TABLE I

Physical Constants and Related Data for Acids from Aryl Fluorides

Compound	Yield, %	M.P., °C.	Neutral Equivalent		Fluorine	
			Calcd.	Found	Calcd.	Found
o-Fluorobenzoic acid	60.0	123–124				
5-Methyl-2-fluorobenzoic acid	58.0	159–160	154	156, 159	12.33	12.45, 12.68
3-Methyl-2-fluorobenzoic acid	2.6	109–110	154	154, 155	12.33	12.10, 12.18
1-Fluoro-2-naphthoic acid	30.0	193–194	190	187, 187	9.99	9.97, 9.81

presence of furan.[7] The same adduct was isolated when o-fluorobromobenzene was shaken for 4 days at 25° with lithium amalgam in furan.[5]

When n-butyllithium which was prepared in tetrahydrofuran[8] was added to fluorobenzene at $-40°$, no reaction was noted, but on warming to $-25°$ a very vigorous reaction occurred, and a small amount of triphenylene was isolated. In order to avoid this almost uncontrollable reaction, the temperature of the reaction mixture was maintained between -50 and $-60°$ for 7 hr. On carbonation o-fluorobenzoic acid was obtained in a crude yield of 60%. By employing these conditions, the metalation of the following aryl fluorides was effected in the same manner (Table I).

EXPERIMENTAL[9]

The following reaction under method A for the metalation of fluorobenzene is described in detail, and this general procedure was employed for the metalation of the other aryl fluorides.

Fluorobenzene and n-butyllithium in tetrahydrofuran a $-50°$. Method A. Into a 3-necked, 500-ml., round-bottomed flask was introduced 9.6 g. (0.1 mole) of fluorobenzene in 100 ml. of tetrahydrofuran.[10] To this slowly stirred solution, which was cooled to $-50°$ by means of a Dry Ice–acetone bath, was added over a period of 5 min. 0.1 mole of n-butyllithium in 55 ml. of tetrahydrofuran.[11] The reaction mixture was stirred at this temperature for 7 hr. and carbonated by pouring jet-wise onto a Dry Ice–ether slurry. The basic extract was acidified to yield 9 g. (60% of crude o-fluorobenzoic acid which melted between 110–116°. On crystallization from water, the m.p. was 123–124°. A mixed melting point with an authentic specimen was undepressed.

In two other preparations which were carried out as described above except that the times were 3 and 12 hours, respectively, the yields of crude o-fluorobenzoic acid were 36 and 33%. When p-fluorotoluene was treated in the same manner for a period of 3 or 12 hr., the yields of 5-methyl-2-fluorobenzoic acid were 20 and 33%, respectively.

Method B. To a stirred solution of 0.1 mole of n-butyllithium in 75 ml. of tetrahydrofuran, was added 9.6 g. (0.1 mole) of fluorobenzene. The temperature was kept at $-40°$ for 35 min. and when no reaction was noted, the temperature was permitted to rise to $-25°$. At this point a vigorous reaction took place, and the temperature rose to 12°. The color of the reaction mixture was brown. The reaction mixture was carbonated and worked up in the preceding manner. No acid was obtained from the basic extract, but from the neutral layer 0.6 g. of triphenylene was isolated. The m.p. was 193–194° on crystallization from 1-propanol. A mixed m.p. with an authentic specimen was undepressed.

The Department of Chemistry
Iowa State College
Ames, Iowa

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(8) This solvent was employed because its base strength is greater than that of diethyl ether; H. C. Brown and R. M. Adams, *J. Am. Chem. Soc.*, **64**, 2557 (1942).

(9) All melting points are uncorrected, and all reactions were carried out in a dry, oxygen-free atmosphere.

(10) The tetrahydrofuran was dried and purified by first shaking with sodium hydroxide pellets, refluxing over sodium metal for several hours, and finally distilling, immediately before use, from lithium aluminum hydride.

(11) H. Gilman and B. Gaj, *J. Org. Chem.*, 22, 447 (1957).

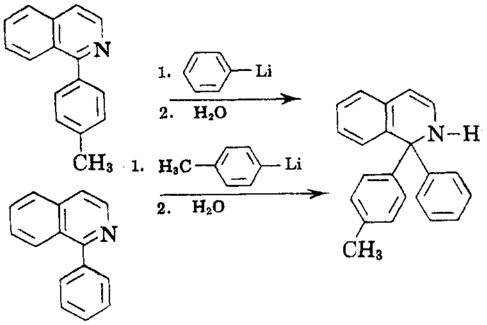
Reaction of Phenyl- and p-Tolyllithium with 1-Arylisoquinolines

Henry Gilman and Theodore Soddy

Received April 9, 1956

In the course of an investigation in this laboratory which involved the preparation of some 1-substituted isoquinolines, there arose the desirability of studying the addition of aryllithium reagents to 1-arylisoquinolines.

In an earlier investigation,[1] the addition of phenyl- and p-tolyllithium to 2-p-tolylquinoline and 2-phenylquinoline, respectively, was found to yield the identical compound, 2-phenyl-2-(p-tolyl)-1,2-dihydroquinoline which resulted from the attack at the azomethine linkage. At that time, also, there was an attempt made to prepare 1-phenyl-1-(p-tolyl)-1,2-dihydroisoquinoline by treating 1-p-tolyl- and 1-phenylisoquinoline with



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(1) H. Gilman and G. C. Gainer, *J. Am. Chem. Soc.*, 69, 877 (1947).

phenyl- and *p*-tolyllithium, respectively,[2] but no product could be isolated. We have been able, however, to carry out this series of reactions and have obtained products which could be isolated and identified. The compounds were purified by fractional crystallization from absolute ethanol. The product from each of the reactions was found to be 1-phenyl-(1-*p*-tolyl)-1,2-dihydroisoquinoline. This fact was demonstrated by a mixture decomposition point and identical infrared spectra. Both of the spectra contained a 1,4 disubstituted phenyl band at 12.3 μ, a phenyl ring band at 6.15 μ, and a N–H band at 3.1 μ.

EXPERIMENTAL[3]

Reaction of p-Tolyllithium with 1-Phenylisoquinoline. Into a 500-ml., 3-necked, round-bottomed flask which was equipped with a mechanical stirrer, reflux condenser, and a dropping funnel, there was placed 16 g. (0.08 mole) of 1-phenylisoquinoline in 200 ml. of anhydrous ether. To this vigorously stirred solution, there was added dropwise a solution of *p*-tolyllithium (0.08 mole) in 90 ml. of anhydrous ether. After the addition of 2, 5, and 8 ml. of the *p*-tolyllithium solution, the reaction mixture became light red, light brown, and, finally, dark green in color. The dark green color was present throughout the remainder of the addition. On completion of the addition, the reaction mixture was refluxed for 45 min. at which time Color Test I[4] was negative. The reaction mixture was hydrolyzed with a saturated solution of ammonium chloride, and the ethereal extract was dried over anhydrous sodium sulfate. The ether was removed by distillation, and the residue was dissolved in absolute ethanol. This solution was treated with charcoal, filtered, and evaporated by means of dry air to give a compound which decomposed between 176–178°. The yield was 0.5 g. or 2.5%.

Anal. Calcd. for $C_{22}H_{18}N$: N, 4.69. Found: N, 4.68, 4.55.

Reaction of phenyllithium with 1-p-tolylisoquinoline. Into a 500-ml., 3-necked, round-bottomed flask, which was equipped as described above, there was placed 19 g. (0.09 mole) of 1-*p*-tolylisoquinoline in 200 ml. of anhydrous ether. To this solution there was added 0.09 mole of phenyllithium in 100 ml. of anhydrous ether. The color of the reaction mixture became dark green after the addition of the first 8 ml. of the phenyllithium solution, and the color was retained for the remainder of the addition. Color Test I[4] was negative within 15 min. after the addition was completed. The reaction mixture was worked up in the same manner as described above to give a product which decomposed between 176–178°. The yield was 0.5 g. or 2.5%.

Acknowledgment. The authors wish to express their appreciation to R. M. McCord, E. M. Layton, and Dr. V. A. Fassel of the Institute for Atomic Research, Iowa State College, for obtaining the infrared spectra of the compounds.

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THE DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

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(2) G. C. Gainer, doctoral dissertation, Iowa State College, Ames, Iowa, 1946.

(3) All melting points are uncorrected.

(4) H. Gilman and J. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

Derivatives of *o*-Phenylenedioxyacetic Acid as Plant Growth-Regulators[1]

HOWARD A. HARTZFELD,[2] ROBERT G. JOHNSON,[3] AND HENRY GILMAN

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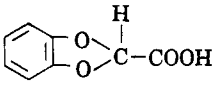
A reasonable extension of studies[4] on the plant growth-regulator activity of phenoxyacetic acid derivatives seemed to be the investigation of derivatives of *o*-phenylenedioxyacetic acid,[5] I.



I

Accordingly, we have prepared and are reporting here the synthesis of a number of derivatives of I. We are also reporting the plant growth-regulating activity of these compounds as measured by the leaf repression method.[6]

The acid (I) and its ethyl ester were reported initially by Christiansen and Dolliver.[7] Subsequently, Burger and coworkers[8] prepared the acid and a number of its derivatives for testing for antispasmodic activity. After the work reported here had been completed, a paper by Cavill and Ford[9] on the subject of *o*-phenylenedioxyacetic acid and its chloro derivatives appeared in the literature. These latter workers seem to be the only ones other

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(1) Abstracted from a Dissertation submitted by H. A. H. to the Graduate School of Iowa State College in partial fulfillment of the requirements for the Ph.D. degree in chemistry, December 1953.

(2) Present address: Research Division, Phillips Petroleum Company, Bartlesville, Okla.

(3) Present address: Department of Chemistry, Xavier University, Cincinnati, Ohio.

(4) Studies carried out under contract with the Chemical Corps of the U.S. Army. Dr. R. L. Weintraub, Fort Detrick, Md., arranged for the biological testing.

(5) Cavill and Ford (ref. 9) name this compound, benzo-1:3-dioxolo-2-carboxylic acid and *Chemical Abstracts* refers to it as 1,3-benzodioxole-2-carboxylic acid.

(6) J. W. Brown and R. L. Weintraub, *Botan. Gaz.*, **111**, 448 (1950).

(7) W. G. Christiansen and M. A. Dolliver, *J. Am. Chem. Soc.*, **66**, 312 (1944).

(8) A. Burger, D. G. Markees, W. R. Nes, and W. L. Yost, *J. Am. Chem. Soc.*, **71**, 3307 (1949).

(9) G. W. K. Cavill and D. L. Ford, *J. Chem. Soc.*, 1388 (1954).