted and the amount of chloroform produced were determined in the manner described in the previous experiment. The data obtained and the values of k_c/k_t are shown in Table II.

Comparative Reactions of Cyclohexane, Toluene, and Cumene (Photoinitiated Reactions).—Equivalent amounts of benzene and trichloromethanesulfonyl chloride were added to 5 equivalents of the hydrocarbon. The resulting mixtures were sealed in Pyrex tubes, supported in a large beaker of boiling water, and illuminated for 4 hr. by means of a sunlamp. In each case, the distance of the sunlamp from the reaction tube was the same (6 in.). The reaction mixtures were chromatographed on a 10 ft. × $^1/_4$ column packed with "Craig Polyester" on Chromasorb W using helium as the carrier gas. The amount of chloroform produced was determined from its peak area using benzene as the internal standard. The relation that existed between the amounts of chloroform and benzene and their gas chromatographic peak areas had been previously determined.

(Peroxide-Induced Reactions).—These reactions were performed in the same manner except that twice as much hydrocarbon was employed and 7 mole % benzoyl peroxide based on the trichloromethanesulfonyl chloride was added to initiate the reactions. The reaction mixtures were heated in a constant temperature oil bath for 16 hr. (about four half-lives of the initiator). The amount of chloroform produced in each case was determined from the gas chromatogram of the reaction mixture in the manner described above.

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Synthetic Applications of the Titanium-Catalyzed Exchange of Olefins with Grignard Reagents[1a]

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The addition of a small amount of titanium tetrachloride to an ether solution of *n*-propylmagnesium bromide and certain olefins brings about a displacement reaction, forming propylene and a new Grignard reagent derived from the added olefin:

$$C_3H_7MgBr + RCH{=}CH_2 \xrightarrow{TiCl_4} C_3H_6 + RCH_2CH_2MgBr$$

A large number of olefins having terminal vinyl groups were exchanged in this way with *n*-propylmagnesium bromide and the reaction mixture was then treated with typical Grignard substrates (CO_2, HCHO, etc.). Products corresponding to the Grignard reagent derived from the olefin were isolated in 20–60% yields. Only the terminal Grignard reagent was obtained from 1-alkenes, but styrenes yielded both alpha- and beta-arylethylmagnesium bromides, with the former predominating. Only the terminal vinyl groups undergo the reaction; internal double bonds and vinylidene groups are unaffected, making it possible to prepare unsaturated Grignard reagents from suitable dienes (for example, β-cyclohexenylethylmagnesium bromide from 4-vinylcyclohexene). The olefin exchange reaction is a useful process for preparation of Grignard reagents in cases where the olefin is available and the corresponding halide is not.

In the previous paper[2] of this series it was shown that a small amount of titanium tetrachloride brings about an exchange between alkylmagnesium bromides and terminal olefins, forming a new Grignard reagent derived from the added olefin; for example, reaction between isopropylmagnesium bromide and 1-pentene yielded propylene and *n*-amylmagnesium bromide:

$$C_3H_7MgBr + CH_3CH_2CH_2CH{=}CH_2 \xrightarrow{TiCl_4} C_3H_6 + CH_3CH_2CH_2CH_2CH_2MgBr \quad (1)$$

The suggested reaction sequence involved the formation of an alkyltitanium compound by reaction of the Grignard reagent with titanium tetrachloride,[3] followed by elimination of the elements of TiH,[4] and addition terminally of the titanium hydride to the olefin. For the reaction to proceed with only catalytic[5] amounts of titanium tetrachloride a rapid and reversible exchange of alkyl groups between Grignard reagent and alkyltitanium compound must also be postulated.[6]

$$C_3H_7MgBr + TiCl_4 \longrightarrow C_3H_7TiCl_3 + MgBrCl \quad (2)$$

$$C_3H_7TiCl_3 \rightleftarrows CH_3CH{=}CH_2 + TiHCl_3 \quad (3)$$

$$CH_3CH_2CH_2CH{=}CH_2 + TiHCl_3 \longrightarrow CH_3CH_2CH_2CH_2CH_2TiCl_3 \quad (4)$$

$$CH_3CH_2CH_2CH_2CH_2TiCl_3 + C_3H_7MgBr \rightleftarrows CH_3CH_2CH_2CH_2CH_2MgBr + C_3H_7TiCl_3 \quad (5)$$

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[1] (a) Presented in part at the 140th Meeting of the American Chemical Society, Chicago, Illinois, September, 1961; (b) present address, New Mexico State University, Box 756, University Park, New Mexico.

[2] G. D. Cooper and H. L. Finkbeiner, *J. Org. Chem.*, **27**, 1493 (1962).

[3] D. F. Herman and W. K. Nelson, *J. Am. Chem. Soc.*, **75**, 3877, 3882 (1953).

[4] Presumably the titanium hydride would make up part of the solid Ziegler-type complex which forms immediately upon the addition of the titanium tetrachloride but for the sake of simplicity it is shown as $TiHCl_3$. The Grignard reagent similarly is shown throughout as RMgBr, although such a structure is no longer considered probable. R. E. Dessy and G. S. Handler, *ibid.*, **80**, 5824 (1958).

[5] Titanium tetrachloride cannot properly be called a "catalyst," as it is converted to other products during the reaction, but no more suitable term appears to be available.

[6] Although this type of exchange has not been reported in the case of alkylmagnesium compounds a similar rapid exchange of alkyl groups between aluminum and titanium has been demonstrated: G. L. Karapinka and W. L. Carrick, *J. Polymer Sci.*, **55**, 141 (1961), and references cited therein.

Although there is no direct evidence for this reaction sequence, which certainly represents an oversimplification,[7] it is nevertheless presented because it has proved useful both in correlating a large number of observations[2] and in suggesting new experiments. Whatever the mechanism, a process by which an olefin is converted in one step to a Grignard reagent appeared to be potentially a useful tool in organic synthesis. For example, a 45% yield of 1-hexanol was obtained when an ether solution of *n*-propylmagnesium bromide and 1-pentene was heated under reflux for sixteen hours with three mole per cent of titanium tetrachloride and then allowed to react with formaldehyde.[2] We have therefore carried out a more extensive survey of this system, with the object of determining the scope and limitations of the Grignard exchange reaction as a synthetic procedure.[8]

Choice of Reaction Conditions.—The Grignard exchange reaction permits a wide choice of reaction variables, for example, the nature and concentration of the Grignard reagent, the ratio of Grignard reagent to titanium tetrachloride, reaction time, etc. For the screening type of operation involved in this work a standard set of reaction conditions appeared desirable. The Grignard reagent should be one which is easily prepared from a readily available alkyl halide, preferably one with no more than four carbon atoms.[9] Previous work[2] indicated that *n*-propylmagnesium bromide was somewhat superior to isopropyl- or ethylmagnesium bromide, and that satisfactory exchange with 1-octene was obtained at a 30:1 ratio of Grignard reagent to titanium tetrachloride and a reaction time (reflux in diethyl ether) of twelve to twenty-four hours.

No attempt has been made to determine exactly the optimum conditions, which in any case are probably different for each olefin, but further investigation showed that higher (100:1) and lower (5:1) ratios of Grignard reagent to titanium tetrachloride resulted in lowered yields of Grignard reagent from 1-octene, so the conditions chosen were approximately those used in the previous work: One-half mole of *n*-propylmagnesium bromide[10] and one-half mole of the olefin in 400 ml. of diethyl ether[11] were refluxed overnight (16–17 hr.) with 0.013 mole of titanium tetrachloride, then allowed to react with the chosen reagent and worked up following standard Grignard procedures.

Olefins with Terminal Vinyl Groups.—Several simple alkenes having terminal vinyl groups were exchanged as described above and allowed to undergo some typical Grignard reactions, with the results listed in Table I. The expected product was obtained in yields of 20–60% based on the alkyl halide. Products were identified by the usual physical constants and in most cases by comparison of their infrared spectra and GPC retention times with those of authentic samples. In each case the product was that corresponding to the terminal Grignard reagent, RCH_2CH_2MgX, with no indication of the secondary isomer which might be produced if the titanium hydride added in the reverse direction to that shown in (4). In two cases the crude product was carefully examined for evidence of the secondary Grignard reagent. No trace of 2-methyl-1-pentanol, which would be expected if the secondary Grignard were present, could be detected when 1-pentene was exchanged and reacted with formaldehyde. Reaction with oxygen yielded a trace (barely detectable by gas chromatography) of material which had a retention time corresponding to 2-pentanol, but the amount was not enough to permit trapping and identification.

The tendency of the metal hydride[12] to form almost exclusively the primary metal alkyl on addition to a terminal double bond agrees with the direction of addition of boron hydrides to similar olefins[13] and accounts for the fact that isopropylmagnesium bromide rearranges to *n*-propylmagnesium bromide in the presence of titanium tetrachloride, while the reverse reaction does not occur.[2,14,15]

Of the various substrates employed (with the exception of water) the best yields were obtained with carbon dioxide, as is usually the case with

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[7] For example, only monoalkyltitanium compounds are shown although polyalkylation must occur at the high ratios of Grignard reagent to titanium tetrachloride employed. The formation of lower valence states of titanium is also not shown, although it is possible that Ti(III) or Ti(II) may be the active species, as appears to be the case when titanium tetrachloride is used in Ziegler polymerizations [W. L. Carrick, F. J. Karol, G. L. Karapinka, and J. J. Smith, *J. Am. Chem. Soc.*, **82**, 1502 (1960)].

[8] A preliminary report of some of this work has been published in the form of a Communication to the Editor [*J. Org. Chem.*, **26**, 4779 (1961)].

[9] The use of low molecular weight alkyl halides facilitates the exchange reaction, since the volatile olefin formed in step 3 does not remain in the reaction mixture to compete with the added olefin, and also simplifies the isolation of the final product. If any of the original Grignard reagent remains after the exchange it reacts with the substrate along with the new Grignard reagent. The product is nearly always obtained by fractional distillation and it is therefore advantageous to have the greatest separation possible between the boiling points of compounds formed from the original and new Grignard reagent.

[10] The Grignard reagent was prepared in each case from 0.5 mole of *n*-propyl bromide and a slight excess of magnesium, so that the amount of Grignard reagent is actually somewhat less than 0.5 mole (approximately 0.45 mole).

[11] In some of the experiments only 200 ml. of ether was used and the titanium tetrachloride was added in two portions. There was no appreciable difference in yields obtained by the two methods.

[12] This may be a titanium hydride as shown in equation 4 or a magnesium hydride. It has been suggested that one mode of termination in Ziegler polymerizations involves addition of an aluminum hydride to a monomer molecule; G. Natta, *J. Polymer Sci.*, **34**, 21 (1959); M. L. Copper and J. B. Rose, *J. Chem. Soc.*, 795 (1959). There is a close analogy between termination by transfer to monomer in the Ziegler polymerization and the Grignard exchange reaction.

[13] H. C. Brown, *Tetrahedron*, **12**, 117 (1961).

[14] It is assumed that isomerization occurs by addition of the metal hydride to the propylene formed in 3.

[15] P. D. George and J. R. Ladd, Paper presented at the 140th Meeting of the American Chemical Society, Chicago, Illinois, September (1961); *J. Org. Chem.*, **27**, 340 (1962).

Table I

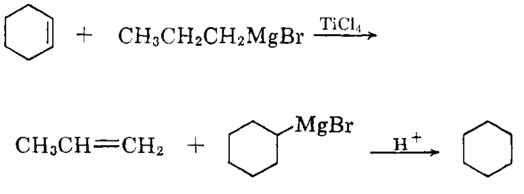
Reactions of Grignard Reagents Prepared by Exchange of Olefins with *n*-Propylmagnesium Bromide

Olefin	Reagent	Product
1-Pentene	HCHO	1-Hexanol (45%)[a]
1-Hexane	Cyclohexanone	1-Hexylcyclohexanol (24%)
1-Octene	CO_2, CH_3OH	Methyl pelargonate (40%)
1-Octene	$HC(OC_2H_5)_3$	Pelargonaldehyde acetal (19%)
3-Methyl-1-butene	C_6H_5CHO	1-Phenyl-4-methyl-pentanol-1 (35%)
4-Methyl-1-pentene	CH_3CHO	6-Methylheptanol-2 (37%)
Allylbenzene	CO_2	γ-Phenylbutyric acid (62%)
Vinylcyclohexane	CO_2	β-Cyclohexylpropionic acid (51%)

[a] Ref. 2.

Grignard reactions,[16] but even with carbon dioxide the maximum yield was 60% (of γ-phenylbutyric acid from allylbenzene) and 40–50% yields were more common.[17] The discrepancy between the observed and theoretical yields is largely due to the side reactions which occur in all Grignard reactions, as well as to the impossibility of obtaining a quantitative recovery of the reaction product on the relatively small scale of these experiments. It appears, however, that this is not the complete explanation. A substantial amount of high-boiling residue remained in each case after distillation of the major product. This residue apparently contains some low molecular weight hydrocarbon polymer,[18] as well as other products not yet identified. An investigation of these by-products is in progress.

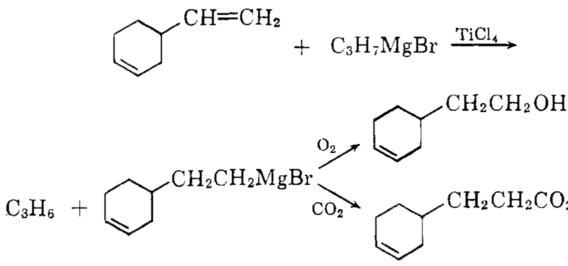
Other Types of Olefins.—The work previously reported indicated that internal olefins exchange only slowly, if at all, with Grignard reagents; no cyclohexanecarboxylic acid was obtained when cyclohexene was refluxed with *n*-propylmagnesium bromide and titanium tetrachloride under the conditions described above and the product then allowed to react with carbon dioxide. A more thorough study has confirmed that internal double bonds do not undergo the exchange reaction and has shown that terminal vinylidene groups are also unaffected. Mixtures of olefin, Grignard reagent, and titanium tetrachloride were heated under reflux in ether and samples were withdrawn periodically, decomposed with dilute acid, and analyzed by gas chromatography for the saturated hydrocarbon which would be produced if exchange occurred, for example:



(6)

No exchange was observed with cyclohexene, 2-pentene, *trans*-stilbene, β-methylstyrene, 2-methyl-1-pentene, or α-methylstyrene under the conditions described above, even with reaction times as long as 144 hours in some cases. Other Grignard reagents (isopropylmagnesium bromide, 3-amylmagnesium bromide, and isobutylmagnesium chloride,[19] and other catalysts (alkylorthotitanates and zirconium tetrachloride) were tested without success with these olefins.

Olefins Containing Two Types of Double Bonds.—The fact that exchange takes place only with terminal vinyl groups ($RCH_2{=}CH_2$) seriously restricts the synthetic uses of the reaction, but at the same time it makes possible the selective reaction of a single double bond in unconjugated dienes. Thus, a 40% yield of β-cyclohexenylethanol was obtained on exchange of 4-vinylcyclohexene with *n*-propylmagnesium bromide followed by air oxidation, and reaction with carbon dioxide produced a 28% yield of β-cyclohexenylpropionic acid.



(7

Selective exchange in a hydrocarbon having both vinyl and vinylidene groups is illustrated by isolation of a 45% yield of 5-methylhex-5-ene-1-ol on exchange of 2-methylhexadiene-1,5-followed by air oxidation.

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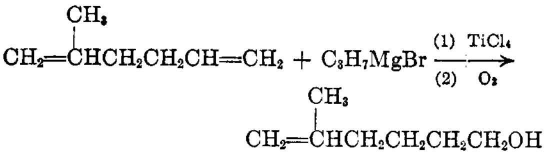
[16] M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, p. 913.

[17] Yields in all cases would be approximately 10% higher if calculated on the basis of the Grignard reagent, which is the actual limiting factor, rather than the alkyl halide, but the method employed is more realistic as a measure of synthetic utility.

[18] The combination of a Grignard reagent and titanium tetrachloride belongs to the family of Ziegler polymerization catalysts, although in ether and at the ratio used in this work it is very ineffective.

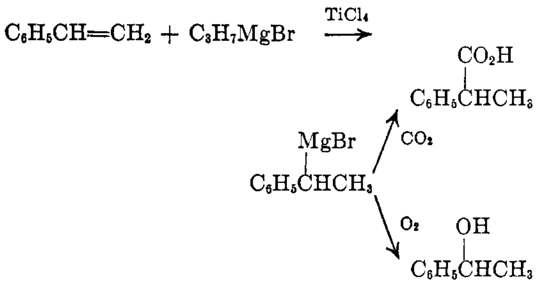
[19] The success of the exchange as ordinarily carried out is due to the removal of propylene from the reaction mixture as it is formed. The discovery that both vinylidene and vinylene double bonds are unreactive leads to the prediction that higher molecular weight Grignard reagents should exchange well provided their structure is such as to yield an unreactive type of olefin in the elimination step 3. This prediction is only partly verified. 2-Methylbutyl- and isobutylmagnesium halides, which form vinylidene compounds, are as effective as *n*-propylmagnesium bromide, but 3-amylmagnesium bromide, which forms 2-pentene, gives much lower yields than *n*-propylmagnesium bromide.



$$CH_2{=}\overset{CH_3}{C}HCH_2CH_2CH{=}CH_2 + C_3H_7MgBr \xrightarrow[(2)\ O_2]{(1)\ TiCl_4} CH_2{=}\overset{CH_3}{C}HCH_2CH_2CH_2CH_2OH \quad (8)$$

Conjugated Dienes with Styrene.—Conjugated dienes such as butadiene or isoprene exchange with n-propylmagnesium bromide, but the reaction is complex and only small yields of products corresponding to the mono Grignard reagent are obtained. Styrene and certain substituted styrenes, however, exchange readily and upon oxidation or carbonation give alcohols or carboxylic acids in yields similar to those obtained from the 1-alkenes listed in Table I. However, the products are those corresponding to the secondary Grignard reagent, $\overset{MgBr}{\text{ArCHCH}_3}$, rather than the terminal Grignard reagent as in the case of the alkenes. Exchange of p-methoxystyrene followed by reaction with carbon dioxide yielded 50% of crude acid from which a 22% yield of p-methoxyhydratropic acid was isolated on recrystallization.[20]

From styrene itself there was obtained a 51% yield of hydratropic acid on carbonation or a 40% yield of α-phenylethyl alcohol on air oxidation of the Grignard reagent.



$$C_6H_5CH{=}CH_2 + C_3H_7MgBr \xrightarrow{TiCl_4} C_6H_5\overset{MgBr}{C}HCH_3 \begin{cases} \xrightarrow{CO_2} C_6H_5\overset{CO_2H}{C}HCH_3 \\ \xrightarrow{O_2} C_6H_5\overset{OH}{C}HCH_3 \end{cases} \quad (9)$$

Gas chromatographic analysis of the oxidation product showed that small amounts of β-phenylethyl alcohol were also formed. In several experiments carried out under the conditions described above the α/β ratio varied from 25:1 to 40:1.[21]

The preferential formation of the alpha Grignard reagent from styrene represents a major difference between the Grignard exchange and the somewhat analogous hydroboration reaction of olefins. In the hydroboration reaction a boron hydride adds across the double bond of the olefin, while the reaction sequence suggested above for the exchange reaction involves addition of a titanium hydride. Inasmuch as the direction of polarization of the M—H bond is the same in both cases it might be expected that the direction of addition also would be the same, but hydroboration of styrene yields predominantly β-phenylethylborane.[13,22]

Alkyllithium and Alkylaluminum Compounds.—In addition to the alkylmagnesium halides, two other organometallic compounds were very briefly investigated. Some exchange occurs with n-propyllithium, as shown by the formation of 9% of n-octane when the reaction mixture from 1-octene, n-propyllithium, and titanium tetrachloride was decomposed with dilute acid. Alkylaluminum compounds do not undergo the exchange reaction to any significant extent under the conditions used in this work; no ethylbenzene could be detected from styrene, triisobutylaluminum and titanium tetrachloride.

Other Catalysts.—In addition to titanium tetrachloride a number of other compounds of titanium and a few other transition metals have been examined as catalysts for the Grignard exchange reaction. The relative effectiveness of some of these compounds may be estimated by comparing the yields of 1-hexanol isolated when a mixture of 1-pentene, n-propylmagnesium bromide, and catalyst, in the ratios and under the conditions described in preceding sections, was allowed to react with formaldehyde (Table II). Titanium tetrachloride was substantially more effective than any of the other compounds tested, but moderate (20–30%) yields of 1-hexanol were obtained with vanadium tetrachloride, zirconium tetrachloride, isopropyl titanate, and dicyclopentadienyltitanium dichloride. In addition to the compounds listed, several other titanium esters were successfully used as catalysts for the exchange of styrene and

TABLE II

1-HEXANOL FROM $CH_3CH_2CH_2MgBr$ + $CH_3CH_2CH_2CH{=}CH_2$ + HCHO

Catalyst	Yield of 1-hexanol (%)
$TiCl_4$	45
$Ti[OCH(CH_3)_2]_4$	23
$(C_5H_5)_2TiCl_2$	20
$ZrCl_4$	31
VCl_4	28

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[20] Although this is not a high yield, it illustrates the preparative value of the Grignard exchange procedure. To assure the identification of this compound an authentic sample was prepared by the only previously reported method [V. N. Gupta and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **44A**, 223 (1957)]. This is a four-step synthesis from p-methoxyacetophenone which requires several days and gives an 8% over-all yield of the acid.

[21] The report (ref. 1) that the α/β ratio in styrene exchange was approximately 100:1 was based on preliminary experiments using isobutylmagnesium chloride as the Grignard reagent. Later work has shown that n-propylmagnesium bromide gives substantially lower ratios, although the alpha isomer is still by far the major product. The product ratio is sensitive to variation in reaction conditions, as well as to the nature of the substituent group in substituted styrenes. These effects are being studied and the results will be reported when the investigation has been completed.

[22] The Grignard exchange reaction yields the thermodynamically more stable isomer (*i.e.*, that corresponding to the more stable carbanion) with both styrene and the 1-alkenes. The order of stability of simple carbanions is primary > secondary > tertiary [A. Schriesheim, J. E. Hofmann, and C. A. Rowe, Jr., *J. Am. Chem. Soc.*, **83**, 3731 (1961)], while resonance with the aromatic ring makes the alpha phenylethyl carbanion more stable than the beta isomer.

n-propylmagnesium bromide.[23] Ferric chloride also catalyzed this exchange, giving a 15% yield (estimated by gas chromatographic analysis) of phenylethyl alcohols on oxidation, but the reaction is extremely complex, and a large number of products, most of which have not yet been identified, are formed. All of the compounds tested gave an immediate precipitate on addition to the Grignard solution except for dicyclopentadienyltitanium dichloride. With this compound no precipitate was formed initially and the solution remained homogeneous for several hours, but there appeared to be a small amount of finely divided solid after seventeen hours.

Utility.—With the exception of the alpha arylethyl compounds the olefin exchange method for preparation of the Grignard reagent is inferior to the conventional method, providing the appropriate alkyl halide is available. Yields of products from *n*-amylmagnesium bromide were 10–20% lower when the Grignard reagent was prepared by exchange of 1-pentene with *n*-propylmagnesium bromide than in experiments on the same scale in which the Grignard reagent was prepared directly from amyl bromide. The method is useful, however, when the olefin is available and the halide is not, particularly as the Grignard reagent produced is not that corresponding to normal Markownikoff addition of hydrogen halide to the olefin. It should be particularly useful in the case of dienes having a terminal vinyl group.

The exchange method is superior to the conventional method for syntheses involving alpha-phenylethylmagnesium bromide, and probably for other alpha-arylethyl compounds. When these Grignard reagents are prepared from the halides. in the usual manner the major products are those arising from coupling and dehydrohalogenation. Stobbe[24] obtained only 2,3-diphenylbutane when he attempted to prepare the Grignard reagent from α-phenylethyl bromide and magnesium, but other workers[25,26] have reported low yields (7–16%) of hydratropic acid from reaction of carbon dioxide with the Grignard reagent prepared in this way. By the Grignard exchange procedure, hydratropic acid was obtained in 51% yield.

Experimental

Preparation of *n*-Propylmagnesium Bromide and Exchange with Olefins.—Two variations of the exchange procedure were used. In both modifications *n*-propylmagnesium bromide was prepared by adding 0.5 mole of *n*-propyl bromide in 50 ml. of diethyl ether to 0.55 g.-atom of magnesium in 150 ml. of ether over a period of 20 min. The solution was then heated under reflux for 10 min. In one method (procedure A) the stirred solution was cooled to 0° and 0.5 mole of the olefin was added, followed by 1.0 ml. of titanium tetrachloride. The mixture was heated under reflux for 2 hr., cooled to 0°, 0.45 ml. of titanium tetrachloride was added, and heating was then continued for an additional 14 hr. The resulting dark mixture, which usually appeared to consist of two liquid phases, was cooled, 200 ml. of ether was added, and the desired reaction carried out. In the other method (procedure B) the Grignard reagent was prepared as above, 200 ml. of ether was added, and the solution was cooled to 0°. The olefin was then added, followed by 1.45 ml. of titanium tetrachloride, and the mixture was refluxed for 16 hr.

1-Hexylcyclohexanol from 1-Hexene.—1-Hexene (42 g., 0.5 mole) was exchanged according to procedure A. The mixture was cooled to 0°, and 73.5 g. (0.75 mole) of cyclohexanone was added dropwise. The mixture was stirred for 1 hr. at room temperature and the magnesium salt decomposed by the addition of a 20% solution of ammonium chloride. The ether layer was decanted and distilled, yielding 21.5 g. (24%) of 1-hexylcyclohexanol, b.p. 114–116° (4 mm.), n^{20}D 1.4645; lit.,[27] b.p. 114–117° (7 mm.), n^{20}D 1.4645. The phenylurethane melted at 85–86°; reported,[27] m.p. 88.5–89°.

Methyl Pelargonate from 1-Octene.—1-Octene (56 g., 0.5 mole) was exchanged according to procedure B. The mixture was cooled and allowed to react with dry gaseous carbon dioxide at −5 to −10°. When the reaction was complete the mixture was cooled with Dry Ice and 200 ml. of methanol was added at −20 to −30°. A rapid stream of dry hydrogen chloride was then passed into the reaction vessel at −20° for 1 hr., after which the mixture was allowed to warm to room temperature and the addition of hydrogen chloride was continued for another hour. The reaction mixture was poured over ice and the organic phase was separated and distilled, yielding 34.3 g. (40%) of methyl pelargonate, b.p. 97–99° (12 mm.), n^{20}D 1.4205; lit.,[28] b.p. 80° (5 mm.), n^{20}D 1.4214. In addition approximately 5 g. of pelargonic acid was isolated.

Pelargonaldehyde Diethylacetal.—1-Octene (56 g., 0.5 mole) was exchanged with *n*-propylmagnesium bromide according to procedure B. The mixture was cooled and ethyl orthoformate (76 g., 0.5 mole) added. The reaction mixture was heated to reflux for 60 hr. and then cooled to room temperature. After the solid material had settled the ether layer was decanted, the solid washed with two 200-ml. portions of ether and the ether extracts combined and dried over magnesium sulfate. Distillation gave 21.2 g. (19%) of pelargonaldehyde diethyl acetal, b.p. 64–66° (0.25 mm.), n^{20}D 1.4219, lit.,[29] b.p. 130° (20 mm.).

Anal. Calcd. for $C_{13}H_{28}O_2$: C, 72.22; H, 12.95. Found: C, 72.8; H, 13.34.

A few drops of the product were converted to the 2,4-dinitrophenylhydrazone m.p. 102–104°; lit.,[30] m.p. 106.5°.

1-Phenyl-4-methylpentanol-1 from 3-Methylbutene-1.—The Grignard reagent was prepared by exchange of 35 g. (0.5 mole) of 3-methylbutene-1 according to procedure B. Benzaldehyde (40 g., 0.38 mole) was added over a period of 1 hr. at room temperature and the mixture was poured over a mixture of ice and 36% hydrochloric acid. The organic phase was washed with 10% sodium carbonate solution, dried over magnesium sulfate, and distilled, yielding 30.9 g. (35%, based on the olefin) of 1-phenyl-4-methylpentanol-1, b.p. 114–115° (5 mm.), n^{20}D 1.5063; lit.,[31] b.p. 130° (8 mm.), n^{19}D 1.5071.

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[23] The alkyl titanates appear to be almost as effective as titanium tetrachloride, but require a somewhat longer reaction time. Yields of hydratropic acid were 40–45% with the titanates, compared to 51% with titanium tetrachloride.

[24] H. Stobbe and G. Posnjak, *Ann.*, **371**, 287 (1909).

[25] J. Salkind and M. S. Peschekerowa, *J. Russ. Phys. Chem.*, **46**, 478 (1913).

[26] H. L. Cohen and G. F. Wright, *J. Org. Chem.*, **18**, 432 (1953).

[27] W. H. Urry, F. W. Stacey, E. S. Huyser, and O. O. Juveland, *J. Am. Chem. Soc.*, **76**, 450 (1954).

[28] H. Walbaum and A. Rosenthal, *J. prakt. Chem.* [2], **124**, 60 (1930).

[29] P. Bagard, *Bull. soc. chim. France* [4], **1**, 352.

[30] G. King, *J. Chem. Soc.*, 387 (1942).

[31] V. Grignard, *Compt. rend.*, 623 (1901).

6-Methylheptanol-2 from 4-Methylpentene-1.—The Grignard reagent was prepared by exchange of 42 g. (0.5 mole) of 4-methylpentene-1 with *n*-propylmagnesium bromide according to procedure A. The mixture was cooled to 0° and a solution of 33 ml. of acetaldehyde in 75 ml. of diethyl ether was added over a period of 1 hr. The magnesium salt was decomposed by the addition of a 20% solution of ammonium chloride and the ether layer was decanted and distilled, yielding 24.2 g. (37%) of 6-methylheptanol-2, b.p. 82–85° (22 mm.), n^{20}_{D} 1.4248. The literature[32] reports b.p. 80° (25 mm.), n^{20}_{D} 1.4250.

γ-Phenylbutyric Acid from Allylbenzene.—Allylbenzene (59 g., 0.5 mole) was exchanged following procedure A. The mixture was cooled in an ice–salt bath, allowed to react with dry carbon dioxide at −5 to −10°, and then decomposed with ice and 20% sulfuric acid. The ether layer was separated and extracted with three 30-ml. portions of 25% sodium hydroxide solution, adding more water when necessary to dissolve the thick soap produced in the first extraction. The combined basic extracts were distilled at atmospheric pressure until most of the volatile organic material was removed, and then cooled and acidified with concentrated hydrochloric acid, causing the separation of a yellow solid. The mixture was extracted with ether and the ether removed at 50° in a rotating film evaporator. On cooling the residual oil solidified, yielding 50.9 g. (62%) of waxy plates of γ-phenylbutyric acid, m.p. 44–46°. Recrystallization from water increased the melting point to 50.5–51°; lit.,[33] m.p. 51°.

β-Cyclohexylpropionic Acid from Vinylcyclohexane.—A Grignard reagent was prepared from 55 g. (0.5 mole) of vinylcyclohexane by exchange with *n*-propylmagnesium bromide following procedure A. The mixture was allowed to react with carbon dioxide, extracted with sodium hydroxide solution, and acidified as in the previous example. The mixture was extracted with diethyl ether and distilled, yielding 38.2 g. (51%) of β-cyclohexylpropionic acid, b.p. 114–115° (1.5 mm.), n^{20}_{D} 1.4634; lit.,[34] b.p. 125–126° (4 mm.), n^{20}_{D} 1.4634. The amide melted at 118–119°; the reported[35] value is 120°.

β-(Δ^3-Cyclohexenyl)ethanol from 4-Vinylcyclohexene.—4-Vinylcyclohexene (54 g., 0.5 mole) was exchanged with *n*-propylmagnesium bromide following procedure B, and the reaction mixture was oxidized with dry air according to the procedure of Goebel and Marvel.[36] Distillation yielded 25.0 g. (40%) of β-(Δ^3-cyclohexenyl)ethanol, b.p. 92–94° (4 mm.), n^{20}_{D} 1.4834; lit.,[37] b.p. 86–87° (6 mm.), n^{20}_{D} 1.4835. The infrared spectrum and GPC retention time of this material were identical with that of an authentic sample prepared by another method.[38]

β-(Δ^3-Cyclohexenyl)propionic Acid from 4-Vinylcyclohexene.—The Grignard reagent was prepared from 54 g. (0.5 mole) of 4-vinylcyclohexene as in the experiment above and was then allowed to react with carbon dioxide as in previous examples. Distillation yielded 22 g. (28.5%) of an unsaturated acid boiling at 99–102° (2 mm.), m.p. 31–32°, n^{38}_{D} 1.4732.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.1; H, 9.2; neut. equiv., 154. Found: C, 69.8; H, 9.3; neut. equiv., 156.

The acid readily absorbed one mole of hydrogen over a platinum catalyst, giving a quantitative yield of β-cyclohexylpropionic acid. The Δ^3 position of the double bond was considered established by analogy with the cyclohexenyl ethanol in the previous experiment, and was confirmed by a study of the proton magnetic resonance spectra of a series of substituted cyclohexenes.[39]

Hydratropic Acid from Styrene.—Styrene (52 g., 0.5 mole) was exchanged with *n*-propylmagnesium bromide according to procedure A, and the product was allowed to react with carbon dioxide and worked up in the usual manner, yielding 37.9 g. (51%) of hydratropic acid, b.p. 122° (3 mm.), n^{20}_{D} 1.5230; lit.,[40] b.p. 131–132° (4.9 mm.), n^{25}_{D} 1.5213.

A similar experiment using a total of 3.6 g. of amyl titanate as the catalyst yielded 34.5 g. (46%) of hydratropic acid, b.p. 127–133° (4–5 mm.), n^{20}_{D} 1.5238.

***p*-Methoxyhydratropic Acid from *p*-Methoxystyrene.**—To a solution of *n*-propylmagnesium bromide prepared from 0.1 mole of *n*-propyl bromide in 40 ml. of ether was added 13.4 g. (0.1 mole) of *p*-methoxystyrene, followed by 0.4 ml. (0.7 g.) of titanium tetrachloride. The mixture was refluxed for 2 hr., cooled to 0°, a second portion of 0.1 ml. (0.176 g.) of titanium tetrachloride was added, and refluxing continued for another 18 hr. After treatment with carbon dioxide the product was worked up in the usual manner by extracting with sodium hydroxide solution, acidifying with hydrochloric acid, and extracting the acid with diethyl ether. After the ether was stripped off there remained 8.6 g. of viscous brown oil having a neutral equivalent of 194 (calcd. for $C_{10}H_{12}O_3$, 180). The oil was refluxed with 500 ml. of water and 5 g. of decolorizing carbon and filtered. On cooling the filtrate to 0°, 2.2 g. of colorless crystals, m.p. 54–56°, were obtained. Extraction of the residue remaining in the flask and the decolorizing carbon with another 500 ml. of boiling water yielded a second crop of 1.1 g., m.p. 54–56°, making up a total yield of 22% of *p*-methoxyhydratropic acid. Recrystallization from benzene–petroleum ether raised the melting point to 55.5–56°; lit.,[20] m.p. 55–57°. A mixture with an authentic sample of *p*-methoxyhydratropic acid, prepared in 8% yield by the method of Gupta and Seshedri,[20] melted at 55–56°.

α-Phenylethyl Alcohol from Styrene.—A Grignard reagent was prepared from 41.5 g. (0.5 mole) of isobutyl chloride and the exchange with styrene was carried out according to procedure B. The mixture was oxidized with air and worked up as previously described, yielding 24.2 g. (40%) of α-phenylethyl alcohol, b.p. 91–92° (7 mm.), n^{20}_{D} 1.5267; lit.,[41] b.p. 91–92° (7 mm.), $n^{22.5}_{\mathrm{D}}$ 1.5248. Analysis by gas chromatography showed less than 1% of β-phenylethyl alcohol. Analysis of the crude product before distillation showed an α/β ratio of 85:1.

5-Methylhex-5-en-1-ol from 5-Methylhexadiene-1,5.—Exchange of 48 g. (0.5 mole) of 5-methylhexadiene-1,5 according to procedure A, followed by air oxidation, yielded 25.7 g. (45%) of alcohol having b.p. 74–76° (10 mm.), n^{20}_{D} 1.4447; the reported constants for 5-methylhex-5-en-1-ol are b.p. 71° (11 mm.), n^{20}_{D} 1.4415.[42]

The infrared spectrum showed a strong vinylidene absorption at 880 cm.$^{-1}$ as well as a very weak band at 975 cm.$^{-1}$, probably due to a small amount of *trans*-vinylene unsaturation, but no detectable absorption attributable to vinyl groups. Gas chromatography indicated that this material was more than 95% a single compound, but with small (1–2%) amounts of two other unidentified compounds and traces of a third.

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[32] V. Herout, M. Zaoral, and F. Sorin, *Collection Czech. Chem. Commun.*, **18**, 122 (1953).

[33] S. Skraup and S. Schwamberger, *Ann.*, **462**, 135 (1928).

[34] G. S. Hiers and R. Adams, *J. Am. Chem. Soc.*, **48**, 2385 (1926).

[35] N. Zelinsky, *Ber.*, **41**, 2676 (1908).

[36] M. T. Goebel and C. S. Marvel, *J. Am. Chem. Soc.*, **55**, 1693 (1933).

[37] H. C. Brown and G. Zweifel, *ibid.*, **83**, 1241 (1961).

[38] This sample was kindly provided by Dr. H. C. Brown.

[39] E. M. Balis, private communication.

[40] C. R. Hauser and W. R. Brasen, *J. Am. Chem. Soc.*, **78**, 494 (1956).

[41] F. D. Greene, *ibid.*, **77**, 4869 (1955).

[42] A. Eschenmoser and A. Frey, *Helv. Chim. Acta*, **35**, 1660 (1952).