

the plots of $\log(1 - F)$ versus time are non-linear and flatten considerably at the higher fractions of exchange. However, initial rates can be easily obtained graphically.

In the experiment where the activities of thio- and isothiocyanate were separately measured, the separation of the two organic species was performed by treating the hexane layer with cyclohexylamine (100% excess, calculated on the isothiocyanate formed) and cooling at 0° for 30 minutes. The crystals (N-cyclohexyl-N'-benzhydrylthiourea) were filtered, washed with hexane and dissolved in ethanol.

Silver nitrate was added and the mixture refluxed. Silver sulfide was filtered off and oxidized to sulfuric acid with bromine. The hexane solution containing the unreacted benzhydryl thiocyanate was diluted with ethanolic silver nitrate and refluxed. The precipitate consisted largely of silver thiocyanate, but contained also traces of silver sulfide, presumably in part from incompletely separated thiourea. It was therefore heated with aqueous ammonia, filtered and the solution treated with nitric acid to precipitate silver thiocyanate, which was oxidized.

[CONTRIBUTION FROM THE SHELL DEVELOPMENT CO., EMERYVILLE, CALIF.]

The Reinterpretation of Several Kharasch Reactions. A Question of Free Radical Displacements at Saturated Carbon Atoms

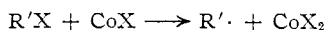
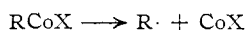
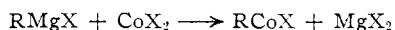
BY LYNN H. SLAUGH

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Many reactions of Grignard reagents with organic halides in the presence of cobaltous salts apparently involve the formation of free radicals by the removal of a halogen atom from the organic halide. It has been found that interchange reactions between the Grignard reagent and the organic halide are important competing reactions and may determine the product. For example, an interchange reaction producing, transiently, 3-phenoxypropylmagnesium bromide and not the formation of the 3-phenoxypropyl radical, as previously postulated, is believed to be responsible for cyclopropane formation during the cobaltous bromide-catalyzed reaction of 3-phenoxypropyl bromide with Grignard reagents. Other reactions of this type have been reinterpreted in light of this finding. The decomposition of di-*t*-butyl peroxide in a chlorobenzene solution containing 1-iodobutane was studied in a further search for a reaction involving a free radical displacement at a saturated carbon atom. *t*-Butyl *n*-butyl ether, the anticipated product of displacement on 1-iodobutane by the *t*-butoxy radical, was not detected in the product.

Introduction

Kharasch discovered that several transition metal salts, e.g., cobaltous chloride, catalyze a reaction between Grignard reagents and organic halides¹ (referred to hereafter as "Kharasch reactions"). He proposed the following mechanism to explain the formation of the observed products.



He postulated the formation of intermediate subhalides (CoX in the present case) which abstract halogen atoms from the organic halides to produce free radicals. The free radicals thus formed disproportionate, couple etc. The following are further evidences for the formation of free radicals. (a) 2,3-Dimethyl-2,3-diphenylbutane is formed when these reactions occur in a solvent containing cumene.² (b) Rearrangement products are obtained from the Kharasch reaction of neophyl chloride (1-chloro-2-methyl-2-phenylpropane).³ (c) 9,10-Dibenzyl-9,10-dihydroanthracene, 10,10'-dibenzyl-9,9',10,10'-tetrahydro-9,9'-dianthryl and a trace of 9,10-dibenzylanthracene result from the Kharasch reaction of benzyl chloride with benzylmagnesium chloride⁴ in the presence of anthracene.⁶

(1) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice Hall, Inc., New York, N. Y., 1954.

(2) M. S. Kharasch and W. H. Urry, *J. Org. Chem.*, **13**, 101 (1948).

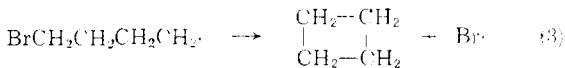
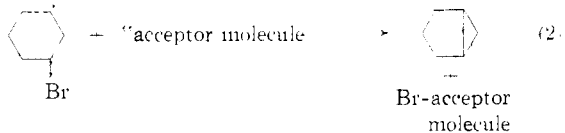
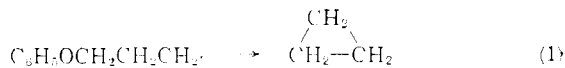
(3) W. H. Urry and M. S. Kharasch, *J. Am. Chem. Soc.*, **66**, 1438 (1944).

(4) Although evidences indicate that some Grignard reagents are best represented as $R_2Mg \cdot MgX_2$ they will be referred to as alkylmagnesium halides for simplicity in this publication.

(5) R. E. Dessy, G. S. Handler, J. H. Wotiz and C. A. Hollingsworth, *J. Am. Chem. Soc.*, **79**, 3476 (1957); R. E. Dessy and G. S. Handler, *ibid.*, **80**, 5824 (1958).

(6) R. O. C. Norman and W. A. Waters, *J. Chem. Soc.*, 950 (1957).

Several particularly interesting Kharasch reactions have resulted in the formation of cyclopropane from 3-phenoxypropyl bromide (I),⁷ bicyclo-[3.1.0]hexane from 1,3-dibromocyclohexane⁸ and cyclobutane from 1,4-dibromobutane⁹ or 4-phenoxybutyl bromide.^{7,9} These reactions have been interpreted as involving free radical intermediates (eq. 1-3).^{8,9}



Although it is unlikely, there is the possibility that the formation of the above products involved free radical displacements at saturated carbon atoms. Since this type of displacement is rare, it seemed of interest to reinvestigate the Kharasch reaction of I to form cyclopropane. It was further hoped that this study would shed light on the mechanisms of these and other Kharasch reactions.

Results and Discussion

Decarbonylation of 4-Phenoxybutyraldehyde.—To check the possibility that the cyclopropane from the Kharasch reaction of I was formed *via* the 3-phenoxypropyl radical, the latter was generated,

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

(8) M. S. Kharasch, J. S. Sallo and W. Nudenberg, *ibid.*, **21**, 129 (1956).

(9) W. B. Smith, *ibid.*, **23**, 509 (1958).

TABLE I
 REACTION OF BROMIDES WITH ETHYLMAGNESIUM BROMIDE

Experiment number Magnesium used to prepare G.R.	132 Reagent ^a	144 Reagent	158 Sublimed ^b	139 ^a Reagent	163 ^a Reagent	165 Reagent	18 ^c Sublimed ^b
Grignard reagent, mole	0.40	0.56	0.35	0.25	0.25	0.25	0.047
Organic bromide ^c	I	I	I	Ethyl	Ethyl	EPB	I
Mole	0.13	0.14	0.16	0.30	0.30	0.052	0.05
Metal halide catalyst	None	CoBr ₂	None	None	CoBr ₂	CoBr ₂	MnCl ₂
Mole % G.R.		3.0			3.0	3.0	3.0
Temperature, °C.	37	37	37	37	37	37	37
Hours for complete react.	10	1.0	>100 ^d	<20	1.0	1.0	~3.0
Gas product, moles/100 moles of organic bromide							
Methane	0.0	1.1	0.0	0.0	0.5	0.0	0
Ethane	100	107	<5.6	81	65	69	34
Ethylene	93	85	0.6	78	54	52	30
Propane } Propylene }	0.8	1.4	0.0	1.7	2.8	2.2	0.4
<i>n</i> -Butane	0.2	5.8	<1.0	0.3	8.8	4.8	0.4
<i>n</i> -Butene	0.8	1.1	<0.6	0.5	0.7	0.6	0
Cyclopropane	71	76	<1.2	0.0	20

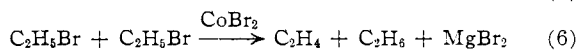
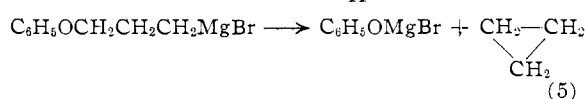
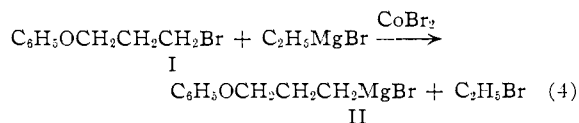
^a Mallinckrodt Grignard reagent grade magnesium; see Experimental section for analysis. ^b Triply-sublimed magnesium furnished by Dow Chemical Co. ^c I = 3-Phenoxypropyl bromide; EPB = 3-ethoxypropyl bromide. ^d No gas evolution observed after first 5 minutes. ^e The yield limiting reactant was the Grignard reagent.

in an unequivocal way, by the free radical-catalyzed decarbonylation of 4-phenoxybutyraldehyde. The 3-phenoxypropyl radical resulting from the decarbonylation should have nearly as much opportunity to form cyclopropane as the radical produced by the Kharasch reaction. The fact that the neophyl radical rearranges to comparable extents when generated by either method^{3,10} is in support of this. Nevertheless, so as to allow maximum opportunity for the 3-phenoxypropyl radical to decompose to cyclopropane, the decarbonylation was effected in chlorobenzene solution which was only 0.13 molar in aldehyde. The amount of carbon monoxide in the gas product corresponded to 56% decarbonylation of the aldehyde. Phenyl *n*-propyl ether, equivalent to 45% of the carbon monoxide, was identified as the major product.

Careful gas analyses showed that cyclopropane was not a product of the decarbonylation. This indicates that the 3-phenoxypropyl radical is not responsible for the cyclopropane formed during the cobaltous bromide-catalyzed reaction of I with Grignard reagents.

Possible Mechanism of Cyclopropane Formation during the Kharasch Reaction of 3-Phenoxypropyl Bromide (I).—Several reactions of excess ethylmagnesium bromide with I and other bromides were studied in the presence and absence of cobaltous bromide and manganous chloride (see Table I). The results of these experiments demonstrate that transition metal-catalyzed interchange reactions occur between Grignard reagents and organic halides during Kharasch reactions. They also suggest that at least part of the cyclopropane formed during the Kharasch reaction of I may be the result of a cobaltous bromide-catalyzed interchange of Grignard reagents with I to form 3-phenoxypropylmagnesium bromide (II) which then decomposes (eq. 4 and 5).

This mechanism, although not rigorously proved, is supported by the following observations: (1) The



catalytic effect of cobaltous bromide on the reaction was confirmed. In the absence of cobaltous bromide, little reaction occurred between I and ethylmagnesium bromide prepared from sublimed magnesium (Table I, 158). It is interesting that when the Grignard reagent was prepared from ordinary reagent grade magnesium (Table I, 132), a slow evolution of cyclopropane occurred. Apparently, some of the impurities in the reagent grade magnesium¹¹ have a catalytic effect similar to cobaltous salts. Manganese is one of the impurities likely to have catalytic activity. In this regard, manganous chloride was shown to be a catalyst for the reaction (Table I, 18). These data illustrate the importance of using sublimed magnesium for studies involving Grignard reagents where interchange reactions are to be avoided.

(2) It has been shown previously that the interchange of Grignard reagents with organic halides ($\text{RMgX} + \text{R}'\text{X} \rightleftharpoons \text{RX} + \text{R}'\text{MgX}$) is catalyzed by cobaltous halides.^{12,13} To demonstrate that

(11) See the Experimental section for detailed analyses of reagent grade and sublimed magnesium metals.

(12) M. S. Kharasch and C. Fuchs, *J. Org. Chem.*, **10**, 292 (1945).

(13) H. Gilman and H. L. Jones, *J. Am. Chem. Soc.*, **51**, 2840 (1929), did not observe interchange reactions between Grignard reagents and organic halides in the absence of transition metal salts. However, R. T. Morrison (Absts., of papers presented at the ACS meeting, Cleveland, Ohio, April 5-14, 1960, p. 20) has recently observed an interchange reaction between Grignard reagents and benzyl chloride in the absence of added transition metal salts. We have re-examined this reaction using ethylmagnesium bromide prepared from sublimed magnesium. Using isotopic tracer techniques we found also that a slow interchange occurred, in the absence of added transition metal salts, to give benzylmagnesium chloride. We found the reaction to

(10) F. H. Seubold, Jr., *J. Am. Chem. Soc.*, **75**, 2532 (1953).

interchange reactions, such as eq. 4, do occur under the present conditions (refluxing ether), 3-ethoxypropyl bromide, similar structurally to I but known to form stable Grignard reagents at 35°,¹⁴ was treated with excess ethylmagnesium bromide in the presence of cobaltous bromide (Table I, 165). Using isotopic tracer techniques (see Experimental section), it was shown that a 63% yield of 3-ethoxypropylmagnesium bromide was formed. It is likely that Compound I also would undergo interchange reactions to form II under these same conditions. However, when this same experiment was repeated with I instead of 3-ethoxypropyl bromide, II was not detected (<0.001%, by isotopic tracer techniques). Cyclopropane was formed instead. Further evidence for the interchange of I with ethylmagnesium bromide to form II was obtained by carrying out the reaction in the presence of cobaltous bromide at -10°. Under these conditions the evolution of cyclopropane was slow and it was possible to show by isotopic tracer techniques that a 6% yield of II was obtained (see Experimental section).

(4) The decomposition of 3-alkoxypropyl Grignard reagents to cyclopropane, as depicted by eq. 5, is well known,¹⁴ and has been used as a preparative procedure for substituted cyclopropanes.¹⁵ For example, 3-ethoxypropylmagnesium bromide decomposes to give cyclopropane when heated in benzene to ~75°. Since the phenoxide ion probably is more easily eliminated than the ethoxide ion, it is not unexpected that II would be too unstable to detect at 35°. This was shown to be the case. 3-Phenoxypropylmagnesium bromide (II) was prepared in low but significant yields (0.020 ± 0.001%; determined by isotopic tracer techniques) by the reaction of sublimed magnesium with I in ether at 5 to 10°. When the cold Grignard solution was separated from the excess magnesium and heated to reflux (35°) for 45 minutes, II completely decomposed (0 ± 0.001% yield).¹⁶

(5) For each mole of ethylmagnesium bromide that interchanges with I or with 3-ethoxypropyl bromide, one mole of ethyl bromide is formed. Consequently, the ethyl bromide should react with a second mole of ethylmagnesium bromide, according to known Kharasch reactions,¹⁷ to give a combined yield of approximately two moles of ethane plus ethylene (eq. 6). This is in accord with the yields obtained experimentally (Table I, 132, 144 and 165). Furthermore, under all experimental conditions where interchange reactions about twenty times faster when unsublimed magnesium was used for the Grignard reagent preparation.

(14) N. Rabjohn and M. S. Cohen, *J. Am. Chem. Soc.*, **74**, 6290 (1952).

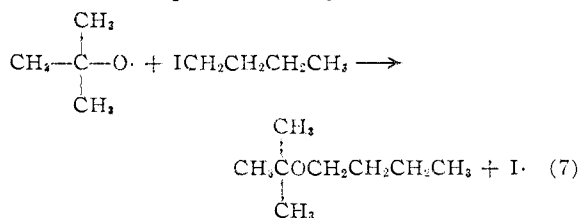
(15) J. T. Gragson, K. W. Greenlee, J. M. Derfer and C. F. Boord, *J. Org. Chem.*, **20**, 275 (1955).

(16) Cyclopropane (0.012 mole) was given off, upon heating, equivalent to a ~50% yield of II. This high yield of cyclopropane was unexpected since only 0.020 ± 0.001% of II was detected by isotopic tracer techniques. It may be that part of the cyclopropane was formed at the lower temperature (in fact, a slow evolution of cyclopropane was observed at 5 to 10°) and was distilled off when the solution was refluxed. Also, it may be that the isotopic tracer technique did not detect all of II present. Most of II may have decomposed to cyclopropane upon treatment with tritium labeled ethanol instead of hydrolyzing to phenyl *n*-propyl ether.

(17) M. S. Kharasch, D. W. Lewis and W. B. Reynolds, *J. Am. Chem. Soc.*, **65**, 493 (1943).

tions occurred, ethyl bromide was shown to react with ethylmagnesium bromide (Table I, 139 and 163).

Decomposition of Di-*t*-butyl Peroxide in a Chlorobenzene Solution Containing 1-Iodobutane.—As shown, the 3-phenoxypropyl radical apparently does not cyclize to give cyclopropane. In a further search for a possible free radical displacement at a saturated carbon atom, the decomposition of di-*t*-butyl peroxide in a chlorobenzene solution containing 1-iodobutane was investigated. The displacement of an iodine atom by the *t*-butoxy radical would produce *t*-butyl *n*-butyl ether (eq. 7).



However, this ether was not detected in the liquid product. Based upon the amount of *t*-butyl alcohol formed (a measure of the minimum amount of *t*-butoxy radicals produced) and the limits of *t*-butyl *n*-butyl ether detection (gas chromatography), the maximum amount of displacement of iodine atoms by the *t*-butoxy radicals could be only 0.4%.

Conclusions and Comments on other Kharasch Reactions.—Many reactions of Grignard reagents with organic halides in the presence of transition metal salts apparently involve the formation of free radicals by the removal of a halogen atom from the organic halide.^{1-3,6} However, care must be exercised when interpreting these Kharasch reactions since interchange reactions between the Grignard reagent and the organic halide are important competing reactions and may determine the product as is probably the case for the formation of cyclopropane from 3-phenoxypropyl bromide (*vide supra*).

Several other cobaltous halide-catalyzed reactions of Grignard reagents with organic halides have been interpreted solely as free radical reactions but may be, in fact, the result of interchange reactions to form unstable Grignard reagents. Examples are the formation of (a) bicyclo[3.1.0]hexane from 1,3-dibromocyclohexane,⁸ (b) cyclohexene from 1,2-dibromocyclohexane,⁸ (c) ethylene from 2-phenoxyethyl bromide,⁷ and (d) cyclobutane from 1,4-dibromobutane⁹ or 4-phenoxybutyl bromide.^{7,9}

Another aspect of Kharasch reactions deserves attention also since the products are frequently obtained by hydrolyzing the reaction mixture. Because of the metal-catalyzed interchange of Grignard reagents with organic halides, the product so obtained may contain an excess of the saturated hydrocarbon formed by hydrolysis of the Grignard reagent corresponding to the organic halide. This is particularly true when large excesses of Grignard reagents are employed. The following examples are illustrative.

(a) The reaction of several Grignard reagents with 1-bromooctane in the presence of cobaltous bromide has been employed to study the inter-

action of octyl radicals with radicals of differing reactivities.¹⁸ Based upon the yields of octanes and octenes, the radicals investigated were arranged in an order of decreasing activity. Although the conclusions may not be changed, it is quite likely that at least part, depending upon the rates of interchange, of the octanes obtained was a result of the hydrolysis of *n*-octylmagnesium bromide formed by the interchange of 1-bromo-octane with the Grignard reagents employed.

(b) Halogen atoms on aromatic compounds have been replaced with hydrogens (40–55% yields) by treating halogenated aromatic compounds with an excess of a Grignard reagent in the presence of cobaltous chloride.¹⁹ It was postulated that the halogen atoms were removed by cobalt subhalide to give aromatic radicals which, in turn, abstracted hydrogens from the ether solvent. However, at least part of the reduced aromatic products likely were formed by the hydrolysis of the corresponding Grignard reagents which were produced by the catalyzed interchange of the halogenated aromatic compounds with the Grignard reagent.

(c) Radicals produced *via* the Kharasch reaction can either disproportionate, couple or abstract hydrogens from the solvent. However, catalyzed interchange reactions may be responsible for the high yields, relative to the corresponding olefins ($C_6H_5OCH_2(CH_2)_nCH=CH_2$), of *n*-butyl phenyl ether (89%) from 4-phenoxybutyl bromide, *n*-pentyl phenyl ether (70%) from 5-phenoxybutyl chloride, and *n*-hexyl phenyl ether (90%) from 6-phenoxyhexyl bromide.⁷ It is unlikely that these high yields of saturated ethers were a result of hydrogen abstraction from the solvent by radicals produced from the corresponding halides.

Experimental

4-Phenoxybutyronitrile.—The nitrile, b.p. 170.1–170.6° (22 mm.), was prepared in 81% yield from 3-phenoxypropyl bromide (600 g.) and sodium cyanide (195 g.) dissolved in alcohol (300 ml.) and water (200 ml.) according to the procedure of Marvel and Tanenbaum.²⁰

Anal. Calcd. for $C_{10}H_{11}ON$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.52; H, 6.91; N, 8.49.

4-Phenoxybutyric acid was prepared in 76% yield, b.p. 184.0–184.4° (8 mm.), by acid (HCl) hydrolysis of 4-phenoxybutyronitrile (560 g.) according to published procedures.²¹

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; acid equiv., 180. Found: C, 66.78; H, 6.73; acid equiv., 179.

4-Phenoxybutyryl Chloride.—To a stirred solution of thionyl chloride (1.20 moles) in anhydrous benzene (200 ml.) was added, over a period of 10 minutes, 4-phenoxybutyric acid (0.522 mole). This solution was refluxed for 2.5 hours and then the excess thionyl chloride and benzene removed by vacuum distillation. Twice, benzene (200 ml.) was added and again removed by vacuum distillation. Obtained upon distillation was 4-phenoxybutyryl chloride (0.27 mole, 53% yd.), b.p. 109° (1.2 mm.).

Anal. Calcd. for $C_{10}H_{11}O_2Cl$: C, 60.5; H, 5.6. Found: C, 61.1; H, 5.7.

Preparation and Decarbonylation of 4-Phenoxybutyraldehyde.—A diglyme solution of lithium tri-*t*-butoxyaluminumhydride was prepared from lithium aluminum hydride (0.27

mole) and *t*-butyl alcohol (0.81 mole), using Brown and Subba Rao's procedure D.²²

In a four-necked flask, protected with drying tubes and equipped with stirrer, dropping funnel and helium inlet, were placed 4-phenoxybutyryl chloride (0.27 mole) and diglyme (200 ml.). The helium swept solution was cooled to –78° and the diglyme solution of lithium tri-*t*-butoxyaluminumhydride added, while stirring, over 1.5 hours. The solution was warmed, over a period of 1 hour, to room temperature.

A 10-ml. aliquot of the diglyme solution (440 ml.) was treated with 2 *N* HCl saturated with 2,4-dinitrophenylhydrazine to obtain a 2,4-dinitrophenylhydrazone derivative (0.8 g.), m.p. 95.0–95.5° (recrystallized from ethanol). The amount of derivative indicated 0.10 mole of 4-phenoxybutyraldehyde to be in the diglyme solution.

Anal. Calcd. for $C_{16}H_{18}N_4O_5$: C, 55.8; H, 4.7. Found: C, 56.1; H, 4.7.

The diglyme solution containing the 4-phenoxybutyraldehyde was added to ice and *o*-dichlorobenzene. The *o*-dichlorobenzene solution was filtered, washed repeatedly with water and dried over magnesium sulfate.

The *o*-dichlorobenzene solution (645 ml.) and di-*t*-butyl peroxide (0.04 mole) were placed in a flask and heated to 140–165°. After the evolution of gas, collected in a gas holder, had subsided, more peroxide (0.04 mole) was added and the solution again heated.

The gas collected had the composition: CO, 0.056 mole; CH_4 , 0.062 mole; $C_2H_6 + C_2H_4$, 0.0021 mole; $C_3H_8 + C_3H_6$, 0.0026 mole; iso- $C_4H_{10} + iso-C_4H_8$, 0.007 mole; cyclopropane, 0.00 mole. The gas composition was determined by gas chromatography (50-ft. column, dimethyl sulfolane on firebrick)²³ and mass spectrometric means. As a final check to demonstrate the absence of any cyclopropane in the gas product, a small sample of cyclopropane was introduced into the remaining gas product and a gas chromatography analysis again performed. As anticipated, a new peak due to cyclopropane appeared on the gas chromatography chart. The amount of CO in the gas product corresponded to 56% decarbonylation of the 4-phenoxybutyraldehyde.

The *o*-dichlorobenzene solution was analyzed by gas chromatography techniques. A sample of a compound corresponding by gas chromatography emergence times to phenyl *n*-propyl ether was collected and identified as such by mass spectrometric analysis. The yield of phenyl *n*-propyl ether (0.025 mole) was 45% of the CO evolved. Allyl phenyl ether was not detected in the product. Other compounds were present which could not be identified.

Preparation of Grignard Reagents.—Grignard reagents used in this study were prepared in the usual manner in an anhydrous atmosphere of helium using sodium-dried ether and 100% excess magnesium metal. The Grignard reagents were filtered under helium pressure either directly into a flask for further reaction or into a helium flushed bottle for temporary storage.

The Grignard reagent content was determined by addition of a 5.00-ml. aliquot to a measured excess of standard HCl and back titrating with sodium hydroxide solution to a phenolphthalein end-point.

Two grades, reagent²⁴ and sublimed,²⁵ of magnesium were used in the present study and were found by emission spectroscopy to contain the impurities shown in the table.

Reaction of Ethylmagnesium Bromide with Bromides.—Into a dry helium-flushed three-necked flask, protected with drying tubes and equipped with a condenser and dropping funnel, was introduced a measured amount of Grignard reagent. A known amount of bromide (3-phenoxypropyl, ethyl or 3-ethoxypropyl bromide) was added through the funnel to the Grignard reagent and refluxing began. The refluxing was continued until gas evolution ceased, the gas being collected in a brine-displacement gas holder.

When anhydrous cobaltous bromide (City Chemical Co.) was used as a catalyst, it was introduced into the Grignard reagent and the bromide added at such a rate as to maintain a gentle reflux from the heat of the reaction. Refluxing was maintained by external heating for 30 minutes after the bromide addition had been completed.

(18) M. S. Kharasch, J. K. Hambling and T. P. Rudy, *J. Org. Chem.*, **24**, 303 (1959).

(19) M. S. Kharasch, D. C. Sayles and E. K. Fields, *J. Am. Chem. Soc.*, **66**, 481 (1944).

(20) C. S. Marvel and A. L. Tanenbaum, *ibid.*, **44**, 2645 (1922).

(21) C. S. Marvel and E. R. Birkhimer, *ibid.*, **51**, 260 (1929).

(22) H. C. Brown and B. C. Subba Rao, *ibid.*, **80**, 5377 (1958).

(23) E. M. Fredericks and F. R. Brooks, *Anal. Chem.*, **28**, 297 (1956).

(24) Mallinckrodt reagent grade magnesium for Grignard Reagents.

(25) Kindly supplied by Dow Chemical Co.

Metal	Sublimed magnesium ²⁶ Wt. %	Reagent grade magnesium ²⁷ Wt. %
Silicon	0.005-0.05	0.005-0.05
Iron	0.005	0.05
Tin	< .005	< .005
Copper	.005	.05
Silver	< .005	Not detd.
Nickel	< .005	.05
Aluminum	< .005	.5
Strontium	< .005	< .005
Calcium	.05	.05
Barium	< .005	< .005
Chromium	Not detd.	.05
Manganese	Not detd.	0.05-0.5

The quantities of reagents used and the gaseous products formed are listed in Table I.

Formation and Decomposition of 3-Phenoxypropylmagnesium Bromide Prepared from 3-Phenoxypropyl Bromide and Sublimed Magnesium.—Sublimed magnesium (0.12 mole) and sodium-dried ether (150 ml.) were placed in a four-necked flask protected with drying tubes and equipped with stirrer, dropping funnel, condenser and nitrogen inlet. Cyclopropane evolution was almost immediate upon the addition of 3-phenoxypropyl bromide (0.025 mole) in ether (15 ml.). The solution was cooled to 5 to 10° and more 3-phenoxypropyl bromide (0.075 mole in 35 ml. of ether) added. After stirring for 2.5 hours, a 45-ml. aliquot of the Grignard solution was placed in a separate flask and refluxed for 45 minutes. This solution and the original cold Grignard solution were hydrolyzed with excess (100 ml.) tritium labeled water and ethanol, respectively. To each of the hydrolyzed Grignard solutions was added phenyl *n*-propyl ether (50 ml., 0.350 mole). The ether solutions, recovered by decantation, were washed repeatedly with dilute sodium hydroxide solution to remove phenol formed during the attempted Grignard preparation, and distilled through a whirling band column. The recovered phenol *n*-propyl ethers were measured for tritium activity. The activity found was not further decreased by additional sodium hydroxide washings: tritium activities found: H₂O, 3.6×10^8 d.p.m./mmole; EtOH³, 1.17×10^7 d.p.m./mmole; recovered phenyl *n*-propyl ether from cold hydrolyzed Grignard solution, 7330 d.p.m./ml.; phenyl *n*-propyl ether recovered from Grignard solution which had been refluxed and hydrolyzed with H₂O, 20 ± 20 d.p.m./ml. Calculations based upon the above data indicate that $0.020 \pm 0.001\%$ yield of 3-phenoxypropylmagnesium bromide was formed at 5 to 10° and that essentially all of it decomposed upon refluxing for 45 minutes.

Determination of the Absence of 3-Phenoxypropylmagnesium Bromide from the Reaction of 3-Phenoxypropyl Bromide with Ethylmagnesium Bromide at 35°.—3-Phenoxypropyl bromide (0.051 mole), ethylmagnesium bromide (0.25 mole) and cobaltous bromide (~3.0 mole% of the 3-phenoxypropyl bromide) in ethyl ether were refluxed as described above until gas evolution ceased. The mixture was hydrolyzed with excess tritium water (105 ml., 9.13×10^8 d.p.m./mmole), phenyl *n*-propyl ether (0.730 mole) added and recovered as described above.

The lack of radioactivity of the recovered phenyl *n*-propyl ether indicated that 3-phenoxypropylmagnesium bromide was not present (<0.001% yield) in the product resulting from the reaction of 3-phenoxypropyl bromide with ethylmagnesium bromide.

Determination of 3-Phenoxypropylmagnesium Bromide from the Reaction of 3-Phenoxypropyl Bromide with Excess Ethylmagnesium Bromide at -10°.—3-Phenoxypropyl bromide (0.05 mole), ethylmagnesium bromide (0.25 mole) and cobaltous bromide (~3.0 mole % of the bromide) in ether were stirred at -10° for 1 hour. A slow evolution of gas occurred at this temperature. The stirred mixture was hydrolyzed with excess tritium water (~90 ml., 1.18×10^8 d.p.m./mmole) while the temperature was maintained below -5°. Phenyl *n*-propyl ether (0.05 mole) was added and recovered as described above. The recovered ether had an activity of 2.13×10^8 d.p.m./mmole which was not reduced by further washing with base and water.

From the amount of phenyl *n*-propyl ether added as a carrier, the activity of the tritium water used for the hydrolysis and the activity of the recovered phenyl *n*-propyl ether, the amount of 3-phenoxypropylmagnesium bromide present from the above reaction is calculated²⁶ to be 0.0031 mole or 6.2% of the 3-phenoxypropyl bromide.

3-Ethoxypropanol, b.p. 160.7-161.6°, $n_{20}^{20,D}$ 1.4151, was prepared in 84% yield by hydrogenating (50°, 500 p.s.i.g.) 3-ethoxypropionaldehyde (525 g.) over water-washed Raney nickel.

Anal. Calcd. for C₆H₁₂O₂: C, 57.66; H, 11.53. Found: C, 57.54; H, 11.61.

3-Ethoxypropyl Bromide.—Phosphorus tribromide (0.43 mole) was added (1.0 hour) to stirred 3-ethoxypropanol (1.30 moles) allowing a free rise in temperature. The cooled solution was poured into ice-water. The bottom layer, washed three times with water, was dried over calcium chloride and distilled through a glass helices packed column. Obtained was 3-ethoxypropyl bromide (0.663 mole, 51% yield), b.p. 57.9-59° (33 mm.), $n_{20}^{20,D}$ 1.448.

Anal. Calcd. for C₆H₁₁OBr: C, 35.94; H, 6.54. Found: C, 35.92; H, 6.63.

Ethyl *n*-propyl ether was prepared, b.p. 62.1-62.9°, $n_{20}^{20,D}$ 1.3680, in a 40% yield from sodium ethoxide and *n*-propyl iodide in ethanol.

Anal. Calcd. for C₅H₁₂O: C, 68.12; H, 13.73. Found: C, 68.03; H, 13.73.

Determination of 3-Ethoxypropylmagnesium Bromide Resulting from the Reaction of 3-Ethoxypropyl Bromide with Ethylmagnesium Bromide in the Presence of Cobaltous Bromide.—The reaction of 3-ethoxypropyl bromide (0.0523 mole) with ethylmagnesium bromide (0.25 mole) in the presence of anhydrous cobaltous bromide (~3 mole % of the bromide) was carried out as described above for 3-phenoxypropyl bromide.

After gas evolution had ceased (1.0 hour), the Grignard solution was hydrolyzed with excess tritium water (100 ml., 1.53×10^8 d.p.m./mmole) and ethyl *n*-propyl ether (0.676 mole) added. The ether solution, washed repeatedly with water, was dried over magnesium sulfate and distilled through a whirling band column. The recovered ethyl *n*-propyl ether had an activity of 2.75×10^4 d.p.m./mmole which was not reduced by further washing with water.

The amount of 3-ethoxypropylmagnesium bromide present from the above reaction is calculated²⁶ to be 0.033 mole. On this basis, 63% of the 3-ethoxypropyl bromide interchanged with ethylmagnesium bromide to form 3-ethoxypropylmagnesium bromide and ethyl bromide. See Table I for the composition of the gas evolved during the reaction.

***t*-Butyl *n*-butyl ether**, b.p. 124-125° was prepared in low yields by heating potassium *t*-butoxide (0.5 mole) with 1-iodobutane (0.50 mole) in *t*-butyl alcohol (500 ml.). Mass spectrometric analysis confirmed the product as being the desired ether.

Decomposition of Di-*t*-butyl Peroxide in a Chlorobenzene Solution of 1-Iodobutane.—In a flask equipped with a condenser attached to a brine-displacement gas holder, was placed purified chlorobenzene (100 ml.), 1-iodobutane (0.40 mole) and di-*t*-butyl peroxide (0.15 mole). The flask was flushed with helium and refluxed for 24 hr.

Gas chromatography and mass spectrometric analyses of the gas product indicated the products: CH₄ (0.007 mole), C₂H₆ + C₂H₄ (0.0022 mole), *n*-C₄H₁₀ (0.0014 mole), *n*-C₃H₁₂ (none), 1-C₄H₈ (0.00112 mole), 2-C₄H₈ (0.0056 mole) and H₂ (0.0047 mole).

The following analysis was obtained by gas chromatography techniques, chlorobenzene, and 1-iodobutane not included, for the liquid product: Biphenyls (not present), *t*-butyl alcohol (0.07 mole), acetone (not determined), *t*-butyl *n*-butyl ether (not detected, <0.0003 mole), CH₃I (0.018 mole), recovered di-*t*-butyl peroxide (0.08 mole).

Radioactivity Measurements.—The tritium activities of the compounds were determined by the coincidence liquid scintillation method.²⁷ In general, counting efficiencies were about 12% for tritium water, and 15-25% for the organic tritium compounds. All net counting rates were

(26) Assuming a tritium isotope effect of 1.3 for the hydrolysis of the Grignard reagent; see L. O. Assarsson, *Acta Chem. Scand.*, **10**, 1599 (1956).

(27) See V. P. Guinn in C. G. Bell, Jr., and F. N. Hayes, "Liquid Scintillation Counting," Pergamon Press, New York, N. Y., 1958, pp. 166-182.

converted to disintegration per minute (d.p.m.) by measurement of the exact counting efficiencies with calibrated tritium solutions.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TENNESSEE, KNOXVILLE, TENN.]

A Study of the Catalytic Hydrogenation of Hydroxybenzenes over Platinum and Rhodium Catalysts

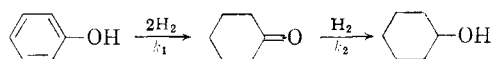
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The catalytic hydrogenation of phenol, catechol, resorcinol, hydroquinone, phloroglucinol and pyrogallol has been studied with platinum and rhodium catalysts. The rates of reduction are of the same order as those found for corresponding methyl- and methoxybenzenes. Some cleavage occurs in the reduction process, the amount depending on both temperature and catalyst. While ketones are produced during the reduction of the phenols, the kinetic evidence indicates that the mechanism of formation of cyclohexanols from the phenols does not require ketone intermediates. It is suggested that cyclohexenols are formed as intermediates, and that these may be reduced to form cyclohexanols, cleaved to form cyclohexanes, or isomerized to form cyclohexanones.

It has been recognized for many years that when phenol undergoes hydrogenation, the predominant product may be cyclohexanol, benzene or cyclohexane, depending on the catalyst employed and the reaction. Under certain conditions and with specific catalysts, cyclohexanone may be isolated during the course of the reaction, and the role of this compound as an "intermediate" in phenol hydrogenation has been investigated.

Vavon and Berton¹ were the first to isolate cyclohexanone as an "intermediate" in the hydrogenation of phenol. They hydrogenated phenol and the cresols over platinum black and isolated the cyclohexanones formed by reaction of the ketone with semicarbazide to produce the semicarbazone derivative. Coussement and Jungers² made a thorough study of the kinetics of catalytic hydrogenation of phenol over Raney nickel. On the basis of the results obtained in these investigations, the following reaction mechanism has been proposed



Wicker³ hydrogenated *o*-, *m*-, *p*-cresol, and the corresponding methylcyclohexanones in acetic acid over Adams platinum catalyst at 20°. Stereochemical evidence obtained indicated that these hydroxy compounds do not hydrogenate *via* a ketone intermediate. It was the purpose of this research to extend the study of phenol hydrogenations to include the isomeric dihydroxybenzenes, catechol, resorcinol and hydroquinone, to find out whether ketones or diketones are formed during the course of the reaction and, if so, in what amounts.

Of interest also was the cleavage of hydroxyl groups from the aromatic ring during the course of hydrogenation. Smith and Thompson⁴ made a sys-

tematic study of the cleavage reaction of the methoxyl group from an aromatic nucleus during hydrogenation, and it was felt that an extension of this study to include hydroxyl cleavage would lead to a further understanding of the reaction. A possible mechanism for the cleavage of the carbon-to-oxygen bond during such catalytic hydrogenations is: The methoxybenzene, anisole for example, is adsorbed on the catalyst surface where hydrogenation takes place to give a methoxycyclohexene as a short-lived intermediate. This intermediate may undergo cleavage and hydrogenation to give cyclohexane and methanol, or it may undergo simple hydrogenation to give methoxycyclohexane. These two reactions would probably occur simultaneously until the double-bonded molecules were saturated.

Finally, it was the purpose of this research to extend the kinetic data for catalytic hydrogenation of hydroxybenzenes.

Experimental

Commercial preparations of platinum oxide were obtained from the American Platinum Works, Newark, N. J., and Goldsmith Brothers, Chicago, Ill. The 5% rhodium-on-alumina catalyst was obtained from Baker and Co., Inc., Newark, N. J.

Glacial acetic acid was purified by fractionation of du Pont C.P. acid through an 8-foot Vigreux column. Commercial hydrogen obtained from the National Cylinder Gas Co. was used without further purification. This hydrogen has been shown previously to be satisfactory for kinetic studies.

Matheson (Coleman and Bell Division) phenol was fractionated through a 2-foot Vigreux column and the fraction boiling at 181.6° (745.8 mm.) was used. Eastman Kodak Co. white label catechol and Merck and Co., Inc., hydroquinone were purified by recrystallization from benzene. Melting points are 108.5° and 175.4–176.6°, respectively. Matheson (Coleman and Bell Division) resorcinol was recrystallized from toluene (m.p. 111.2–111.6°). Eastman Kodak Co. white label phloroglucinol and cyclohexanone were used without further purification. Baker Chemical Co. pyrogallol was recrystallized from an ethanol-benzene solution (m.p. 136°).

A much simpler method than has been reported previously was used to prepare dihydroresorcinol. Ten grams of resorcinol was hydrogenated at room temperature in 20 ml. of water containing 4.36 g. of sodium hydroxide over 2.0

(1) G. Vavon and A. L. Berton, *Bull. soc. chim.*, **37**, 296 (1925).

(2) F. Coussement and J. C. Jungers, *Bull. soc. chim. Belges*, **59**, 295 (1950).

(3) R. J. Wicker, *J. Chem. Soc.*, 3299 (1957).

(4) H. A. Smith and R. G. Thompson, "Advances in Catalysis," Vol. IX, Academic Press, Inc., New York, N. Y., 1957, p. 727.