fractions which were analyzed by gas chromatography using a 0.25″ × 6′ column packed with polypropylene glycol (30%) on firebrick.

The composition of the evolved gases was determined by the method of Kharasch, Lewis and Reynolds[21] and verified by gas chromatography with a 0.25″ × 50′ column packed with dimethyl sulfolane (30%) on firebrick.

The results of these experiments are given in Table I.

Reaction of Phenyllithium and Propylene Oxide in the Presence of Ferric Chloride.—Propylene oxide (17.4 g., 0.3 mole) in 100 ml. of ether was added dropwise into an ethereal solution of phenyllithium (0.77 mole) containing 5.5 g.

(21) M. S. Kharasch, D. W. Lewis and W. B. Reynolds, J. Am. Chem. Soc., 65, 495 (1943)

(0.0385 mole) of ferric chloride. The mixture was refluxed for 1 hour following the addition. No gas evolution was observed. After being cooled to 0–5°, the mixture was decomposed with a minimum quantity of saturated aqueous ammonium chloride solution. The ethereal layer was decanted and the residue was washed with ether (2 × 10 ml.). The combined ethereal solution was concentrated to a light brown oily residue (29 g.). A portion of the oil (14.5 g.) was chromatographed over alumina (200 g., Woelm Activity III). Biphenyl (0.75 g.) was isolated from the petroleum ether eluent. A yellow liquid (13.1 g.) was isolated from the ether eluent. Distillation of this liquid yielded 1-phenyl-2-propanol (12.6 g., 61%), b.p. 98–100° (15 mm.), n^{20}D 1.5210; 1-naphthylurethan, m.p. 92° alone or admixed with an authentic sample.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE INSTITUTE OF ORGANIC CHEMISTRY, THE UNIVERSITY OF CHICAGO, CHICAGO 37, ILL.]

Factors Influencing the Course and Mechanism of Grignard Reactions. XXIV. Reactions of 1,3-Disubstituted Compounds, 1,2-Hydrogen Atom Shift[1]

BY M. S. KHARASCH,[2] M. WEINER, W. NUDENBERG, ANIMA BHATTACHARYA,[3] TING-I WANG AND N. C. YANG[4]
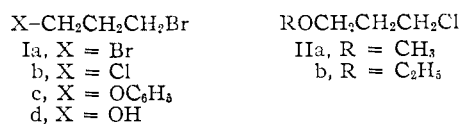
The reactions of 3-substituted 1-alkyl halides with phenylmagnesium bromide in the presence of ferric chloride were investigated. 1,3-Dibromopropane and 1-bromo-3-chloropropane gave cyclopropane; 3-ethoxy-1-chloropropane and 3-methoxy-1-chloropropane gave pure propylene, while 3-phenoxy-1-bromopropane gave a mixture of these two products. The formation of propylene in these reactions is interpreted via a 1,2-hydrogen atom shift of the intermediate 3-alkoxy-1-alkyl radical.

Simple alkyl halides react with Grignard reagents in the presence of transition metal halides to give alkanes, alkenes and alkyl dimers in various proportions.[5] The formation of these products may be rationalized from the disproportionation and dimerization of the intermediate alkyl radicals.

$$RX + R'MgX \xrightarrow[\text{halides}]{\text{transition metal}} R\cdot$$

$$R\cdot \begin{cases} R-R \\ RH + R_{-H} \end{cases}$$
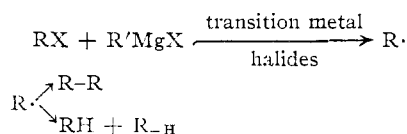
In several instances, the presence of these radicals was detected in appreciable concentration.[6] The introduction of a second functional group to the alkyl halide molecule has a direct influence on these reactions. In 2-substituted 1-alkyl halides, the main product was an alkene derived from the elimination of both functional groups.[7] This observation led subsequently to a systematic study of the reactions of modified Grignard reagents, i.e., combinations of Grignard reagents and transition metal salts, and bifunctional organic compounds. The present communication deals with the reactions of modified Grignard reagents

(1) Supported by grants from the National Science Foundation, No. NSF G-2624, and from the Research Corporation.

(2) Deceased.

(3) Firestone Tire and Rubber Co. Postdoctoral Fellow, 1957–1958.

(4) To whom inquiries on this paper may be sent; Alfred P. Sloan Foundation Fellow.

(5) M. S. Kharasch, J. K. Hambling and T. P. Rudy, J. Org. Chem., 24, 303 (1959), and references therein.

(6) (a) M. S. Kharasch and W. H. Urry, ibid., 13, 101 (1948); (b) M. S. Kharasch, R. D. Mulley and W. Nudenberg, ibid., 19, 1477 (1954); and (c) R. O. C. Norman and W. A. Waters, J. Chem. Soc., 950 (1957).

(7) M. S. Kharasch, et al., J. Am. Chem. Soc., 83, 3229 (1961).

with 3-substituted 1-alkyl halides, such as 1,3-dibromopropane (Ia), 1-bromo-3-chloropropane (Ib), 3-phenoxy-1-bromopropane (Ic), 3-methoxy-1-chloropropane (IIa), 3-ethoxy-1-chloropropane (IIb) and 3-bromo-1-propanol (Id), and trimethylene oxide.

$X-CH_2CH_2CH_2Br$	$ROCH_2CH_2CH_2Cl$
Ia, X = Br	IIa, R = CH₃
b, X = Cl	b, R = C₂H₅
c, X = OC₆H₅	
d, X = OH	

(Table values corrected: IIa, R = CH_3; b, R = C_2H_5)

1,3-Dihalopropanes and 3-halopropyl ethers do not react with phenylmagnesium bromide prepared from sublimed magnesium. In the presence of a small amount of ferric chloride, 1,3-dibromopropane (Ia) or 1-bromo-3-chloropropane (Ib) reacts with phenylmagnesium bromide to give a good yield (81–84%) of cyclopropane contaminated with small amount of propylene, while 1-methoxy-3-chloropropane (IIa) or 1-ethoxy-3-chloropropane (IIb) under similar conditions gives exclusively pure propylene (60–78%). In view of this surprising finding, the formation of propylene from 1,3-disubstituted propanes, the reaction of 3-phenoxy-1-bromopropane (Ic) with modified Grignard reagents[8] was reinvestigated. The result showed that a mixture of cyclopropane and propylene was obtained. The effectiveness of various transition metal salts as modifiers in these reactions were investigated and ferric chloride was found to be the most effective. 3-Bromo-1-propanol (Id) reacts with phenylmagnesium bromide in the presence of ferric chloride to give a moderate yield of propylene (38%); trimethylene oxide is quite

(8) M. S. Kharasch, G. Stampa and W. Nudenberg, J. Org. Chem., 18, 575 (1953).

unreactive under similar conditions. The results of these experiments are summarized in Table I.

Substrate, mole	Mole of C₆H₅· MgBr	Transition metal salt (mole)	Products, yield, %
BrCH₂CH₂CH₂Br, 0.35	0.76	FeCl₃, 0.038	Cyclopropane, 84ᵃ
BrCH₂CH₂CH₂Cl, 0.13	.29	FeCl₃, 0.006	Cyclopropane, 81ᵇ
PhOCH₂CH₂CH₂Br, 0.2	.5	FeCl₃, 0.025	Cyclopropane, 33 Propylene, 25
PhOCH₂CH₂CH₂Br, 0.2	.5	CoBr₂, 0.025	Cyclopropane, 26 Propylene, 25
CH₃OCH₂CH₂CH₂Cl, 0.3	.69	FeCl₃, 0.035	Propylene, 60–78ᶜ
CH₃OCH₂CH₂CH₂Cl, 0.2	.5	TiCl₄, 0.025	Propylene, 60
CH₃OCH₂CH₂CH₂Cl, 0.2	.5	CrCl₃, 0.025	Propylene, 11
CH₃OCH₂CH₂CH₂Cl, 0.2	.5	CoBr₂, 0.025	Propylene, 10
C₂H₅OCH₂CH₂CH₂Cl, 0.2	.5	FeCl₃, 0.025	Propylene, 66
C₂H₅OCH₂CH₂CH₂Cl, 0.2	.5	TiCl₄, 0.025	Propylene, 61
BrCH₂CH₂CH₂OH, 0.2	.8	FeCl₃, 0.04	Propylene, 38, 1-propanol, 5%, and 3-phenyl-1-propanol, 15
Trimethylene oxide, 0.2	.66	CoBr₂, 0.033	No gas evolution
Trimethylene oxide, 0.2	.66	FeCl₃, 0.033	Propylene, 7, 1-propanol (trace) and 3-phenyl-1-propanol, 5

ᵃ Cyclopropane is contaminated with 3.4% of propylene and traces (<0.05%) of ethane and ethylene. ᵇ Cyclopropane is contaminated with 4.6% of propylene and traces of ethane and ethylene. ᶜ Propylene is contaminated with less than 0.5% of cyclopropane. The yield of propylene ranges from 60–78% in six runs.
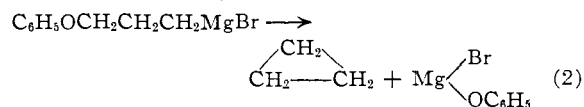
Discussion

3-Alkoxy-1-halopropanes (II) react with phenylmagnesium bromide in the presence of ferric chloride to give pure propylene, while 1,3-dihalopropanes gave essentially pure cyclopropane in over 80% yield under identical conditions. The formation of cyclopropane from 1,3-dihalopropanes indicated that cyclopropane does not undergo appreciable isomerization to propylene under the reaction conditions, nor does 1,3-dihalopropane isomerize to 1,2-dihalopropane prior to the reaction. Therefore, the formation of propylene from II cannot be attributed to the isomerization of cyclopropane and it is extremely unlikely that II would undergo appreciable isomerization to 1-alkoxy-2-halopropane (III) during the reaction. The latter assumption was substantiated by an experiment in which II was recovered unchanged from a boiling ethereal Grignard reagent.
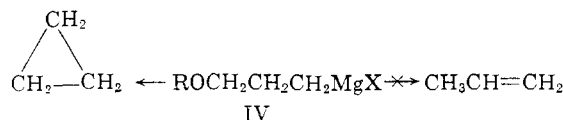
$$\underset{\underset{\text{X}}{|}}{ROCH_2CHCH_3} \quad III$$
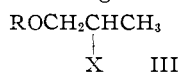
Recently Slaugh[9] suggested that functional exchange reaction may play an important role in the Kharasch reaction, i.e., modified Grignard reaction. The basis of his suggestion was derived from the isolation of cyclopropane from 3-phenoxy-1-bromopropane; 3-phenoxy-1-propylmagnesium bromide was postulated as a reaction intermediate (eq. 1) which underwent intramolecular displacement to give cyclopropane (eq. 2). Our recent finding indicated that the product is actually a mixture of propylene and cyclopropane. Functional exchange in modified Grignard reaction
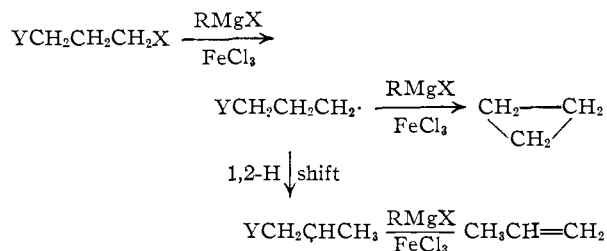
(9) L. Slaugh, J. Org. Chem., 26, in press (1961).

has been observed earlier in this Laboratory as a minor side reaction.[10] 3-Alkoxy-1-propylmagnesium bromide (IV) cannot be a key intermediate in the formation of propylene from II and modified Grignard reagent, because IV is known to be stable under the reaction condition which decom-

$$C_6H_5OCH_2CH_2CH_2Br + RMgBr \xrightarrow{CoBr_2}$$
$$C_6H_5OCH_2CH_2CH_2MgBr + RBr \quad (1)$$

$$C_6H_5OCH_2CH_2CH_2MgBr \longrightarrow$$
$$\underset{CH_2\text{------}CH_2}{\overset{CH_2}{\diagup \diagdown}} + Mg\underset{OC_6H_5}{\overset{Br}{\diagdown}} \quad (2)$$

poses upon warming to give cyclopropane and no propylene (eq. 3).[11] Functional exchange does not play an important role, if at all, in these reactions.

$$\underset{IV}{\underset{CH_2\text{------}CH_2}{\overset{CH_2}{\diagup \diagdown}}} \longleftarrow ROCH_2CH_2CH_2MgX \longrightarrow\!\!\!\!/\longrightarrow CH_3CH=CH_2$$

The formation of propylene from 3-alkoxy-1-halopropanes indicates there is a hydrogen migration during the reaction. Due to the high yield of propylene, there is no rational intermolecular hydrogen transfer process plausible to account for its formation. A rational explanation of the general reaction of 3-substituted 1-halopropanes with phenylmagnesium bromide in the presence of ferric chloride may be indicated by the equations

$$YCH_2CH_2CH_2X \xrightarrow[FeCl_3]{RMgX}$$

$$YCH_2CH_2CH_2· \xrightarrow[FeCl_3]{RMgX} \underset{CH_2}{\overset{CH_2\text{------}CH_2}{\diagdown \diagup}}$$

$$1,2\text{-H}\downarrow\text{shift}$$

$$YCH_2\overset{·}{C}HCH_3 \xrightarrow[FeCl_3]{RMgX} CH_3CH=CH_2$$

By analogy of the reactions between simple alkyl halide and 2-phenoxyethyl bromide with modified Grignard reagents,[6] it is reasonable to assume the formation of 3-substituted 1-alkyl radical as the initial step. The radical may undergo two possible reactions: (1) further attack by a reductant to give cyclopropane, or (2) rearrangement to give a more stable secondary radical followed by further reduction to give propylene. The relative proportions of the two products, cyclopropane and propylene, then will depend on the relative rates of these two competing reactions, which in turn will depend on the reactivity of the 3-substituents. In the case of 1,3-dihalopropane, owing to the high reactivity of the halogen atom toward reduction by the reduced iron salt, the radical is further attacked at the 3-position to give cyclopropane with the ring closure and the reduction taking place in rapid succession or in a concerted manner. In the case of 3-alkoxy-1-chloropropane (II), the alkoxyl group is relatively inert toward reduction, and the
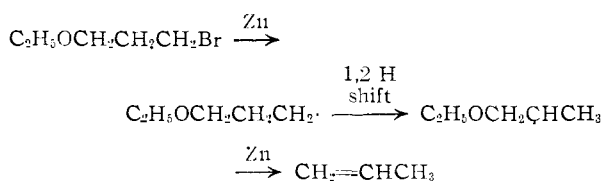
(10) M. S. Kharasch and C. F. Fuchs, ibid., 10, 292 (1945).

(11) J. G. Gragson, K. T. Greenlee, J. M. Derfer and C. E. Boord, ibid., 20, 275 (1955).

3-alkoxy-1-propyl radical generated will undergo a 1,2-hydrogen atom shift to give 1-alkoxy-2-propyl radical prior to further reduction by another equivalent of reduced iron salt. Therefore, only propylene is formed. Finally, in the case of 3-phenoxy-1-bromopropane, the phenoxyl groups are cleaved by modified Grignard reagents,[12] yet more sluggishly than the corresponding halides; reactions 1 and 2 become competitive and a mixture of propylene and cyclopropane is formed.

It has been generally accepted that the formation of cyclopropane from 1,3-dibromopropane and metals is due to an internal Wurtz reaction, i.e., an internal anionic displacement reaction.[13] However, Wolkoff and Menschutkin[13b] demonstrated that 3-ethoxy-1-bromopropane reacted with zinc in boiling ethanol yielding only propylene as the sole product of the reaction and they had postulated a rather complicated mechanism for its formation. The formation of propylene from the reaction of zinc and ethoxybromopropane parallels directly the modified Grignard reaction and it is best interpreted as a radical reaction. Therefore, the possible role of free radical intermediates in the reactions of metals and organic halides should be emphasized.

$$C_2H_5OCH_2CH_2CH_2Br \xrightarrow{Zn}$$

$$C_2H_5OCH_2CH_2CH_2\cdot \xrightarrow[\text{shift}]{1,2\ H} C_2H_5OCH_2CHCH_3$$

$$\xrightarrow{Zn} CH_2=CHCH_3$$

The reaction of 3-bromo-1-propanol with phenylmagnesium bromide in the presence of ferric chloride gives only a moderate yield (38%) of propylene with an appreciable amount of the bromohydrin recovered. The result may be rationalized by the low solubility of the magnesium salt of the bromohydrin in ether. Trimethylene oxide does not undergo cleavage to an appreciable extent by magnesium bromide[14] to give the magnesium salt of 3-bromo-1-propanol under the reaction conditions[15]; therefore, virtually no reaction was observed. Among transition metal salts tested as modifiers for the reaction of 3-methoxy-1-chloropropane and phenylmagnesium bromide, the high

(12) M. S. Kharasch and R. L. Huang, J. Org. Chem., 17, 669 (1952); R. L. Huang, J. Chem. Soc., 3084 (1954), and later papers.

(13) (a) A. Freund, J. prakt. Chem., [2] 26, 367 (1882); [2] 36, 300 (1887); (b) A. Wolkoff and B. W. Menschutkin, Ber., 31, 3067 (1898); (c) N. Zelinsky and J. Gutt, ibid., 40, 3049 (1907); and (d) J. F. Sirks, Rec. trav. chim., 62, 193 (1943).

(14) R. E. Dessy and G. S. Handler, J. Am. Chem. Soc., 80, 5824 (1958), and related papers.

(15) S. Searles, ibid., 73, 125 (1951).

efficiency of ferric chloride as a modifier may be attributed to its high solubility in ether.

Experimental[16]

1,3-Dibromopropane, 1-bromo-3-chloropropane and 3-bromo-1-propane were purchased from Eastman Kodak Co. 3-Phenoxy-1-bromopropane was prepared by the reaction of 1,3-dibromopropane and sodium phenolate.[8] 3-Ethoxy-1-chloropropane was prepared by the method of Smith and Sprung[17]; b.p. 128–129°, $n^{20}D$ 1.4160. 3-Methoxy-1-chloropropane was prepared by two alternative methods[18]; b.p. 110–111°, $n^{20}D$ 1.4130–1.4138. Trimethylene oxide was prepared by the method of Searles.[15] All these compounds were freshly distilled from a 0.5 × 60 cm. tantalum spiral column at 10:1 reflux ratio before use and were shown to be better than 96% purity by gas chromatography on a 0.25″ × 20′ column packed with 30% TCP on firebrick.

Phenylmagnesium bromide was prepared from freshly distilled bromobenzene and an excess of sublimed magnesium in ether. The solution was filtered under an atmosphere of nitrogen and its concentration was determined by acid–base titration. Aliquots of standardized solution were used for the experiments.

The Reaction Proper.—The reaction was performed in a three-neck flask fitted with a Friederichs condenser, a Tru-Bore stirrer and a Y-tube connected to two dropping funnels. The apparatus was flame-dried and flushed with nitrogen before the reaction. The exit of the condenser then was connected to a gas collecting bottle. Ice-water was circulated through the condenser to exclude ether from the evolved gas. The Grignard solution was placed in the flask. The reactant diluted with 3 volumes of ether was placed in one of the dropping funnels and a saturated solution of ferric chloride in ether was placed in the other. When transition metal halides other than ferric chloride was used, the salt was added directly to the Grignard reagent and a single dropping funnel was used instead of the Y-tube. About one-fourth of the ferric solution was added to the Grignard reagent followed by dropwise addition of the reactant. The rates of addition of the two solutions were adjusted so that a smooth reflux of the reaction mixture was maintained. The time for addition varied from 1–2 hours and the mixture was refluxed for 1 hour following the addition.

The composition of the evolved gas was determined either by infrared spectroscopy with a 15-cm. gas cell at gas pressures from 4–8 cm. and by gas chromatography with a 0.25″ × 50′ column packed with 25% dimethyl sulfolane on firebrick and helium as the carrier gas at flow rate of approximately 80 ml. per minute. The relative composition of cyclopropane and propylene was determined by the absorbance at 868 and 914 cm.$^{-1}$, respectively, in the infrared spectrum or by the relative peak area at 30 and 16 minutes, respectively, in the gas chromatogram. The quantitative values were checked by comparison with mixtures of known composition.

In certain cases, the high-boiling products were isolated by fractional distillation or by chromatography[7] and they were identified by preparation of derivatives and by comparison with authentic samples.

(16) All boiling points and melting points are uncorrected, gas chromatographic analyses were performed on a model 1111A Shell–Hallikainen chromograph, and infrared spectra were determined on a Perkin–Elmer model 21 infrared spectrophotometer.

(17) L. J. Smith and J. A. Sprung, J. Am. Chem. Soc., 65, 1279 (1943).

(18) (a) R. Paul, Ann. Chem., [10] 18, 315 (1932); and (b) E. Haworth and W. H. Perkin, J. Chem. Soc., 65, 597 (1894).