pounds are probably a result of addition to the bromodimethoxybenzoylpropiolic ester formed by loss of two molecules of hydrogen bromide from the dibromo ester. This acetylenic ester has not been isolated but two intermediate ethylenic bromo esters have been prepared and shown to give two of the products obtained from the dibromo ester. The reaction of this dibromo methyl ester with methyl alcoholic potash has also been studied.

The dibromo ethyl ester gives with sodium ethylate products corresponding to all those obtained from the methyl ester with one exception but the dibromo acid is unreactive compared with its esters and loses only one molecule of hydrogen bromide on treatment with sodium methylate, forming isomeric ethylenic bromo acids. With potash the dibromo acid gives products which are a result of addition to bromodimethoxybenzoylpropiolic acid.

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THE REACTION OF THE GRIGNARD REAGENT WITH γ-CHLOROPROPYL PARA-TOLUENESULFONATE. A METHOD OF LENGTHENING CARBON CHAINS BY THREE CARBON ATOMS

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In synthetic organic work it is often necessary to build up the higher homologs of any series of compounds from the lower ones. Recently the practice of increasing carbon chains by one or two methylene groups by use of the Grignard reagent and formaldehyde or ethylene oxide, respectively, has become fairly common and laboratory details for these methods are available.[1] Gilman and Beaber[2] have published a preliminary paper on the reaction of the Grignard reagent with halogenated alkyl esters of aryl sulfonic acids in which they mention the possibility of the practical use of this reaction for the lengthening of the carbon chain in alkyl halides according to the following equation: $CH_3C_6H_4SO_2O(CH_2)_xCl + RMgX \longrightarrow R(CH_2)_xCl + CH_3C_6H_4SO_2OMgX$. Most of the work reported in this paper dealt with β-chloro-ethyl *p*-toluenesulfonate, but one reaction using γ-chloropropyl *p*-toluenesulfonate was recorded. While the yields reported in this preliminary work were not exceptionally good, the reaction seemed worthy of further study.[3]

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[1] "Organic Syntheses," **6**, 22, 54 (1926).

[2] Gilman and Beaber, THIS JOURNAL, **45**, 839 (1923).

[3] Before beginning this study, we were informed by Dr. Gilman that he did not expect to extend his researches on this particular reaction and that he did not object to our undertaking a further study of it.

Since the reaction of the Grignard reagent with ethylene oxide runs rather smoothly to give the primary alcohol with two more methylene groups, we have confined our attention mainly to the reaction of the Grignard reagent with γ-chloropropyl *p*-toluenesulfonate in the hope of obtaining a practical method of increasing the chain by three methylene groups.

In preliminary experiments using equimolecular proportions of the Grignard reagent (RMgX) and γ-chloropropyl *p*-toluenesulfonate, the expected product ($R(CH_2)_3Cl$) was obtained in approximately the same yields that Gilman has reported in similar reactions between other alkyl sulfonates and the Grignard reagent. However, there were obtained as by-products in these experiments the dihalogen derivative $X(CH_2)_3Cl$ (where X is the halogen of the Grignard reagent) and the hydrocarbon RH (where R is the hydrocarbon group of the Grignard reagent).

The simplest reactions which suggest themselves as a satisfactory explanation[4] of these products are as follows

$$CH_3C_6H_4SO_2O(CH_2)_3Cl + RMgX \longrightarrow R(CH_2)_3Cl + CH_3C_6H_4SO_2OMgX \qquad (1)$$

$$CH_3C_6H_4SO_2O(CH_2)_3Cl + RMgX \longrightarrow X(CH_2)_3Cl + CH_3C_6H_4SO_2OMgR \qquad (2)$$

$$CH_3C_6H_4SO_2OMgR + H_2O \longrightarrow CH_3C_6H_4SO_2OMgOH + RH \qquad (3)$$

It was thought that if the reaction represented by Equation 2 actually took place, the compound[5] $CH_3C_6H_4SO_2OMgR$ might be expected to react with another molecule of the chloropropyl ester as follows

$$CH_3C_6H_4SO_2O(CH_2)_3Cl + CH_3C_6H_4SO_2OMgR \longrightarrow (CH_3C_6H_4SO_2O)_2Mg + R(CH_2)_3Cl \qquad (4)$$

With this in mind the proportions used in the reaction were changed and two molecules of the chloropropyl ester were used to one of the Grignard reagent. With this change in the procedure the reaction becomes a useful synthetic process, as the yields obtained are usually about 50% of the theoretical amount when the higher alkyl magnesium halides are used.

A double decomposition similar to that represented by Equation 2 takes place when simple alkyl esters of *p*-toluenesulfonic acid react with the Grignard reagent. Thus when butyl *p*-toluenesulfonate reacts with one mole of benzylmagnesium chloride, the reaction products include *n*-amyl benzene (previously reported by Gilman and Beaber),[6] *n*-butyl chloride and toluene.

Gilman and Beaber[7] have reported that the lower alkyl magnesium halides do not react with the alkyl *p*-toluenesulfonates to give good yields of the expected products. This observation has been confirmed in the

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[4] Since this paper was written Gilman and Heck have advanced a much simpler explanation for these reactions. (Private communication.)

[5] This type of compound has been formulated before by Kenyon, Phillips and Turley, *J. Chem. Soc.*, **127**, 402 (1925).

[6] Gilman and Beaber, THIS JOURNAL, **47**, 523 (1925).

[7] Ref. 6, p. 519.

reaction of ethylmagnesium bromide and *n*-butylmagnesium bromide with γ-chloropropyl *p*-toluenesulfonate. As by-products in these reactions, certain unidentified volatile sulfur compounds are formed. A yield of 23% of *n*-amyl chloride was obtained from ethylmagnesium bromide. The exact yield of heptyl chloride from the *n*-butyl Grignard reagent was not determined on account of the difficulties of separating a pure product.

High boiling products which do not hydrolyze with alkali are sometimes formed and these indicate the possibility of some formation of sulfones. The amounts of these products thus far obtained are not sufficient for their isolation in pure condition and identification.

From the results thus far obtained, this method of lengthening carbon chains by three methylene groups is satisfactory when a Grignard reagent with six or more carbon atoms is used as the starting material.

Experimental Part

γ-Chloropropyl *p*-Toluenesulfonate.[8]—A mixture of 210 g. (1.1 moles) of *p*-toluenesulfonyl chloride and 189 g. (2 moles) of trimethylene chlorohydrin was placed in a 3-liter, three-necked flask fitted with a mechanical stirrer, a separatory funnel and a thermometer. The flask was placed in an ice-water bath and stirring was started. When the temperature had dropped to about 8°, the addition of 320 cc. of 5 *N* sodium hydroxide solution through the separatory funnel was begun. The rate of addition was regulated to maintain the temperature between 8 and 15°. Stirring was continued for about an hour after the addition of the alkali. Then a second portion of 210 g. of *p*-toluenesulfonyl chloride was introduced into the mixture and a second 320 cc. of 5 *N* sodium hydroxide solution was added as before. Stirring was continued for about three hours after the addition of the last of the alkali. The ester was extracted with ether and the ether layer was washed with water, then with a little 20% sodium hydroxide and was finally dried over anhydrous potassium carbonate. The ether was distilled at ordinary pressure and the residue under reduced pressure. The ester boiled at 188–192° at 5 mm. The yield varied from 248–275 g. (50–55% of the theoretical amount).

The ester has been prepared before by Gilman and Beaber[9] who report the following physical constants: d_4^{20}, 1.2674; n_D^{20}, 1.5230; b. p. 216–217° (17 mm.). Our product had the following constants: sp. gr. $\frac{25}{25}$, 1.2396; n_D^{21}, 1.5225; and b. p. 188–192° at 5 mm. In some cases the ester was obtained as a semi-solid but it never completely crystallized.

Anal. Subs., 0.6543: $BaSO_4$, 0.6009. Calcd. for $C_{10}H_{13}SO_3Cl$: S, 12.86. Found: S, 12.60.

Reaction of One Mole of the Grignard Reagent with One Mole of γ-Chloropropyl *p*-Toluenesulfonate.—The Grignard reagent was prepared in the usual manner in a three-necked flask of suitable size, which was fitted with a separatory funnel, mechanical stirrer and reflux condenser. The chloro ester was then added at such a rate that the ether refluxed gently. Preliminary experiments seemed to indicate that there was no change in yields at different reaction temperatures. The reaction mixture was stirred and maintained at gently boiling temperature for about eight hours after the addition of the last of the chloro ester. Additional ether was added from time to time in order to keep the mixture fluid enough for efficient stirring.

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[8] This method is based on the method for *n*-butyl *p*-toluenesulfonate by Gilman and Beaber. Private communication.

[9] Ref. 2, p. 842.

The reaction mixture was then decomposed with cracked ice and treated with enough dilute hydrochloric acid to dissolve the basic magnesium salts. The ether layer was separated, the water layer extracted with ether and the extract combined with the original ether solution. The ether solution was then carefully distilled with a fractionating column. When ethylmagnesium bromide and *n*-butylmagnesium bromides were the Grignard reagents used, the lower boiling fractions obtained in this distillation had the very disagreeable odor that is characteristic of the volatile sulfur compounds. When these fractions were washed with cold concd. sulfuric acid the material which carried this odor was dissolved and pure halogen derivatives could be obtained by fractionation of the insoluble material.

On pouring the sulfuric acid which was used for the purification onto crushed ice a few cc. of a substance with a very disagreeable odor was obtained. Not enough of this material was isolated for identification.

The reactions studied and the products isolated are described in Table I. In every case a gram molecule of the alkyl halide and equivalent amounts of magnesium and γ-chloropropyl *p*-toluenesulfonate were used. The amount of ether used for the preparation of the Grignard reagent was 300–400 cc. but as mentioned before more ether was added to the reaction mixture as it was needed.

TABLE I

PRODUCTS OBTAINED BY THE REACTION OF ONE MOLE OF RMgX WITH ONE MOLE OF γ-CHLOROPROPYL *p*-TOLUENESULFONATE

						Physical constants	
Alkyl halide	Amt., g.	Products isolated	Wt., g.	Yield, %	B. p., °C.	Sp. gr., $\frac{25}{25}$	n_D^{25}
n-C_4H_9Cl	93	$Cl(CH_2)_3Cl$	27	..	123–125	1.080	1.4362
n-C_4H_9Br	137	$Cl(CH_2)_3Br$	50	..	138–140	1.4718	1.4732
n-C_4H_9I	184	$Cl(CH_2)_3I$ (not pure)	60	..	47–59 at 6 mm.	1.6703	1.5312
n-$C_7H_{15}Br$	179	$Cl(CH_2)_3Br$	63	..	138–140	....	....
		$C_7H_{15}(CH_2)_3Cl$	20	11.4	137–142 at 24 mm.	0.8850	1.4400
$C_6H_{11}Br$	163	$Cl(CH_2)_3Br$	73	..	138–140	....	....
		$C_6H_{11}(CH_2)_3Cl$[a]	24	14	76–79 at 5 mm.	0.9977	1.4660
$C_6H_5CH_2Cl$	127	$Cl(CH_2)_3Cl + C_6H_5CH_3$[b]	34	..	114–120	....	....
		$C_6H_5(CH_2)_4Cl$	72	42	98–102 at 6 mm.	1.0295	1.5183
$C_6H_5(CH_2)_4Cl$	169	$Cl(CH_2)_3Cl$	36	..	123–125	....	....
		$C_6H_5(CH_2)_3CH_3$	50	..	178–180	0.8754	1.4920
		$C_6H_5(CH_2)_7Cl$[c]	53	25	131–136 at 6 mm.	0.9899	1.5152

[a] *Anal.* Subs., 0.2100: 13.1 cc. of 0.1001 *N* $AgNO_3$. Calcd. for $C_9H_{17}Cl$: Cl, 22.14. Found: Cl, 22.09.

[b] This mixture could not be separated by fractional distillation. The odor of each of the constituents was apparent. The toluene was identified by conversion to benzoic acid. A mixture of equimolecular amounts of these two constituents was prepared and its boiling point and density agreed with that of the mixture isolated in this experiment.

[c] *Anal.* Subs., 0.2090: 9.6 cc. of 0.1010 *N* $AgNO_3$. Calcd. for $C_{13}H_{19}Cl$: Cl, 16.8. Found: Cl, 16.4.

It will be noted that no heptyl chloride was isolated when the butylmagnesium halides were used. Volatile sulfur compounds were produced rather abundantly in these experiments.

Reaction of One Mole of the Grignard Reagent with Two Moles of γ-Chloropropyl *p*-Toluenesulfonate.—These reactions were run exactly as described in the preceding experiments with the exception that two equivalents of the ester were used for one equivalent of the Grignard reagent. No hydrocarbons were isolated except in one case. A high boiling residue of unchanged ester was recovered in a few cases. This indicates that in certain cases less than two moles of ester could be used with as good yields of final product. The results of these experiments are collected in Table II.

TABLE II

PRODUCTS OBTAINED BY THE REACTION OF ONE MOLE OF RMgX WITH TWO MOLES OF γ-CHLOROPROPYL *p*-TOLUENESULFONATE

Alkyl halide	Amt., g.	Products isolated	Wt., g.	Yield, %	B. p., °C.	Physical properties Sp. gr. $\frac{25}{25}$	Physical properties n_D^{25}
$C_6H_5CH_2Cl$	127	$Cl(CH_2)_3Cl$	50	..	123–125	1.080	1.4362
		$C_6H_5(CH_2)_4Cl$	99	50	98–102 at 6 mm.	1.0295	1.5183
C_6H_5Br	157	$Cl(CH_2)_3Br$	51	..	138–140	1.4718	1.4732
		$C_6H_5(CH_2)_3Cl$	93	62	89–93 at 6 mm.	1.0801	1.5160
C_2H_5Br	109	$Cl(CH_2)_3Br$	100	..	138–140	....	....
		$C_2H_5(CH_2)_3Cl$	25	23	106–108	0.8890	....
n-$C_6H_{13}Br$	165	$Cl(CH_2)_3Br$	100	..	138–140	....	....
		$C_6H_{13}(CH_2)_3Cl$	83	52	76–79 at 4 mm.	0.8931	1.4400
n-$C_{12}H_{25}Br$	55	$Cl(CH_2)_3Br$	33	..	138–140	....	....
		$C_{12}H_{25}(CH_2)_3Cl$	20	30[a]	119–121 at 6 mm.	0.8433	1.4470
$C_6H_{11}Br$	163	$Cl(CH_2)_3Br$	98	..	138–140	.. ..	....
		$C_6H_{11}(CH_2)_3Cl$	100	62	76–79 at 5 mm.	0.9977	1.4660
$C_6H_5(CH_2)_4Cl$	173	$Cl(CH_2)_3Cl$	60	..	123–125	....	....
		$C_6H_5(CH_2)_7Cl$	62	44[b]	131–136 at 6 mm.	0.9899	1.5152
		$C_6H_5(CH_2)_3CH_3$	28	..	178–180	0.8754	1.4920
$C_7H_{15}Br$	179	$Cl(CH_2)_3Br$	101	..	138–140	....	....
		$C_7H_{15}(CH_2)_3Cl$	87	50	137–142 at 24 mm.	0.8850	1.4400

[a] The lower yield in this case is due in part to the fact that smaller quantities were used and mechanical losses lowered the yield and in part to the fact that the Grignard reagent is formed in only about 70% yield from lauryl bromide. The yield of pentadecyl chloride based on the Grignard reagent is about 42%.

[b] This yield is based on the actual amount of Grignard reagent used as determined by titration with standard acid.

Benzylmagnesium Chloride and *n*-Butyl *p*-Toluenesulfonate.—When one mole of benzylmagnesium chloride and one mole of *n*-butyl *p*-toluenesulfonate were allowed to react according to the method described by Gilman and Beaber,[4] careful fractionation of the products showed that 18 g. of *n*-butyl chloride (b. p. 75–81°), 22 g. of toluene (b. p. 106–112°) and 45 g. of *n*-amylbenzene (b. p. 198–201°) were obtained.

If the ratio was changed so that one mole of the Grignard reagent reacted with two moles of the ester, the products isolated were 24 g. of *n*-butyl chloride (b. p. 76–80°) and 74 g. of *n*-amylbenzene (b. p. 198–201°).

Summary

1. The reactions of various Grignard reagents with γ-chloropropyl *p*-toluenesulfonate have been studied.

2. Conditions have been described which make this a useful synthetic reaction in converting RX to $R(CH_2)_3Cl$.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

THE MECHANISM OF CARBOHYDRATE OXIDATION. VIII. THE ACTION OF POTASSIUM HYDROXIDE ON FRUCTOSE

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It has been shown that temperature and concentration of alkali are experimental factors which exert a marked influence on the quantity of reaction products which may be obtained when glucose, fructose, mannose and galactose are oxidized with potassium permanganate in aqueous solutions of potassium hydroxide.[1] A quantitative study of the reaction products obtained by the action of aqueous solutions of potassium hydroxide on glucose and galactose under definitely chosen conditions of temperature and concentration of the base, and in the absence of potassium permanganate, shows that the equilibrated reacting system is one that is easily disturbed by a change in one or both of these experimental factors.[2] By reason of the fact that fructose in alkaline solutions is converted, in part, to glucose,[3] it became of much interest to know whether this ketohexose would show the same general behavior toward potassium hydroxide as that observed for the aldohexose by Evans, Edgar and Hoff.[2a] To determine this point was the first objective in these experiments.

When fructose-3,4-enediol is ruptured at the double bond, two molecules of the active form of glyceric aldehyde should be formed.[4] Hence, it follows that in those alkaline solutions of the hexoses in which the equilibrium between the enediols has been shifted largely to the 3,4-form, the action of the alkali on the carbohydrate should involve the same general mechanism as that observed by Hass,[5] and Cornthwaite and one of us[6] concerning the behavior of glyceric aldehyde and dihydroxy-acetone

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[1] (a) Evans, Buehler, Looker, Crawford and Holl, THIS JOURNAL, **47**, 3085 (1925); (b) Evans and Buehler, *ibid.*, **47**, 3098 (1925).

[2] (a) Evans, Edgar and Hoff, *ibid.*, **48**, 2665 (1926); see (b) Amick, *J. Phys. Chem.*, **31**, 1473–7 (1927); (c) Wolfrom with Lewis, THIS JOURNAL, **50**, 838 (1928).

[3] (a) De Bruyn and van Ekenstein, *Rec. trav. chim.*, **14**, 156 (1895); (b) **14**, 203 (1895); (c) **15**, 92 (1896); (d) **16**, 257 (1897); (e) **16**, 262 (1897); (f) **16**, 274 (1897); (g) **19**, 1 (1900); (h) **27**, 1 (1908).

[4] Ref. 1a, p. 3093.

[5] Evans and Hass, THIS JOURNAL, **48**, 2703 (1926).

[6] Evans and Cornthwaite, *ibid.*, **50**, 486 (1928).