TABLE I

ALKYLATION OF NAPHTHALENE WITH BORON FLUORIDE AND ALCOHOLS

Alcohol	Product (yield[a])	B. p. °C.	B. p. Mm.	$n^{20}D$	d^{25}_{25}	MD Calcd.	MD Found	Picrate, m. p., °C.
Cyclohexyl	β-Cyclohexyl- (63%)	190–195	15	1.5973[d]	1.020[d]	69.95	69.7	100[d]
(1.2 moles)	Dicyclohexyl-[b] (9%)	215–225	7					
Tertiary butyl	β-*t*-Butyl- (62%)	140–145	13	1.5685	0.979	60.1	58.3	99[e]
(2.3 moles)	Di-*t*-butyl- (5%)	180–185	13					154[g]
Isopropyl (1.5 moles)	β-Isopropyl- (35%)	265–270	760	1.5775	.974	55.5	57.5	..
Isopropyl (4 moles)	Triisopropyl-[c] (57%)	265–270	760	1.5566	.946	87.15	86.6	..
Benzyl	α-Benzyl- (28%)	200–205	9	(m. p. 58°)[f]				100[f]
(1.1 moles)	β-Benzyl- (2%)							93[f]
	Dibenzyl- (15%)	265–275	9					
	Tribenzyl- (20%)	320–330	9					

[a] Yield calculated on the basis of naphthalene consumed. [b] Mol. wt. calcd. 292; mol. wt. found (ebullioscopically in benzene), 291. [c] Mol. wt. calcd. 254; mol. wt. found 255, 246. *Anal.* Calcd. for $C_{19}H_{26}$: C, 89.76; H, 10.24. Found: C, 89.93; H, 10.62. [d] Bodroux, *Ann. chim. phys.*, [10] 11, 536 (1927). [e] Barbot, *Bull. soc. chim.*, [4] **47**, 1314 (1930). [f] Roux, *Ann. chim. phys.*, [6] **12**, 330 (1887). [g] Fieser and Price, THIS JOURNAL, **58**, 1842 (1936).

tive, m. p. 82°. This seems to prove that under conditions of rapid and easy alkylation no olefin formation occurred.

Cyclohexylnaphthalene from Cyclohexene.—That olefins will react with naphthalene in the presence of boron fluoride alone, however, was demonstrated by bubbling this catalyst through 50 g. of naphthalene in 48 cc. of cyclohexene for an hour and a half. No layers separated in this case. After standing for a day the mixture was washed with water and alkali, 15 g. of naphthalene was recovered and the mixture dried and distilled. A yield of 20 g. (35%) of β-cyclohexylnaphthalene was obtained. It was identified by its physical constants and the melting point of its picrate.

Summary

The alkylation of naphthalene with alcohols using boron fluoride as a catalyst leads to the formation of the β-alkyl derivatives, with the exception of benzyl alcohol which yields largely α-benzylnaphthalene.

A mechanism for the catalytic effect of boron fluoride in aromatic alkylation is proposed involving the formation of alkyl cations which may then react with the aromatic nucleus.

A mechanism is suggested for the formation of meta-dialkylbenzene from the alkylation of benzene by the Friedel–Crafts reaction.

URBANA, ILLINOIS RECEIVED JULY 5, 1938

[CONTRIBUTION FROM RÖHM & HAAS COMPANY, INC.]

Friedel-Crafts Condensation with Arylalkylene Ether Chlorides

BY HERMAN ALEXANDER BRUSON AND JOHN W. EASTES

While attempting to treat β-phenoxy-β′-chlorodiethyl ether with anhydrous aluminum chloride so as to form a possible chain condensation product by the elimination of hydrogen chloride from a plurality of molecules according to equation (A)

$$C_6H_5—O—C_2H_4—O—C_2H_4Cl— \xrightarrow{AlCl_3}$$
$$C_6H_5—O—C_2H_4—O—C_2H_4(—C_6H_4—O—C_2H_4—O—$$
$$C_2H_4)_x—C_6H_4—O—C_2H_4—O—C_2H_4 \ldots + HCl \quad (A)$$

it was observed that practically no reaction occurred at temperatures as high as 70°, and that the starting material could be recovered substantially unchanged.

The unusual resistance of the ether linkages to splitting by the aluminum chloride, and the failure of the terminal aliphatically bound chlorine atom to react with the phenyl nucleus at temperatures of about 50–60°, where Friedel–Crafts reactions ordinarily take place with ease, suggested the possibility that other typical alkylating or acylating agents would condense probably with the benzene ring according to the customary synthesis, so as to alkylate or acylate the phenyl nucleus without affecting the ether linkages or the terminal chlorine atom.

Such compounds, where the alkyl group is of sufficient chain length and of the proper configuration, are intermediates for the synthesis of newer detergents and wetting agents, and are of interest also in other fields of organic research.[1]

---

(1) Bruson, U. S. Patents (a) 2,097,441; (b) 2,098,203; (c) 2,107,366; (d) 2,107,367; (e) 2,115,250; (f) 2,115,192.

It was therefore of interest to try various alkylating and acylating agents upon aryloxyalkylene ethers of the type $R–O–CH_2CH_2Cl$ and $R–O–CH_2CH_2–O–CH_2CH_2Cl$ where R is an aryl nucleus.

It was found that aromatic ether chlorides of this type condensed with acid anhydrides, acyl halides, alkyl halides or olefinic compounds in the presence of anhydrous aluminum chloride to yield the corresponding nuclear acyl or alkyl derivatives without any appreciable scission of the ether linkages or elimination of the terminal chlorine atom.

Phthalic anhydride, for example, condensed with β-phenoxy-β′-chlorodiethyl ether to give β-chloroethoxyethoxybenzoyl-*o*-benzoic acid (I). Similarly, β-phenoxyethyl chloride yielded the corresponding acid (II). Both are crystalline compounds. Attempts to obtain the next higher homolog (III) by the use of β-phenoxyethoxy-β′-chlorodiethyl ether yielded a sirupy acid.

$$C_6H_4(COOH)—CO—C_6H_4—O—CH_2—CH_2—O—CH_2CH_2Cl \quad (I)$$

$$C_6H_4(COOH)—CO—C_6H_4—O—CH_2CH_2Cl \quad (II)$$

$$C_6H_4(COOH)—CO—C_6H_4—O—CH_2CH_2—O—CH_2—CH_2—O—CH_2CH_2Cl \quad (III)$$

The tendency for these compounds to form is so great that they may be obtained even when benzene is employed as an "inert" solvent for the reactants since no appreciable quantity of benzoyl-*o*-benzoic acid is formed under the conditions used.

The introduction of an ortho substituent, namely, a chloro, methyl, or methoxy group in the phenyl radical of the chloro alkylene ether used, did not prevent the condensation from taking place, the corresponding compounds IV, V and VI being obtained in crystalline form. However, the presence of a para alkyl substituent (methyl) prevented the condensation under the same conditions. It is believed therefore that the para position to the phenol ether link, is the position occupied by the entering phthaloyl group.

$$C_6H_4(COOH)—CO—C_6H_3(Cl)—O—CH_2CH_2—O—CH_2CH_2Cl \quad (IV)$$

$$C_6H_4(COOH)—CO—C_6H_3(CH_3)—O—CH_2CH_2—O—CH_2CH_2Cl \quad (V)$$

$$C_6H_4(COOH)—CO—C_6H_3(OCH_3)—O—CH_2CH_2—O—CH_2CH_2Cl \quad (VI)$$

The condensation of β-(2-naphthoxy)-β′-chlorodiethyl ether with phthalic anhydride likewise yielded the corresponding chloroethoxyethoxy naphthoyl-*o*-benzoic acid (VII) in crystalline form.

In a similar manner, succinic anhydride and maleic anhydride each were condensed with β-phenoxy-β′-chlorodiethyl ether to form the corresponding chloroethoxyethoxybenzoylpropionic acid (VIII) and chloroethoxyethoxybenzoylacrylic acid (IX), respectively.

$$ClCH_2CH_2—O—CH_2CH_2—O—C_6H_4—CO—CH_2CH_2COOH \quad (VIII)$$

$$ClCH_2CH_2—O—CH_2CH_2—O—C_6H_4—CO—CH=CH—COOH \quad (IX)$$

Finally, β-phenoxy-β′-chlorodiethyl ether condensed with acetic anhydride or acetyl chloride to yield chloroethoxyethoxyphenyl methyl ketone (X) and with *n*-butyl chloride to give butylphenoxyethoxyethyl chloride (XI), both of which were oils.

The unusual stability of the linkages and the terminal chlorine atom in the beta-aryloxy ether chlorides of the type $R–O–CH_2CH_2Cl$ and $R–O–CH_2CH_2–O–CH_2CH_2Cl$ was still more striking when attempts were made to alkylate the aromatic nucleus by means of olefins or alcohols.

Diisobutylene condensed readily with β-phenoxy-β′-chlorodiethyl ether in the presence of concentrated sulfuric acid to give the corresponding β-(*p*-*t*-octylphenoxy)-β′-chlorodiethyl ether (XII), which was identical with the product obtained by the half etherification of β,β′-dichlorodiethyl ether and *p*-α,α,γ,γ-tetramethylbutylphenol.[1b]

Furthermore, even at temperatures as high as 180° it was possible to alkylate the aromatic nucleus of these ethers with a long chain higher alcohol, in the presence of surface-active siliceous clays ("Tonsil") without appreciable splitting off of hydrochloric acid or scission of the ether linkages. In this manner, octanol-2 condensed with β-phenoxy-β′-chlorodiethyl ether to yield *s*-octyl phenoxyethoxy-ethyl chloride (XIII); and lauryl alcohol condensed with β-phenoxyethyl chloride to yield dodecylphenoxyethyl chloride (XIV). In these compounds the position and the configuration of the alkyl groups has not been determined.

Experimental

(I) β-Chloroethoxyethoxybenzoyl-*o*-benzoic Acid.—(a). To a mixture of 50 g. of phthalic anhydride, 90 g. of anhydrous powdered aluminum chloride and 250 cc. of carbon disulfide in a 1-liter 3-necked flask fitted with a sealed stirrer and reflux condenser, there was added gradually 68 g. of β-phenoxy-β′-chlorodiethyl ether[2] while stirring the reaction mixture. The temperature was maintained at gentle refluxing during the addition and for five hours

---

(2) Cretcher, Koch and Pittenger, THIS JOURNAL, **47**, 1174 (1925).

thereafter, during which time hydrogen chloride was evolved copiously. The carbon disulfide was then distilled off on a water-bath and the residue decomposed with 250 cc. of 3 *N* hydrochloric acid on ice, giving a white precipitate which was filtered off and dried. It was purified by dissolving in 10% soda solution, filtering and extracting the oil impurities from the filtrate with ether. After removal of the ether by boiling, the clear, alkaline solution obtained was acidified with hydrochloric acid. The waxy precipitate which at first formed gradually solidified to a hard white mass; yield 72 g., after recrystallization from glacial acetic acid. The compound formed colorless crystals, m. p. 123–124°.

Anal. Calcd. for $C_{18}H_{17}O_5Cl$: C, 62.00; H, 4.91; Cl, 10.18. Found: C, 62.44; H, 4.58; Cl, 10.16.

(**b**). By adding 45 g. of aluminum chloride in small portions at a time to a solution of 67 g. of β-phenoxy-β′-chlorodiethyl ether and 49 g. of phthalic anhydride in 400 cc. of dry benzene while stirring and cooling with tap water, stirring thereafter for eight hours at 25–30°, and decomposing with ice and hydrochloric acid in the usual manner followed by steaming off the benzene, there was obtained 40 g. of the above chloroethoxyethoxybenzoyl-*o*-benzoic acid, m. p. 124°, and containing 10.09% Cl, indicating that no appreciable quantity of benzoyl-*o*-benzoic acid was formed.

(**II**) **β-Chloroethoxybenzoyl-*o*-benzoic Acid.**—A mixture consisting of 49 g. of phthalic anhydride and 90 g. of anhydrous aluminum chloride in 200 cc. of carbon disulfide was treated with 52 g. of β-phenoxyethyl chloride as described in (Ia) above and worked up in the same manner. The product crystallized from benzene in colorless crystals, m. p. 145°.

Anal. Calcd. for $C_{16}H_{13}O_4Cl$: C, 63.05; H, 4.30; Cl, 11.65. Found: C, 62.69; H, 4.18; Cl, 10.05.

(**IV**) **4-(β-Chloroethoxyethoxy)-3-chlorobenzoyl-*o*-benzoic Acid.**—Seventy-eight grams of β-(2-chlorophenoxy)-β′-chlorodiethyl ether was added slowly to a mixture of 49 g. of phthalic anhydride and 90 g. of anhydrous aluminum chloride in 200 cc. of carbon disulfide. The reaction mixture was stirred and heated for five hours on a steam-bath under reflux and then worked up as described in (I). The product crystallized from glacial acetic acid in colorless crystals, m. p. 85°.

Anal. Calcd. for $C_{18}H_{16}O_5Cl_2$: C, 56.38; H, 4.20; Cl, 18.52. Found: C, 56.46; H, 4.37; Cl, 17.5.

(**V**) **4-(β-Chloroethoxyethoxy)-3-methylbenzoyl-*o*-benzoic Acid.**—Seventy-one grams of β-(2-methylphenoxy)-β′-chlorodiethyl ether was added slowly to a mixture of 49 g. of phthalic anhydride and 90 g. of aluminum chloride in 200 cc. of carbon disulfide and after heating for five hours the product worked up as above; crystals, m. p. 87–88.5° (from acetic acid).

Anal. Calcd. for $C_{19}H_{19}O_5Cl$: C, 62.89; H, 5.29; Cl, 9.79. Found: C, 62.31; H, 5.33; Cl, 10.00.

(**VI**) **4-(β-Chloroethoxyethoxy)-3-methoxybenzoyl-*o*-benzoic Acid.**—Seventy-seven grams of β-(2-methoxyphenoxy)-β′-chlorodiethyl ether was added gradually to a mixture of 49 g. of phthalic anhydride and 90 g. of anhydrous aluminum chloride in 200 cc. of carbon disulfide. After four hours of boiling on a steam-bath while stirring under reflux, the product was worked up as above; colorless crystals, m. p. 188–190° (from acetic acid).

Anal. Calcd. for $C_{19}H_{19}O_6Cl$: C, 60.25; H, 5.07; Cl, 9.37. Found: C, 60.13; H, 4.90; Cl, 9.40.

(**VII**) **(2-β-Chloroethoxyethoxy)-naphthoyl-*o*-benzoic Acid.**—Seventy-six grams of β-2-naphthoxy-β′-chlorodiethyl ether was added slowly to 49 g. of phthalic anhydride and 90 g. of aluminum chloride in 200 g. of carbon disulfide. The mixture was stirred and boiled for six hours under reflux and worked up in the usual manner. The product was crystallized first from benzene and then from glacial acetic acid; colorless crystals, m. p. 125°.

Anal. Calcd. for $C_{22}H_{19}O_5Cl$: C, 66.25; H, 4.82; Cl, 8.91. Found: C, 66.22; H, 4.63; Cl, 8.84.

(**VIII**) **4-(β-Chloroethoxyethoxy)-benzoyl-β′-propionic Acid.**—To a gently refluxing mixture of 33 g. of succinic anhydride, 90 g. of aluminum chloride and 200 cc. of carbon disulfide there was added gradually 67 g. of β-phenoxy-β′-chlorodiethyl ether while stirring. Refluxing was continued for five hours thereafter. The product was then decomposed with ice and hydrochloric acid. After two crystallizations from benzene and three recrystallizations from ethylene dichloride, the pure compound was obtained in colorless crystals, m. p. 97–98°.

Anal. Calcd. for $C_{14}H_{17}O_5Cl$: C, 55.91; H, 5.69; Cl, 11.81. Found: C, 55.94; H, 5.60; Cl, 11.63.

(**IX**) **4-(β-Chloroethoxyethoxy)-benzoyl-β′-acrylic Acid.**—Sixty-seven grams of β-phenoxy-β′-chlorodiethyl ether was treated with a mixture of 33 g. of maleic anhydride and 90 g. of aluminum chloride in 250 cc. of carbon disulfide for five hours. The product was decomposed with ice and hydrochloric acid and the crude waxy acid obtained purified by dissolving in a *cold* solution of 50 g. of sodium carbonate in 1200 cc. of water and filtering. The clear filtrate upon acidification with dilute hydrochloric acid gave a yellow precipitate of the crude product. This was recrystallized from benzene giving pale yellow crystals, m. p. 100°.

Anal. Calcd. for $C_{14}H_{15}O_5Cl$: C, 56.30; H, 5.06; Cl, 11.88. Found: C, 56.24; H, 5.05; Cl, 11.45.

(**X**) **β-(4-Acetylphenoxy)-β′-chlorodiethyl Ether.**—(**a**). A solution consisting of 34 g. of acetic anhydride and 67 g. of β-phenoxy-β′-chlorodiethyl ether was added slowly to a well-stirred mixture of 90 g. of aluminum chloride and 200 cc. of carbon disulfide cooled in an ice-bath. Stirring was continued for one hour in the ice-bath and then for two hours at room temperature with occasional cooling when the temperature tended to rise. The reaction mixture was decomposed with iced 3 *N* hydrochloric acid and the carbon disulfide distilled off. The residual oil was washed and distilled under vacuum. The product came over at 210–222° (10 mm.) as a yellow oil.

Anal. Calcd. for $C_{12}H_{15}O_3Cl$: C, 59.36; H, 6.23; Cl, 14.63. Found: C, 60.04; H, 6.09; Cl, 14.30.

(**b**). The same compound was obtained from 50 g. of aluminum chloride in 200 cc. of carbon disulfide treated with a mixture of 16.5 g. of acetyl chloride and 67 g. of β-phenoxy-β′-chlorodiethyl ether.

(**XI**) **β-Butylphenoxy-β′-chlorodiethyl Ether.**—A solution of 31 g. of *n*-butyl chloride and 67 g. of β-phenoxy-β′-chlorodiethyl ether was added slowly to a stirred mixture of

45 g. of aluminum chloride and 200 cc. of carbon disulfide. The mixture was then refluxed on the steam-bath for sixteen hours, after which the carbon disulfide was removed by distillation. The residue was decomposed with iced dilute hydrochloric acid, the oil layer separated, washed, and distilled *in vacuo*. The product distilled over at 170–185° (9 mm.) as a colorless oil.

Anal. Calcd. for $C_{14}H_{21}O_2Cl$: C, 65.45; H, 8.27; Cl, 13.83. Found: C, 66.44; H, 8.02; Cl, 13.35.

(XII) **β-(*p*-(α,α,γ,γ-Tetramethylbutylphenoxy))-β'-chlorodiethyl Ether.**—To a solution of 100 g. of β-phenoxy-β'-chlorodiethyl ether and 56 g. of diisobutylene (b. p. 100–104°) there was added dropwise during forty-five minutes while stirring and occasionally cooling, 20 g. of 98% sulfuric acid. The mixture was then stirred for seven hours at room temperature and allowed to stand for eighteen hours. The thick oil obtained was warmed with 145 cc. of 10% sodium hydroxide solution, the oil layer separated, washed and distilled *in vacuo*. The fraction of b. p. 157–167° (1 mm.) was the desired product; yield 107.5 g. or 68%.

Anal. Calcd. for $C_{18}H_{29}O_2Cl$: Cl, 11.34. Found: Cl, 11.68.

(XIII) **β-(*s*-Octylphenoxy)-β'-chlorodiethyl Ether.**—A mixture consisting of 180 g. of β-phenoxy-β'-chlorodiethyl ether, 117 g. of octanol-2 and 20 g. of "Tonsil" clay was heated with stirring for four hours at 160–175° under reflux attached to a water trap. The clay was then filtered off and the *s*-octylphenoxyethoxyethyl chloride, b. p. 175–185° (3 mm.), isolated by vacuum distillation; yield 60%.

Anal. Calcd. for $C_{18}H_{29}O_2Cl$: Cl, 11.34. Found: Cl, 10.78.

(XIV) **β-Dodecylphenoxyethyl Chloride.**—A mixture consisting of 56 g. of β-phenoxyethyl chloride, 66.5 g. of lauryl alcohol and 15 g. of "Tonsil" clay was boiled with rapid stirring for three and one-half hours under a reflux condenser attached to a water trap. The temperature gradually rose from 165 to 195° during this period. Heating was continued for sixteen hours at 180–195°. The mixture was then cooled, diluted with toluene and filtered hot by means of a Büchner funnel. The filtrate was fractionated under reduced pressure. Dodecylphenoxyethyl chloride distilled over at about 185–195° (1 mm.) as a colorless oil, the chlorine analysis of which indicated a purity of 97.5%.

Summary

Aromatic alkylene ether chlorides or polyalkylene ether chlorides of the type R–(O-alkylene)$_n$Cl readily undergo Friedel–Crafts nuclear alkylation or acylation reactions without splitting the ether links, loss of the terminal chlorine atom, or appreciable polymeric intercondensation. A number of acylations with phthalic, succinic, maleic and acetic anhydrides and alkylations with butyl chloride, capryl alcohol, diisobutylene and lauryl alcohol are described.

PHILADELPHIA, PENNA. RECEIVED AUGUST 5, 1938

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

The Effect of the Composition of the Medium upon the Growth of Yeast in the Presence of Bios Preparations. II. The Response of Several Strains of Saccharomyces Cerevisiae[1]

BY JAMES B. LESH, L. A. UNDERKOFLER AND ELLIS I. FULMER

In a previous communication from these Laboratories[2] data were presented showing that, for the one strain of yeast employed, the presence of magnesium sulfate markedly increased the growth of the yeast in the presence of Bios II or a mixture of Bios II and Bios I (*i*-inositol). The present paper deals with the response of several strains of *Saccharomyces cerevisiae* to the above-mentioned reagents. While 23 strains of yeast were studied during the present investigation, data are presented here for only the 13 of these which can be obtained readily from standard sources: these strains are listed in Table I. Lucas,[3] Williams, Warner and Roehm,[4] Williams and Saunders,[5] Stantial[6] and Farrell[7] have noted significant differences among various strains of yeast as to their response to various Bios preparations, but the effect of magnesium sulfate had not been considered previously. Magnesium sulfate is a customary ingredient of most media used for growing yeast. However, the media developed in these Laboratories by Fulmer, Nelson and Sherwood[8] for the growth of yeast in the

---

[1] This work was supported in part by a grant from the Industrial Science research funds of the Iowa State College for studies on the fermentative utilization of agricultural products.

[2] E. I. Fulmer, L. A. Underkofler and J. B. Lesh, THIS JOURNAL, **58**, 1356 (1936).

[3] G. H. W. Lucas, *J. Phys. Chem.*, **28**, 1180 (1924).

[4] R. J. Williams, M. E. Warner and R. R. Roehm, THIS JOURNAL, **51**, 2764 (1929).

[5] R. J. Williams and D. H. Saunders, *Biochem. J.*, **28**, 1887 (1934).

[6] Helen Stantial, *Trans. Roy. Soc. Can.*, **26**, Sec. III, 163 (1932).

[7] Leone N. Farrell, *ibid.*, **29**, Sec. III, 167 (1935).

[8] E. I. Fulmer, V. E. Nelson and F. F. Sherwood, THIS JOURNAL, **43**, 191 (1921).