little, if any, interaction with the 9-position (methylene group) took place. The identity of the acid formed by carbonation was confirmed by permanganate oxidation of a portion to fluorenone-2-carboxylic acid, both acids having appropriate melting points. The Grignard reaction may furnish a convenient source of small amounts of fluorene-2-carboxylic acid.

Experimental[3]

The 2-bromofluorene was obtained by the method of Thurston and Shriner.[4] The preparation was studied in two ways, varying the time of reaction and the amount of ethyl bromide used.

In the preferred method of reaction, 5 g. of 2-bromofluorene with excess magnesium in 100 ml. of ether were treated dropwise with 20 ml. of ethyl bromide in 100 ml. of ether during one hour. The solution was then refluxed one-half hour and carbonated while still warm with Dry Ice. The mixture was hydrolyzed with dilute hydrochloric acid and the organic layer removed and washed with water. It was extracted with three portions of sodium carbonate solution and the extracts combined and acidified. This caused precipitation of the acid as a cream colored powder. After filtering, washing and drying it weighed 900 mg. (21%). From the filtrate from the acid precipitation, on standing overnight, 50 mg. of a more soluble white acid, m.p. 216–221°, was formed. This was not identified but did not decompose on boiling its alkaline solution or on melting.

The fluorene-2-carboxylic acid was recrystallized from acetone–water and from ether, m.p. 260–267° with some sublimation and darkening. The ether solution was decolorized with charcoal and the acid crystallized again by concentrating the solution. This gave a product m.p. 275–277° with sublimation, on rapid heating. Schiessler and Eldred[5] list 265–274° with decomposition as the m.p. of the acid obtained by one method and 271–275° without decomposition as the m.p. of the acid formed by another process.

In this Grignard synthesis, all of the aryl bromide was initially present and maximum utilization of the entraining action of ethyl bromide was achieved. The large excess of ethyl bromide was employed to improve the yield further if possible. Some of the unreacted 2-bromofluorene may be recovered from the neutral reaction products.

The second method of carrying out the reaction employed less ethyl bromide and the mixture was refluxed overnight. A mixture of 0.5 g. of 2-bromofluorene with 0.5 ml. of ethyl bromide in 50 ml. of ether reacted with excess magnesium (about 5 g.) until the action was slow. A solution of 4.5 g. of 2-bromofluorene and 1.5 ml. of ethyl bromide in 100 ml. of ether was then added slowly during one-half hour. Twenty ml. of benzene was also added during this time. The resulting orange-brown solution was refluxed overnight (16.5 hours) and carbonated. The mixture was hydrolyzed and the acid isolated as before. The yield was 750 mg. or 17.5%.

A portion of the fluorene-2-carboxylic acid was oxidized in aqueous alkaline solution by an excess of permanganate by heating several hours on the steam-bath. The excess of permanganate was destroyed by oxalic acid, and the solution filtered. Acidification of the filtrate furnished the fluorenone-2-carboxylic acid which formed yellow crystals from ether. It had m.p. about 330° with much sublimation and some decomposition. Schiessler and Eldred[5] give 333–335° with decomposition as the m.p. of fluorenone-2-carboxylic acid.

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(3) Melting points are uncorrected.

(4) J. T. Thurston and R. L. Shriner, THIS JOURNAL, **57**, 2163 (1935).

(5) R. W. Schiessler and N. R. Eldred, *ibid.*, **70**, 3958 (1948).

Arylsulfonic Esters of Bromophenols in Grignard Preparations[1]

BY D. C. MORRISON

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The work of Gilman and others[2] on reactions of aryl esters of arylsulfonic acids with Grignard reagents showed that only slight action took place at 35°. During the course of work on Grignard preparations, the possibility of obtaining a reaction of magnesium with bromophenyl esters of aromatic sulfonic acids was examined. It was hoped to use these bromophenol esters as aryl halides and obtain protection of the phenolic group by this esterification.

Some of the bromophenyl esters reacted successfully under entrainment conditions giving about 25% yields of the desired Grignard reagent ($Ar\cdot SO_2\cdot O\cdot C_6H_4\cdot MgX$) whose presence was proved by carbonation and isolation of the corresponding acid. The latter and other reaction products of these Grignard reagents could be hydrolyzed, removing the sulfonate group and forming the corresponding hydroxy derivatives.

Bromoalkyl esters of arylsulfonic acids would not be expected to function as alkyl halides in a similar reaction as alkyl esters of these acids have labile alkyl groups.

p-Bromophenol was used in most of the work and its esters with benzene- and toluenesulfonic acids were studied. These reacted difficultly or not at all with magnesium alone but more facile reaction occurred if the ester bromide was entrained with excess ethyl bromide. Carbonation with Dry Ice and isolation of the acids in the usual manner furnished the arylsulfonic esters of *p*-hydroxybenzoic acid ($Ar\cdot SO_2\cdot O\cdot C_6H_4\cdot COOH$). The tosyl ester was hydrolyzed to *p*-hydroxybenzoic acid.

This type of Grignard reaction is apparently not general, as esters of several other bromophenols gave little or none of the desired carboxylic acids or unknown substances. Thus, the ester of *o*-bromophenol yielded a product different from the known desired acid (arylsulfonate of salicylic acid) and which was not identified. The phenyl ester of *p*-bromobenzenesulfonic acid, entrained with ethyl bromide and carbonated, gave two acids according to the conditions. These were not further examined.

As the hydroxy derivatives ultimately desired were organophosphorus acids with a *p*-hydroxy group, the reaction of the *p*-bromophenyl ester Grignards with $POCl_3$ was examined. This reaction was carried out in accordance with the directions of Kosolapoff[3] who has demonstrated that, under suitable conditions, phosphinic acids (R_2POOH) can be prepared by this method. The expected product was the bis-(arylsulfonate) of di-(*p*-hydroxyphenyl)-phosphinic acid. However,

(1) The work described in this paper was sponsored by the Atomic Energy Commission. It was supported in part by a grant from the Henry, Laura and Irene B. Dernham Fund of the American Cancer Society and the Christine Breon Fund.

(2) H. Gilman, N. J. Beaber and C. H. Myers, THIS JOURNAL, **47**, 2047 (1925).

(3) G. M. Kosolapoff, *ibid.*, **64**, 2982 (1942).

the product which was isolated was the arylsulfonate ester of ethyl-(*p*-hydroxyphenyl)-phosphinic acid, obviously formed by incorporation of the ethyl Grignard entrainer into the reaction product (an excess of ethylmagnesium bromide was present). The acid was hydrolyzed to the parent *p*-hydroxy acid, $C_2H_5(p\text{-}HOC_6H_4)POOH$.

An attempt to conduct the entrainment reaction with butyl bromide in place of ethyl bromide and so to include a butyl group in the phosphorus compound, gave a poor yield of an acid of the desired type. Separation of this substance from the main product, dibutylphosphinic acid, was difficult.

The reactions of other ester Grignards with $POCl_3$ were not examined as the main object of the work was preparation of *p*-hydroxyphosphinic acids.

This method of forming *p*-hydroxy derivatives through organometallic intermediates may possibly serve as a supplement to the method of Gilman[4] involving exchange (interconversion) of butyllithium with *p*-bromophenol.

Experimental

All melting points are uncorrected.

The aryl esters of aromatic sulfonic acids were prepared according to Slagh and Britton's modification of the Hinsberg method.[5] These phenol esters were previously made by Hazlett[6] and by Sekera.[7]

Preparation of *p*-Carboxyphenyl Benzenesulfonate.—The method used for the preparation of the ester Grignards and their carbonation is illustrated by the synthesis of *p*-carboxyphenyl benzenesulfonate.

A solution of 6.55 g. of *p*-bromophenyl benzenesulfonate and 2 ml. of ethyl bromide in 50 ml. of ether reacted with a considerable excess of magnesium until the reaction was slow. A solution of 16 ml. of ethyl bromide in 50 ml. of ether was then added dropwise at room temperature during 1.5 hr. The solution may be refluxed after the addition but this is not necessary and in some cases is deleterious. The large excess of ethyl bromide enables more of the aryl bromide to be utilized than would otherwise occur and may possibly be increased still further with advantage. The Grignard solution was carbonated by pouring into a suspension of crushed Dry Ice in ether. The ether layer of the hydrolysis product was extracted three times with sodium carbonate solution and the combined carbonate extracts were acidified to precipitate the acid. The yield was 1.59 g. or 24.3%. The acid was recrystallized several times from ether, m.p. 170–171.5°. A German patent gives m.p. 170° for this acid.[8] The non-acidic fraction of the reaction product may be used to recover unreacted bromophenyl ester.

A similar preparation of the *p*-toluenesulfonate of *p*-hydroxybenzoic acid (*p*-carboxyphenyl *p*-toluenesulfonate) gave a 28.3% yield of the acid. This, after several recrystallizations from ether, also melted 170–171.5°. The German patent literature gives m.p. 168–170° for this acid.[9]

The reaction of *o*-bromophenyl *p*-toluenesulfonate (3.7 g.) entrained with 25 ml. of ethyl bromide as before, and the mixture carbonated, gave 830 mg. of a white acid, m.p. 216–217° after ether recrystallization. This is not the desired tosylate of salicylic acid which has m.p. 154–156°.[9,10]

Entrainment of phenyl *p*-bromobenzenesulfonate with ethyl bromide and carbonation gave an acid m.p. 206° if the solution was not refluxed after ethyl bromide addition. When refluxed one-half hour and then carbonated, an acid m.p. above 260° resulted. One of these (possibly the first) may be the expected $p\text{-}HOOC\cdot C_6H_4\cdot SO_2\cdot OC_6H_5$.

Hydrolysis of *p*-Carboxyphenyl *p*-Toluenesulfonate.—This substance was hydrolyzed quantitatively by four hours of boiling with 10% sodium hydroxide solution. Acidification and several ether extractions removed the *p*-hydroxybenzoic acid. This was recrystallized from water. The m.p. and mixed m.p. with authentic material was 214–216°. Literature values for this constant vary from 210–216°. Heilbron[11] gives m.p. 213–214° for *p*-hydroxybenzoic acid.

Preparation of Ethyl-(4-[*p*-toluenesulfonyloxy]-phenyl)-phosphinic Acid.—A solution of 5 g. of *p*-bromophenyl toluenesulfonate and 5 ml. of ethyl bromide in 100 ml. of ether reacted with excess magnesium and when the action was slow, a solution of 17 ml. of ethyl bromide in 50 ml. of ether was started in dropwise. This was added in one hour and the reaction mixture was then left one-half hour in the cold.

It was transferred to a separatory funnel along with any gum which may form (using benzene). This solution was added during one hour to 30 ml. of $POCl_3$ in 200 ml. of benzene at an average temperature of 30°. Twenty minutes after addition was complete, the product was hydrolyzed by ice and hydrochloric acid. The mixture was shaken thoroughly to decompose any excess $POCl_3$. The washed organic layer was extracted three times with sodium carbonate solution to extract the acid, which was obtained on acidifying the extracts. A partly gummy product was precipitated but this solidified on cooling and standing. When cooled in ice an additional amount separated. The weight of washed and dried crude acid was 1.105 g. or 21.3%.

The acid is best recrystallized by solution in acetone and dilution with water and then boiling off the organic solvent. If the solution is boiled too long, some decomposition occurs. It was recrystallized in this manner several times. The analytical sample was recrystallized from ether–petroleum ether and again from acetone–water, m.p. 153–153.5°. It forms a white powder.

Anal. Calcd. for $C_{15}H_{17}PSO_5$: C, 52.94; H, 5.00. Found: (I) C, 52.85; H, 5.18; (II) C, 52.77; H, 5.12.

Preparation of Ethyl-(*p*-hydroxyphenyl)-phosphinic Acid.—This was obtained by hydrolysis of the preceding acid. A mixture of 1.52 g. of this substance and 10 g. of sodium hydroxide dissolved in 50 ml. of water was heated for four hours on the steam-bath. The solution was cooled, diluted and acidified with excess hydrochloric acid. It was filtered, concentrated by boiling and filtered again to eliminate some resin. The water soluble acid could then be recovered by repeated extraction with ether (10 times or more) or by evaporation and repeated and thorough extraction of the dry residue with ether and acetone. The acid was obtained in crude yield of 580 mg. or 69.7%. It was purified by continued recrystallization from benzene–acetone (10:1). Finally it was recrystallized from benzene alone by boiling out acetone from the mixed solvent solution. The powder was washed with ether and air dried. The highest melting point observed was 160–161°.

Anal. Calcd. for $C_8H_{11}PO_3$: C, 51.61; H, 5.91. Found: C, 51.35; H, 5.91.

Entrainment of *p*-Bromophenyl Toluenesulfonate with Butyl Bromide and Reaction with Phosphoryl Chloride.—This was carried out similarly to the reaction with ethyl bromide except that butyl bromide was employed. The reaction gave a mediocre yield of acid which was difficult to purify. It was recrystallized a number of times from ether and from ether–petroleum ether but was not obtained quite free from dibutylphosphinic acid. The highest melting point observed was 141–142.5°.

Anal. Calcd. for $C_{17}H_{21}PSO_5$, butyl-(4-[*p*-toluenesulfonyloxy]-phenyl)-phosphinic acid: C, 55.43; H, 5.71. Found: C, 54.77; H, 5.44.

Preliminary work indicates that the phenolic group in bromophenols may also be protected by esterification with diphenylphosphoryl chloride, $(C_6H_5O)_2POCl$. Thus, the compound diphenyl *p*-bromophenyl phosphate, $(C_6H_5O)_2\text{-}PO\text{-}OC_6H_4Br$, can be made to react with magnesium by ethyl bromide entrainment and the resulting solution used in a similar manner as an arylmagnesium halide.

(4) H. Gilman, C. E. Arntzen and F. J. Webb, *J. Org. Chem.*, **10**, 374 (1945).

(5) H. R. Slagh and E. C. Britton, THIS JOURNAL, **72**, 2808 (1950).

(6) S. E. Hazlett, *ibid.*, **59**, 287 (1937).

(7) V. C. Sekera, *ibid.*, **55**, 421 (1933).

(8) B.A.S.F. German Patent 162,322, "Beilstein," 4th Ed., Vol. XI, p. 34.

(9) B.A.S.F. German Patent 162,322 and *Frdl.*, **8**, 155; "Beilstein," 4th Ed., Vol. XI, p. 103.

(10) An authentic sample of the *p*-toluenesulfonate of salicylic acid made by acylation of salicylic acid had m.p. 158–159° after recrystallization from water (depressed when mixed with salicylic acid which itself has m.p. 158°).

(11) Heilbron, "Dictionary of Organic Compounds," Vol. II, Eyre-Spottiswoode Publ., London, 1934, p. 233.

Acknowledgment.—The author is indebted to Drs. J. G. Hamilton, K. G. Scott, E. Hoerger and W. D. Kumler for advice received during this work.

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Quinoxaline Studies. IV. The Preparation of *dl*-2,6-Dimethyl-1,2,3,4-tetrahydroquinoxaline and *dl*-2,7-Dimethyl-1,2,3,4-tetrahydroquinoxaline

BY MORTON MUNK[1] AND HARRY P. SCHULTZ

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Hinsberg[2] condensed 3,4-diaminotoluene with chloroacetone to give a substance which was either a mixture of 2,6- and 2,7-dimethylquinoxaline, or one of the pure compounds. The purpose of this investigation was to determine whether the Hinsberg condensation of chloroacetone with 3,4-diaminotoluene gave both of the above isomers, or only one.

All attempts in this Laboratory to synthesize either 2,6- or 2,7-dimethylquinoxaline failed; hence, an indirect proof of the identity of Hinsberg's compound was achieved in the following manner. Both 2-hydroxy-3,6- and -3,7-dimethylquinoxaline had been previously prepared unequivocally by Marks and Schultz[3]; replacement of the 2-hydroxy group in these two known compounds with a hydrogen atom should have given the desired 2,6- and 2,7-dimethylquinoxalines. This attempt, produced instead the tetrahydro derivatives of 2,6- and 2,7-dimethylquinoxaline.

Since the preparations of 2-hydroxy-3,6- and -3,7-dimethylquinoxaline were tedious, initial experimental work was carried out on 2-hydroxy-3-methylquinoxaline. Treatment of this compound with phosphorus oxychloride gave 2-chloro-3-methylquinoxaline. Catalytic reduction of the chloro derivative over palladium-on-charcoal gave *dl*-2-methyl-1,2,3,4-tetrahydroquinoxaline, previously prepared by Ris[4] by a different method.

In an analogous fashion 2-hydroxy-3,6- and -3,7-dimethylquinoxaline were transformed into *dl*-2,7- and -2,6-dimethyltetrahydroquinoxaline, respectively. In the course of this portion of the work a new synthesis of 2-hydroxy-3,6-dimethylquinoxaline, superior to that of Marks and Schultz,[3] was developed. This was achieved by condensation of 3-amino-4-nitrotoluene with α-bromopropionic acid to give N-(2-nitro-5-methylphenyl)-*dl*-α-alanine; reductive cyclization and subsequent oxidation gave the known 2-hydroxy-3,6-dimethylquinoxaline.

A mixed melting point curve (Fig. 1) of the two pure isomers, *dl*-2,6- and -2,7-dimethyl-1,2,3,4-tetrahydroquinoxaline, indicated a eutectic, m.p. 88–89° at a 1:1 composition of isomers. The ultraviolet absorption spectra of these two compounds were very similar; these data are summarized in Table I.

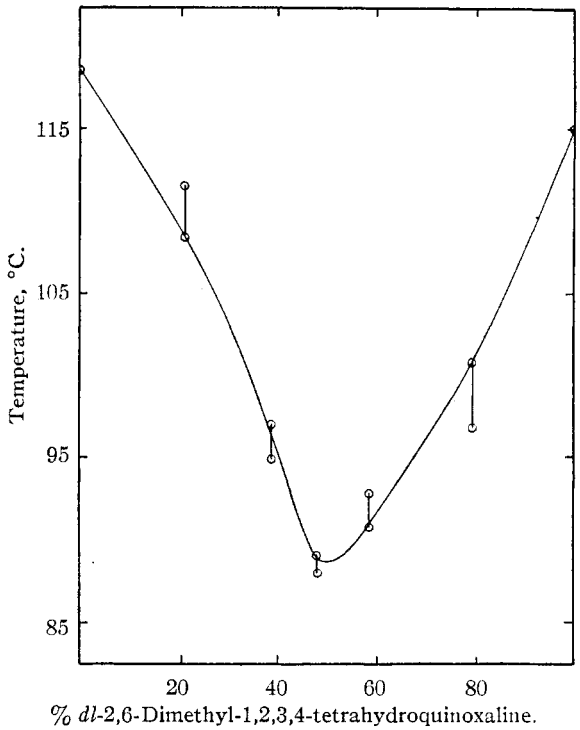

Fig. 1.—Melting point–composition curve of *dl*-2,6- and 2,7-dimethyl-1,2,3,4-tetrahydroquinoxaline; melting point range of each mixture indicated by O–O.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF *dl*-2,6-DIMETHYL-1,2,3,4-TETRAHYDROQUINOXALINE AND *dl*-2,7-DIMETHYL-1,2,3,4-TETRAHYDROQUINOXALINE

1,2,3,4-Tetrahydroquinoxaline	Solvent	Maxima mμ	Maxima ε × 10⁻³
dl-2,6-Dimethyl-	Ethanol, 95%	256	4.95
		314	3.83
	HCl, 0.1 *N*	243	5.16
		294	1.31
dl-2,7-Dimethyl-	Ethanol, 95%	256	5.19
		314	4.27
	HCl, 0.1 *N*	244	4.26
		295	0.92

Hinsberg's mixture was prepared by condensing 3,4-diaminotoluene with chloroacetone. The product, collected over a wide boiling range, was reduced to give a mixture of *dl*-2,6- and -2,7-dimethyl-1,2,3,4-tetrahydroquinoxaline. The melting point of this purified mixture was 88–89°, about 30° lower than that of either of the pure isomers, comparing exactly with the melting point of the eutectic obtained by mixing the pure isomers together in a 1:1 ratio. Hence, a mixture of 2,6- and 2,7-dimethylquinoxaline was indicated to exist in Hinsberg's mixture. Attempts to achieve separation by fractional crystallization of the two isomers in the reduced Hinsberg mixture failed.

Experimental Procedures

2-Chloro-3-methylquinoxaline.—A solution of 2.0 g. of 2-hydroxy-3-methylquinoxaline[2] in 90 ml. of phosphorus oxychloride was refluxed for one-half hour. The excess phosphorus oxychloride was distilled off, and the residue

(1) Abstracted in part from a thesis by Morton Munk, presented to the Graduate Faculty of the University of Miami, in partial fulfillment of the requirements for the degree of Master of Science in Chemistry, January, 1952.
(2) O. Hinsberg, *Ann.*, **237**, 368 (1887).
(3) H B. Marks and H. P. Schultz, THIS JOURNAL, **73**, 1368 (1951).
(4) C. Ris, *Ber.*, **21**, 382 (1888).