Synthesis of Seven New Phenoxyphenoxybiphenyls

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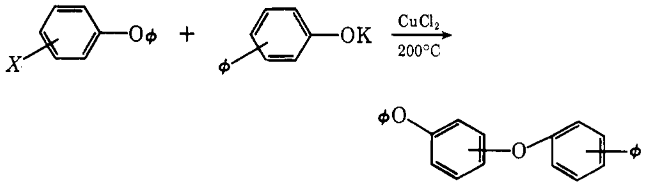
Seven new phenoxyphenoxybiphenyls were synthesized utilizing the Ullmann condensation reaction so that all nine possible isomers are known. Percent yields, physical properties, and thermal stabilities are given. Although all isomers have equivalent thermal stabilities, for application as heat transfer or hydraulic fluids, the isomers containing meta links gave the widest liquid range.

In a search for low-cost organic fluids suitable for use as heat transfer fluids in the temperature ranges up to 700–800°F, we evaluated diphenoxybiphenyls (*10*) and phenoxyphenoxybiphenyls (*11*). These compounds were expected to have the thermal stability of the polyphenyl ethers, which have proved useful as high-temperature functional fluids (*9*) and more recently as gas-liquid chromatographic substrates (*6*), but to be attainable at lower cost.

To compare the properties of the biphenylyl compounds, we prepared all of the nine phenoxyphenoxybiphenyls of which seven are new. These compounds were all prepared by the Ullmann condensation, the most general method for the formation of diaryl ether links (*18*) and recently utilized for the synthesis of seven new polyphenyl ethers containing the biphenyl unit as the central core (*12*). The mechanism and parameters of this reaction have been studied in detail by a number of workers (*5, 20, 21*). In the Ullmann reaction, phenols with phenoxy (*3*) substituents and halides with phenoxy (*1*), and chloro (*17*) substituents have been used successfully. The reaction, therefore, proved valuable not only for the synthesis of the phenoxyphenoxybiphenyls but for the intermediates as well.

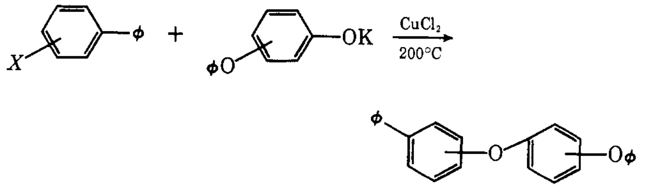
The reaction schemes depicted here allow the choice either of reaction between a halophenyl phenyl ether and a phenylphenol or of reaction between a halobiphenyl and a phenoxyphenol.

Scheme A:



(I, III, VII, and IX)

Scheme B:



(II, IV, V, VI, and VIII)

While copper is the standard catalyst for the synthesis of ethers from aryl bromides, cupric chloride was more effective with aryl chlorides. With this catalyst, the phenoxyphenoxybiphenyls listed in Table I were obtained in an average yield of 70%. Gas-liquid chromatographic (glc) analyses of each compound showed their purity to be greater than 99%.

The thermal stabilities of all the phenoxyphenoxybiphenyls as determined by the decomposition point fell within experimental error in the range 819–842°F, indicating that orientation has no influence on this property. As expected, the melting points varied widely and as in the case with the bis(*x*-phenoxyphenyl) ethers, the meta isomers were lowest melting. 3-(*m*-Phenoxyphenoxy)biphenyl, the analog of bis(3-phenoxyphenyl) ether, which is the lowest melting bis(*x*-phenoxyphenyl) ether (mp 40°C), did not crystallize. Of the two analogs of 3-phenoxyphenyl and 4-phenoxyphenyl ether (mp 109°C), one 3-(*p*-phenoxyphenoxy)biphenyl did not crystallize while 4-(*m*-phenoxyphenoxy)biphenyl melted at 55°C. Thus, for heat transfer or hydraulic fluid applications, these three compounds would be the most desirable.

Reaction conditions, ratio of reactants, and physical properties of the phenoxyphenoxybiphenyls are listed in Table I. Excess potassium phenate was used over the halide to "force" reaction. Examination of the data from this study did not suggest any optimum level of phenate to halide.

EXPERIMENTAL

All boiling points and melting points are uncorrected. Microanalyses were performed by Gailbraith Laboratories, Inc., Knoxville, Tenn. Analytical gas-liquid chromatograms were determined using an F and M 720 dual-column gas chromatograph. The dual columns were 20 ft, 0.25 o.d. packed with 12% Dow Corning High Vacuum grease dispersed on 45–50 mesh Chromosorb P. Column temperatures were generally in the range of 250–275°C using a helium flow of 70 ml/min. Sample sizes of 0.1 μl. were used at maximum attenuation to obtain optimum resolution and detection of any trace impurities for the $C_{24}H_{18}O_2$ molecular-weight range reported herein. Our standard for the thermal stability is the "decomposition point," previously defined as the temperature in °F at which a compound decomposes so as to give an isothermal rate of pressure rise of 0.014 mm of Hg/sec (*4*).

The phenoxyphenols used in these syntheses were obtained using the procedure given for the preparation of *o*-phenoxyphenol.

o-**Phenoxyphenol.** *o*-Chlorophenol (256 grams, 2 moles), phenol (940 grams, 10 moles), potassium hydroxide (336 grams, 6 moles), and copper powder (6.3 grams) were heated at 195°C for 6 hr, cooled, poured onto a 2-liter solution of 15% hydro-

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Table I. Synthesis and Properties of Phenoxyphenoxybiphenyls

			Starting materials											
	Compound[a]	Scheme	KOH, mol	Phenol	Mol	Aryl halide	Mol	Time, hr	Temp, °C	Yield, %	Mp,°C.	Bp,°C/mm	$n^{25}_{\rm D}$	T_D,°F
I	2-(*o*-Phenoxyphenoxybiphenyl)	A	0.4	*o*-Phenyl-[b]	0.5	2-Chlorophenyl-phenyl ether (*7*)	0.3	6	200	62	60–1	182/0.07		819
II	2-(*m*-Phenoxyphenoxybiphenyl) (*13*)	B	0.4	*m*-Phenoxy- (*16*)	0.5	2-Chlorobiphenyl (*2*)	0.3	6	200	79	51	191–2/0.07	1.6372[c]	837
III	2-(*p*-Phenoxyphenoxybiphenyl) (*16*)	A	0.4	*o*-Phenyl-[b]	0.5	4-Bromophenyl-phenyl ether[b]	0.4	6	200	68	85–6	194/0.07		820
IV	3-(*o*-Phenoxyphenoxybiphenyl)	B	0.4	*o*-Phenoxy- (*19*)	0.43	3-Chlorobiphenyl (*8*)	0.26	4	220	82	62–3	205/0.15	1.6417[c]	829
V	3-(*m*-Phenoxyphenoxybiphenyl)	B	0.5	*m*-Phenoxy- (*16*)	1.0	3-Chlorobiphenyl (*8*)	0.15	12	195–205	87	. . .	210–12/0.35	1.6414	824
VI	3-(*p*-Phenoxyphenoxybiphenyl)	B	0.5	*p*-Phenoxy- (*14*)	0.43	3-Chlorobiphenyl (*8*)	0.27	6	210	75	. . .	218/0.1	1.6428	827
VII	4-(*o*-Phenoxyphenoxybiphenyl)	A	0.4	*p*-Phenyl-[b]	0.5	2-Chlorophenyl-phenyl ether (*7*)	0.4	6	200	43	122–3	210–12/0.05		822
VIII	4-(*m*-Phenoxyphenoxybiphenyl)	B	1.5	*m*-Phenoxy- (*16*)	2.7	4-Bromobiphenyl[b]	1.0	12	200–10	75	55	230/0.4		842
IX	4-(*p*-Phenoxyphenoxybiphenyl)	A	0.4	*p*-Phenyl-[b]	0.5	4-Bromophenyl-phenyl ether[b]	0.4	6	250	71	132–3	220–30/0.1		840

[a] Elemental analyses (C,H) in agreement with theoretical values have been obtained and were submitted for review. [b] Purchased and purified by crystallization to 99% glc purity. [c] Supercooled.

chloric acid; the oily layer separated. Distillation through a Vigreux column gave 248 grams (66% yield) of *o*-phenoxyphenol, bp 160–5°C/15 mm, mp 106–7°C (from benzene and hexane). Lit. mp 104–5°C (*19*). *m*-Phenoxyphenol (*16*), bp 120–25°C/0.25 mm, $n^{25}_{\rm D}$ 1.5975 (79% yield). *p*-Phenoxyphenol (*14*), bp 126–8°C/0.25 mm, mp 83–5°C (57% yield).

The phenylphenols and 4-bromophenyl phenyl ether were purchased and purified by crystallization to 99% purity by glc analysis before use.

2-Chlorophenyl Phenyl Ether. A mixture of phenol (144 grams, 1.53 moles), potassium hydroxide (56 grams, 1 mole), and toluene (30 ml) to azeotrope, the water formed was heated at 130°C to prepare potassium phenate. The excess toluene was removed by heating to 170°C followed by rapid addition of diglyme (300 ml) and copper powder (5 grams). Excess *o*-dichlorobenzene (735 grams, 5 moles) was next added at temperatures ranging from 125–40°C over a 1.5-hr period. The reactants were stirred for 18 hr at 140°C, cooled, and filtered through Hyflo Super Cel. Excess diglyme was removed in vacuo, the concentrates were taken up in benzene, washed with excess 1.5*N* potassium hydroxide, and dried ($MgSO_4$). Distillation gave a 70% yield, bp 95–6°C/0.65 mm, mp 45°C (from methanol). Lit., mp 43.5°C (*7*).

The only halobiphenyl purchased for this study was 4-bromobiphenyl. This compound was crystallized (mp 91°C) and glc analyzed (99% purity). The chlorobiphenyls used, namely 2- and 3-chlorobiphenyl, were prepared via the diazotization of *o*-chloro-and *m*-chloroaniline, respectively, in benzene (*2*, *8*).

2-(*o*-Phenoxyphenoxy)biphenyl (I). A mixture of *o*-phenylphenol (85 grams, 0.5 mole), potassium hydroxide (22.4 grams, 0.4 mole), and toluene (25 ml) was heated at 130°C. After all of the water had been azeotroped off, the potassium *o*-phenylphenate was heated to 170°C and cupric chloride dihydrate (5 grams) added. 2-Chlorophenyl phenyl ether (61.2 grams, 0.3 mole) was next added to the reaction mixture over a 0.5 hr, and a vigorous reaction ensued at 210–20°C reflux. The reactants were heated for 6 hr at 200°C with stirring, cooled, and dissolved in excess benzene and 3*N* potassium hydroxide. The resulting heterogeneous mixture was filtered through Hyflo Super Cel, the organic layer separated, washed with excess 1.5*N* potassium hydroxide, and dried ($MgSO_4$). Distillation through an 18-in. Vigreux column gave a 62% yield of I, bp 182°C/0.07 mm. Compounds III, VII, and IX were prepared using essentially the same reaction conditions, the appropriate halophenyl phenyl ether, and potassium salt of the appropriate phenylphenol (Table I).

Compounds II, IV, V, VI, and VIII were also prepared using essentially the same reaction conditions as those described for 2-(*o*-phenoxyphenoxy)biphenyl. Selection of the potassium salt of the appropriate phenoxyphenol and the appropriate halobiphenyl for Ullmann condensation gave the desired phenoxyphenoxybiphenyls listed in Table I.

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Synthesis of Ten New Diphenoxybiphenyls

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Ten new diphenoxybiphenyls were synthesized utilizing the Ullmann condensation reaction so that all 12 possible isomers are known. Percent yields, physical properties, and thermal stabilities are given. Although all isomers have equivalent thermal stabilities, for application as heat transfer or hydraulic fluids, the isomers containing meta links give the widest liquid range.

The use of diphenyl ether as a heat transfer fluid at temperatures up to 700–800°F. in pressurized systems is well established. In unpressurized systems, however, no organic fluids for this temperature range were available at suitable costs until the diphenoxybiphenyls (*10*) and the phenoxyphenoxybiphenyls (*11*) were reported for this application.

To evaluate these related aryl ethers on a cost-performance basis as heat transfer fluids at 800°F, we prepared all of the 12 diphenoxybiphenyl isomers of which 10 are new. To our knowledge this is the first complete set of disubstituted biphenyl derivatives.

The diphenoxybiphenyls were prepared either by the Ullmann condensation (*14*, *19*, *20*) or the Ullmann biphenyl coupling reaction (*9*). The mechanism and parameters of the Ullmann condensation have been studied in detail by a number of workers (*4*, *5*, *23–25*). It has been used recently for the synthesis of seven new polyphenyl ethers containing the biphenyl unit as the central moiety (*12*).

Since the Ullmann condensation is the most general method for the formation of diaryl ether links, this reaction was also used to prepare aminophenyl phenyl ethers directly from chloroanilines. These latter compounds were easily diazotized to key intermediate iodophenyl phenyl ethers and utilized as depicted in Schemes C and D.

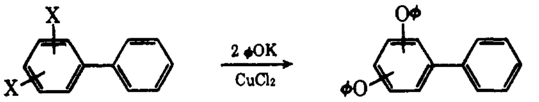
The Ullmann coupling reaction was used to obtain not only symmetrical dichlorobiphenyls having one chlorine in each ring, but also to obtain key intermediate chlorophenoxybiphenyls. The marked difference in reactivity of aryl iodides as compared to aryl chlorides allowed us to obtain chlorophenoxybiphenyl intermediates from Ullmann coupling reaction mixtures. The differences in physical properties of the reaction products allowed us to obtain separable mixtures via prior selection of reactants.

Monochlorobiphenyls and dichlorobiphenyls containing chlorines in the same ring of the biphenyl nucleus were prepared by the Gomberg reaction.

The reaction schemes A and B used for the diphenoxybiphenyls involve the choice either of reaction between a *x,x*-dichlorobiphenyl and potassium phenate or of reaction between *x,x'*-dichlorobiphenyls and potassium phenate. Reaction schemes C and D used for the diphenoxybiphenyls involve the choice of the Ullmann coupling reaction leading to either symmetrical diphenoxybiphenyls or chlorophenoxybiphenyls, easily converted to unsymmetrical diphenoxybiphenyls using potassium phenate.

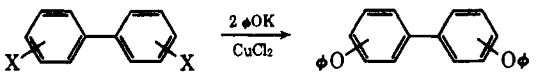
While copper is the standard catalyst for the synthesis of ethers from aryl bromides, cupric chloride was found to be more effective with aryl chlorides. With this catalyst the diphenoxybiphenyls listed in Table I were obtained in a range of 50–87% yield (68% average yield) from the aryl halides. The average yield for the six isomers prepared via scheme A was 74%, for the four isomers prepared via scheme B 71%, and for the two isomers prepared via scheme D 80%. Gas-liquid chromatography (glc) analyses of each compound showed their purity to be

Scheme A:



(I, II, III, IV, V, and VI)

Scheme B:



(VII, VIII, IX and X)

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