(0.005 mole) of *p*-bromobenzyl bromede and 10 ml. of 95% ethyl alcohol were then added and the mixture was refluxed. The refluxing was continued for an hour after the solution had again cleared. When necessary, more alcohol was added in order to bring the reagent into solution. The solution was then cooled rapidly in a stream of cold water and finally in an ice mixture. The esters were filtered and recrystallized from alcohol until constant melting points were obtained. Departures from this general procedure are noted in Table I. All given temperatures are uncorrected.

Analysis.—The Parr bomb was used in conjunction with the Volhard titration method.

TABLE I

p-BROMOBENZYL ESTERS OF SOME AROMATIC CARBOXYLIC ACIDS

Acid	Obs., m. p., °C. Acid	Obs., m. p., °C. Ester	Halogen, % Calcd. Ester	Halogen, % Found Ester
Benzoic	122	45	27.47	27.54
o-Hydroxybenzoic	159	71	26.04	26.20
m-Hydroxybenzoic	201	97[a]	26.04	26.10
p-Hydroxybenzoic	213	146	26.04	26.04
o-Nitrobenzoic	147	69	23.79	23.87
m-Nitrobenzoic	141	114	23.79	23.90
p-Nitrobenzoic	242	121	23.79	23.93
Cinnamic	133	79[b,d]	25.21	25.29
o-Nitrocinnamic	240	98[c,d]	22.08	22.19
p-Nitrocinnamic	286	136[d]	22.08	22.24
o-Toluic	104	46	26.25	26.33
m-Toluic	109	Oil		
p-Toluic	179	72[e]	26.25	26.29
o-Chlorobenzoic	142	57	35.47	35.59
Anisic	184	95	24.89	25.01

[a] Crystallized with partial evaporation. [b] 5 ml. excess of water required to dissolve the salt. [c] Potassium salt of the acid was prepared from potassium carbonate. [d] Acetone replaced alcohol as solvent for this reaction. [e] Slightly more than 5 ml. excess of water required to dissolve the salt.

Acknowledgment.—The authors are pleased to acknowledge an experimental survey of this problem done by J. Benotti under the direction of T. L. Kelly.

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cis and *trans* Forms of β-(*p*-Chlorophenyl)-cinnamic Acid

BY REYNOLD C. FUSON AND HAROLD L. JACKSON

In view of results communicated to us privately by Dr. F. Bergmann,[1] we have modified the procedure of Alexander, Jacoby and Fuson[2] for the preparation of β-(*p*-chlorophenyl)-cinnamic acid by the Reformatsky method and have been able to isolate the acid in *cis* and *trans* modifications.

In the revised procedure 5 g. of crude ethyl β-phenyl-β-(*p*-chlorophenyl)-β-hydroxypropionate, made by the method of Alexander, Jacoby and Fuson,[2] was heated under reflux for two hours with 50 ml. of glacial acetic acid and 25 ml. of acetic anhydride. The acetic acid and acetic anhydride were removed by distillation at the aspirator. The residue was distilled under 1–2 mm. pressure, and the product that distilled between 65 and 69° was collected.

This distillate was treated with 10 g. of sodium hydroxide dissolved in 20 ml. of water and 10 ml. of ethanol. The alkaline hydrolysis mixture was heated under reflux for twenty hours. When the cooled solution was poured into 100 ml. of cold water, a white crystalline solid precipitated. The mixture was made acid with dilute hydrochloric acid. The product melted over a range of 140 to 157°; yield, 3.4 g. Fractional crystallization of this product from dilute ethanol yielded two isomers; one melted at 164.8–165.7° and the other at 173.0–173.8°. Mixed melting point determinations with samples, kindly supplied by Dr. Bergmann, showed these acids to be identical with his low-melting and high melting compounds.

Infrared absorption spectra[3] indicated that the two forms were *cis* and *trans* isomers. The presumption that the low-melting isomer was the *cis* modification was supported by the observation that it was more soluble in diethyl ether than the high-melting isomer.

From these results it appears that the compound described by Alexander, Jacoby and Fuson[2] and melting at 168° must have been an impure sample of the *trans* acid, the contaminant being presumably the *cis* isomer.

[1] See Bergmann, THIS JOURNAL, **70**, 1612 (1948).

[2] Alexander, Jacoby and Fuson, *ibid.*, **57**, 2208 (1935).

[3] Infrared absorption spectra were determined by Mrs. J. L. Johnson.

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2-Benzofuryllithium and 3-Benzofuryllithium

BY HENRY GILMAN AND DONALD S. MELSTROM

2-Bromobenzofuran does not react with magnesium, under conventional conditions, to give a Grignard reagent.[1] However, Reichstein and Baud[2] showed that the activated magnesium-copper alloy[3] react with 3-bromobenzofuran to give, subsequent to carbonation, about 1% of 3-benzofurancarboxylic acid in addition to 28% of *o*-hydroxyphenylacetylene.

By means of the recently developed halogen-metal interconversion reaction, we have shown that 2-bromobenzofuran reacts with *n*-butyllithium to give, on carbonation, a 62% yield of pure 2-benzofurancarboxylic acid.

The yield of 3-benzofurancarboxylic acid, from 3-bromobenzofuran and *n*-butyllithium, was 12%. However, this reaction was particularly interesting because of the formation of appreciable quantities of the isomeric 2-benzofurancarboxylic acid. It is probable that the 2-acid was formed from the 3-bromo compound in essential accordance with

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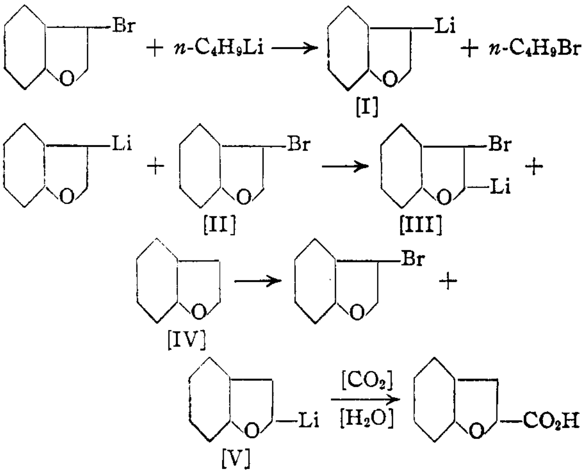
[1] E. W. Smith, unpublished studies.

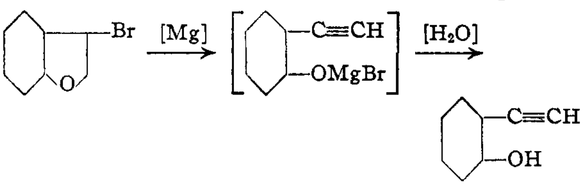
[2] Reichstein and Baud, *Helv. Chim. Acta*, **20**, 892 (1937).

[3] Gilman, Peterson and Schulze, *Rec. trav. chim.*, **47**, 19 (1928).

the following transformations. That is, the initially formed 3-benzofuryllithium [I] metalated [II] in the highly reactive *ortho*- or 2-position to give 3-bromo-2-benzofuryllithium [III] which then metalated the unsubstituted benzofuran [IV] in the expected 2-position to give 2-benzofuryllithium [V]. Another possible explanation involves intramolecular metalation, or essentially rearrangement of the 3-lithium compound to the 2-lithium compound. A related transformation occurs when 3-bromodibenzofuran is treated with n-butyllithium and the acids obtained were 3-dibenzofurancarboxylic acid and 4-dibenzofurancarboxylic acid.[4] It is highly probable that a related so-called rearrangement will be observed with other systems in which there is available a hydrogen which is quite sensitive to metalation.[5]



From a room temperature reaction between 3-bromobenzofuran and three equivalents of n-butyllithium we obtained a 67% yield of o-hydroxyphenylacetylene. It has been suggested[2] that this compound, isolated from the reaction between magnesium and 3-bromobenzofuran, owes its formation to an intramolecular cleavage. In support of this postulate is the difficulty of forming Grignard reagents from β-halogen ethers like β-bromoethyl phenyl ether (which gives phenol and ethylene),[6a] and 2-bromomethyltetrahydrofuran (which gives γ-vinylpropyl alcohol).[6b]



However, substituents may have a marked effect because 2,4,5-triphenyl-3-furyllithium is formed in yields of at least 66% from 2,4,5-triphenyl-3-bromofuran and n-butyllithium[7]; and 3-furylsodium and -potassium are formed by the direct action of 3-iodofuran with sodium–potassium alloy.[8] Also, there is a possibility that the cleavage reaction is not confined to β-halogen ethers because the reaction mixture of 2-bromobenzofuran and n-butyllithium appeared to contain some of the o-hydroxyphenylacetylene as evidenced by the unusually characteristic odor of this compound.

Experimental

2-Bromobenzofuran and n-Butyllithium.—First, the 2-bromobenzofuran was prepared from benzofuran dibromide[9] in accordance with the following directions of E. W. Smith.[1] One-tenth mole of crude, dry benzofuran dibromide was distilled at atmospheric pressure. A vigorous evolution of hydrogen bromide occurred, and the oily fraction distilling at 200–235° was collected. This distillate was dissolved in ether, and then washed successively with water, 10% sodium carbonate solution, and again with water. After drying over sodium sulfate, the ether was removed and the 2-bromobenzofuran was obtained (55% yield) by fractional distillation.

Then, a solution of 2 g. (0.01 mole) of 2-bromobenzofuran in a few cc. of ether was added all at once to a solution of 0.014 mole of n-butyllithium in 50 cc. of ether, cooled to −70° in a Dry Ice–acetone bath. The reaction mixture was stirred for two minutes and then carbonated. The yield of crude 2-benzofurancarboxylic acid, melting at 187–189°, was 1.4 g. (86%). Crystallization from dilute ethanol yielded 1.04 g. (62%) of pure acid melting at 192.5–193°. The compound was identified by a mixed m. p. determination with an authentic specimen.[9] In experiments carried out at room temperature, the yield of crude 2-benzofurancarboxylic acid after a reaction period of twenty minutes was 62%, and after forty minutes the yield was 28%. The aqueous filtrates from the acid had the characteristic odor of o-hydroxyphenylacetylene, indicating that some cleavage of the benzofuran ring had taken place.

3-Bromobenzofuran and n-Butyllithium.—The 3-bromobenzofuran was prepared by the following sequence of reactions: coumarin dibromide → 2-benzofurancarboxylic acid → benzofuran[2] → benzofuran dibromide → 3-bromobenzofuran.[1,2,10] The compound, which melted at 35.5–36° after crystallization from petroleum ether (b. p. 28–38°) at −20°, appeared to be unstable and discolored on standing.

A solution of 2 g. (0.01 mole) of 3-bromobenzofuran in a few cc. of ether was added quickly to a solution of 0.014 mole of n-butyllithium in 50 cc. of ether at −70°. The reaction was then stirred for two minutes, and after carbonation there was obtained 0.23 g. (14%) of acid melting at 154–159°. Crystallization from a mixture of benzene and petroleum ether (b. p. 60–68°) gave 0.19 g. (12%) of acid melting at 160–161°, with no change in melting point subsequent to another crystallization from dilute ethanol. The reported melting point is 162° (cor.).[11] A mixed melting point with the 2-isomer showed a depression.

Anal. Calcd. for $C_9H_6O_3$: neut. equiv., 162. Found: neut. equiv., 164 and 161.

Then a series of experiments was carried out varying the time of the reaction and the temperature, and in each case

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[4] Gilman, Willis and Swislowsky, THIS JOURNAL, **61**, 1371 (1939).

[5] A case in point is the simple monocyclic furan type. The phenyl alkyl ethers may not show the reaction under usual conditions because the metalation proceeds generally with more difficulty than the halogen-metal interconversion reaction. See, Gilman, Moore and Baine, *ibid.*, **63**, 2479 (1941), for some factors influencing the rates of these reactions.

[6] (a) Grignard, *Compt. rend.*, **138**, 1048 (1904); (b) Robinson and Smith, *J. Chem. Soc.*, 195 (1936).

[7] Gilman and Melstrom, THIS JOURNAL, **68**, 103 (1946).

[8] Gilman and Wright, *ibid.*, **55**, 2893 (1933).

[9] Fittig and Ebert, *Ann.*, **216**, 162 (1883).

[10] Stoermer and Kahlert, *Ber.*, **35**, 1636 (1902).

[11] Titoff, Müller and Reichstein, *Helv. Chim. Acta*, **20**, 883 (1937).

the only acid isolated was 2-benzofurancarboxylic acid in the following crude yields: 13, 10, 23.5, 13 and 16%. From an experiment carried out in petroleum ether (b. p. 28–38°) with 3 g. (0.025 mole) of 3-bromobenzofuran and a slight excess of *n*-butyllithium, there was obtained, after carbonation and hydrolysis, 0.15 g. of crude *o*-hydroxyphenylacetylene and a trace of unidentified acid melting at 127–129° (possibly *o*-hydroxyphenylpropiolic acid).

***o*-Hydroxyphenylacetylene from 3-Bromobenzofuran.**—A solution of 10 g. (0.051 mole) of 3-bromobenzofuran in 30 cc. of ether was added during five minutes to a solution of 0.154 mole of *n*-butyllithium in 220 cc. of ether at room temperature. The solution was stirred for one hour and then hydrolyzed by pouring on iced dilute hydrochloric acid. The yield of *o*-hydroxyphenylacetylene, distilling at 95–98° under 10 mm., was 4 g. (67%). A part of the phenol was converted to the *p*-nitrobenzoate by treatment with *p*-nitrobenzoyl chloride in pyridine. The melting point was 108–109°, and the reported melting point is 107–108° (cor.).[2]

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Syntheses in the Pyrazene Series: The Preparation and Properties of Pyrazine Sulfonic Acid

BY EUGENE HORT AND PAUL E. SPOERRI

Although recent electron diffraction studies have shown that benzene and pyrazine have very similar structures,[1] direct substitution with the usual electrophilic reagents, which proceeds so well with benzene operates only with great difficulty or not at all with pyrazine. This deactivation seems to be due to the electron-withdrawing inductive and resonance effects of the nitrogen atoms.[2] Even under such severe conditions as those used in the cleavage of lumazine,[3] *i. e.*, treatment with 100% sulfuric acid at 240°, sulfonation has not been observed. In fact, no direct sulfonation of the pyrazine nucleus has ever been reported. It seemed, therefore, of interest to attempt the synthesis of pyrazine sulfonic acid by means of indirect methods.

Methods based on the oxidation of pyrazine thiol were considered impractical because of the susceptibility of pyrazine to strong oxidizing agents. The reaction of chloropyrazine with sodium sulfite solutions was therefore investigated. Since chloropyrazine had previously been found to possess a chlorine atom intermediate in activity between an alkyl and aryl halide,[4] this method was adopted for the preparation.

Chloropyrazine was obtained by the following sequence of operations. Lumazine prepared according to Cain, Mallette and Taylor,[5] was cleaved to 2-hydroxy-3-pyrazinoic acid and then to hydroxypyrazine according to Weijlard, Tishler and Erickson.[3] Chloropyrazine was then prepared by the method of Erickson and Spoerri[4] with the notable exception that phosphorus oxychloride (in a ratio of five moles to one of hydroxypyrazine) was used as sole chlorinating agent.[6]

Experimental[7]

Chloropyrazine was heated in a sealed tube for twelve hours at 150° with a solution of sodium sulfite. The resulting solution was evaporated and the product crystallized from alcohol as bundles of white needles. Analysis after drying at room temperature *in vacuo* showed that the product was sodium pyrazine sulfonate monohydrate. It was extremely soluble in water, slightly soluble in alcohol, insoluble in ether and petroleum ether, and melted at 295°. Neither silver nitrtae nor barium chloride precipitated an insoluble salt.

The free pyrazine sulfonic acid was prepared by treatment of the sodium salt suspended in dry ether with dry hydrogen chloride gas followed by filtration and evaporation of the ether. It was found to be extremely hygroscopic and unsuitable for an analysis even after extensive drying at 50° *in vacuo*. Its aqueous solution gave a strong acid reaction with hydrion paper.

Three grams (0.026 mole) of 2-chloropyrazine, 4.0 g. (0.032 mole) of anhydrous sodium sulfite, and 25 ml. of water were sealed in a Carius tube and thoroughly mixed. The 2-chloropyrazine remained as a separate layer and some of the sodium sulfite remained undissolved. After keeping the tube at 150° for twelve hours and then allowing to cool, it was opened and the homogeneous yellow solution was evaporated to dryness *in vacuo*. The yellow solid residue was extracted with three 50-ml. portions of boiling 95% ethanol. On cooling the solution, masses of white needle clusters separated and were filtered. The filtrate was evaporated to dryness and extracted with two 8-ml. portions of boiling 95% ethanol. The combined extracts were allowed to stand (crystallization is slow), filtered, and the crystals added to the previously obtained portion; yield, 0.75 g. (15%) of colorless needles, m. p. 295°.

The analytical sample was recrystallized twice from 95% ethanol and dried at room temperature for sixty hours *in vacuo* over phosphorus pentoxide. *Anal.* Calcd. for $(C_4H_3N_2)SO_3Na\cdot H_2O$: C, 24.00; H, 2.52; S, 16.02; Na, 11.49. Found: C, 24.08; H, 2.79; S, 16.02; Na, 11.50.

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(1) Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., Schomaker and Pauling, THIS JOURNAL, **61**, 1776 (1939).

(2) Krems and Spoerri, *Chem. Rev.*, **40**, 328 (1947).

(3) Weijlard, Tishler and Erickson, THIS JOURNAL, **67**, 802 (1945).

(4) Erickson and Spoerri, *ibid.*, **68**, 401 (1946).

(5) Cain, Mallette and Taylor, *ibid.*, **68**, 1996 (1946).

(6) Suggested in a personal communication from B. Klein of G. D. Research Inst., Inc.

(7) Microanalyses performed by Dr. Otto Schwarzkopf, 62-12 79th Street, Elmhurst, Long Island, New York.

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3,4,5-Triiodobenzoyl Chloride as a Reagent for Alcohols

BY DAVID C. O'DONNELL, JOHN K. KELLEY, JR.,[1] ROBERT F. O'MALLEY[1] AND ROY H. UPHAM[1]

The use of 3,4,5-triiodobenzoyl chloride for the identification of cellosolves and carbitols has been reported previously.[2] Since the compound is relatively stable to water, it was applied to the monohydric alcohols. The alcohols were used as obtained from the manufacturer without further purification. The acid chloride of the 3,4,5-triiodobenzoic acid was prepared by the method of Klemme and Hunter.[3]

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(1) Taken from theses submitted in partial fulfilment for the M.S. degree.

(2) O'Donnell and Carey, THIS JOURNAL, **68**, 1865 (1946).

(3) Klemme and Hunter, *J. Org. Chem.*, **5**, 508–511 (1940).