

Synthesis and Thermal Reaction of 2-[4-(4-Ethynylphenoxy)phenylene]-3-phenylquinoxaline

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2-[4-(4-Ethynylphenoxy)phenylene]-3-phenylquinoxaline was prepared by two routes and was thermally reacted at various temperatures. The intermediate reactants, the acetylene containing phenylquinoxaline, and its thermally induced reaction product were characterized by high pressure liquid chromatography and mass spectroscopy. The principal component in the 350° reaction product was a dimer from addition of an acetylene group to another.

J. Heterocyclic Chem., 13, 993 (1976).

As part of a high temperature structural resin program, work was directed towards the preparation and thermal chain extension of acetylene terminated phenylquinoxaline oligomers (2). A representative model compound, 2-[4-(4-ethynylphenoxy)phenylene]-3-phenylquinoxaline, was prepared and studies were conducted to obtain information regarding reaction conditions required for the polymer chain extending reaction and to identify the major component resulting from the thermally induced reaction of the acetylene group.

4-Ethynylphenoxybenzil was prepared as shown in reaction Scheme 1. Phenylacetyl chloride was reacted with excess diphenyl ether in the presence of anhydrous alu-

minum chloride in methylene chloride to provide 4-phenylacetylphenoxybenzil (I). Compound I was oxidized in glacial acetic acid with selenium dioxide to provide 4-phenoxybenzil (II). Acetylation of II was performed with acetyl chloride in the presence of aluminum chloride in

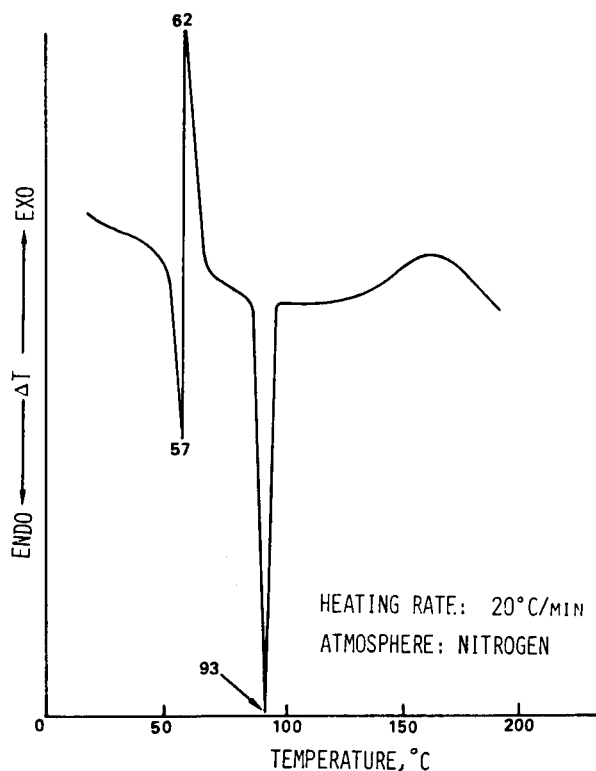
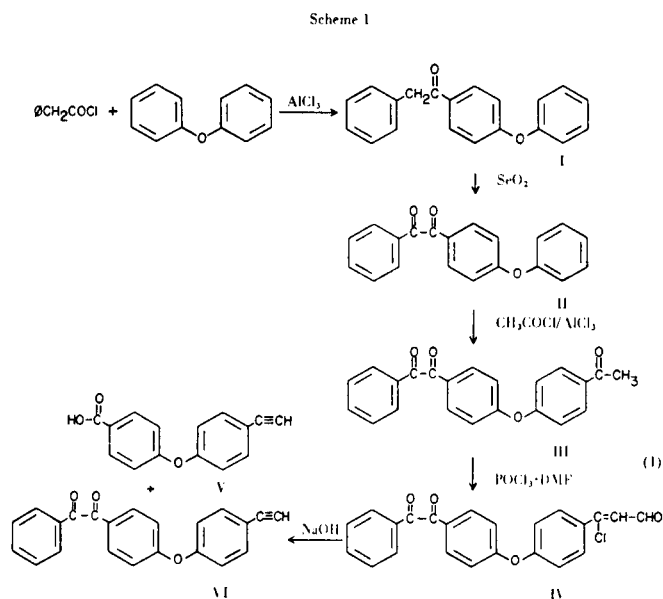


FIGURE 1. DIFFERENTIAL THERMAL ANALYSIS OF III

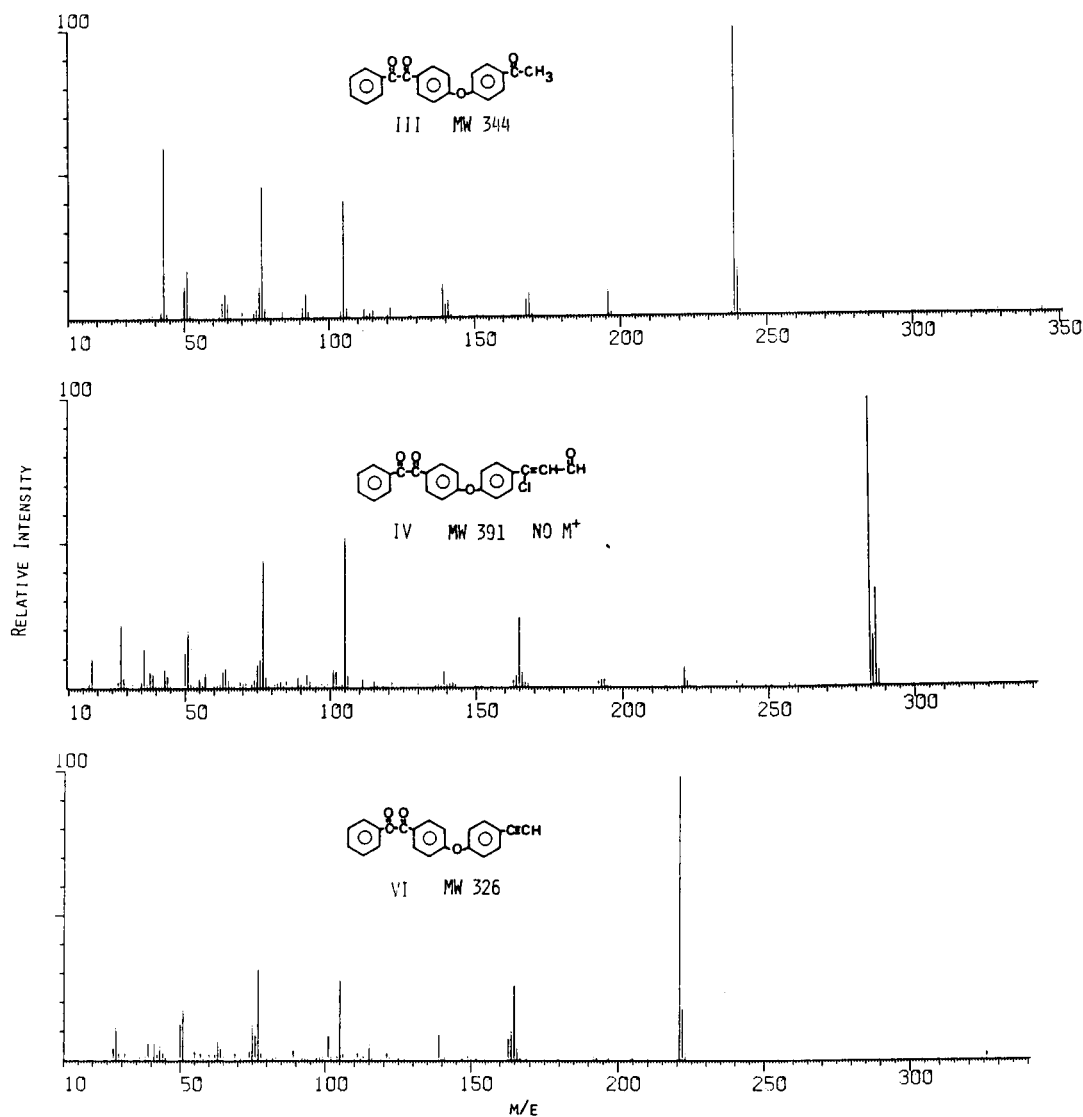


FIGURE 2. MASS SPECTRA OF COMPOUNDS III, IV AND VI

methylene chloride to provide 4-acetylphenoxybenzil (III), as a yellow solid which melted initially at 55-59°, reorganized and remelted at 91-93°. Recrystallization from methanol with fast cooling in an ice bath provided the kinetically favored yellow crystalline form, m.p. 59-61°, which reorganized and remelted at 93-94° [differential thermal analysis (DTA) curve in Figure 1]. Upon standing at ambient temperature for several days, the yellow crystals turned near-white and melted at 93-94°. Recrystallization of III from methanol with slow cooling provided the thermodynamically favored near-white crystalline form, m.p. 93-94° (mass spectrum in Figure 2).

Compound III was treated with excess Vilsmeier reagent (a 1:1 complex of phosphorus oxychloride and *N,N*-dimethylformamide, DMF) in dry DMF to provide an orange

gum. High pressure liquid chromatography (HPLC) of the orange gum showed two major peaks of about equal magnitude which were well resolved and permitted separate isolation. Mass spectral fragmentation patterns of the two components were essentially identical and consistent with that expected for 4-phenylglyoxalylphenoxy-β-chloro-cinnamaldehyde (IV). The orange gum was extracted with cyclohexane to provide IV as pale yellow crystals (mass spectrum in Figure 2). The nmr spectrum was consistent with the assigned structure with a doublet centered at δ 6.84 for the vinyl proton and a doublet centered at δ 10.64 for the aldehyde proton. The cyclohexane insoluble portion was dissolved in dioxane, treated with charcoal, filtered, and quenched in water to provide a yellow gum which changed to a glassy orange solid upon

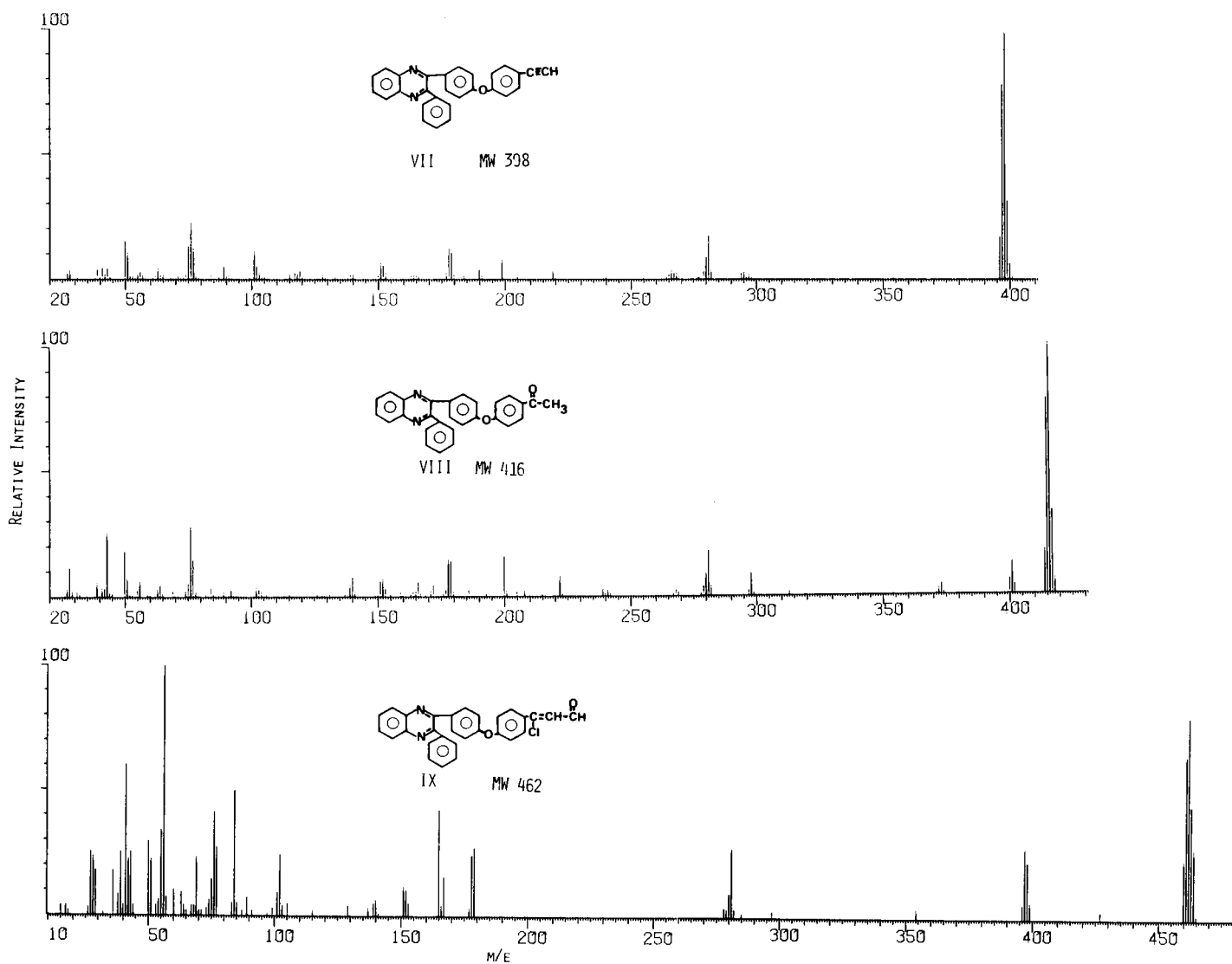


FIGURE 3. MASS SPECTRA OF COMPOUNDS VII, VIII, AND IX

Table I

Reaction of 4-Phenoxybenzil with Sodium Hydroxide (a)

Reaction Temperature, °C	Reaction Time, hours	Weight of 4-phenoxybenzoic acid, g. (yield, %)	Weight of recovered 4-phenoxybenzil, g. (recovery, %)
93	0.33	0.7 (50)	1.0 (50)
55-60	2.5	0.7 (50)	0.9 (45)
26	3.0	0.6 (43)	1.0 (50)

(a) Added solution of 2.0 g. of sodium hydroxide in 20 ml. of water to a solution of 2.0 g. of 4-phenoxybenzil in 25 ml. of dioxane and stirred.

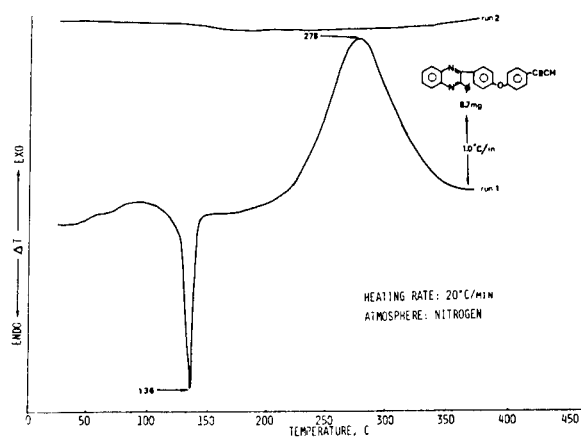


FIGURE 4. DIFFERENTIAL SCANNING CALORIMETRY OF VII

drying. Although the mass spectrum was essentially identical to that obtained for the yellow crystals and the elemental analysis agreed well with the theoretical values for IV, the nmr spectrum was not consistent with the *cis* or the *trans* form of IV. The nmr spectrum was consistent with that expected for an α -chlorocinnamaldehyde.

Compound IV in the form of yellow crystals and glassy orange solid was treated separately in dioxane with aqueous sodium hydroxide to provide 4-ethynylphenoxybenzoic

acid (V, identified by mass spectroscopy and ir) as the major product and 4-ethynylphenoxybenzil (VI) in the form of a yellow gum as the minor product. Several attempts to recrystallize VI from a variety of solvents resulted in the recovery of the yellow gum (mass spectrum in Figure 2). No detectable difference was observed in the reaction of the yellow crystalline or glassy orange solid form of IV with aqueous sodium hydroxide.

1,2-Dicarbonyl compounds (α -diketones) are known to rearrange (3) or cleave in the presence of strong base. Therefore, prior to the preparation of 4-ethynylphenoxybenzil, a brief study as shown in Table I was conducted on the reaction of 4-phenoxybenzil in dioxane with aqueous sodium hydroxide. 4-Phenoxybenzoic acid was the only product isolated with unreacted 4-phenoxybenzil.

2-[4-(4-Ethynylphenoxy)phenylene]-3-phenylquinoxaline was prepared by two routes as shown in reaction Scheme 2. Condensation of 1,2-diaminobenzene with VI in ethanol provided 2-[4-(4-ethynylphenoxy)phenylene]-3-phenylquinoxaline (VII) as a glassy yellow solid which melted at 61-65°, resolidified, and remelted at 132-134°. After several days at ambient temperature, the yellow solid sintered at 126° and melted at 132-134°.

The alternate route to VII involved condensation of 1,2-diaminobenzene with III in ethanol to provide 2-[4-

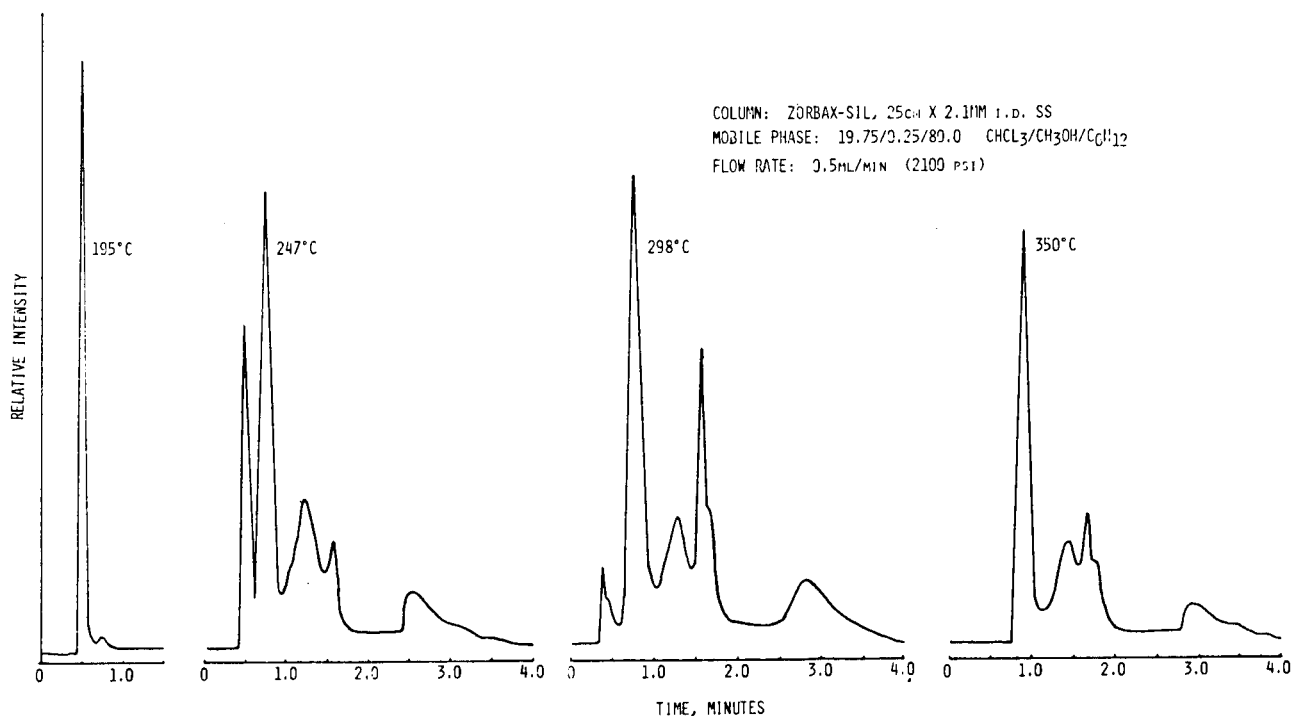
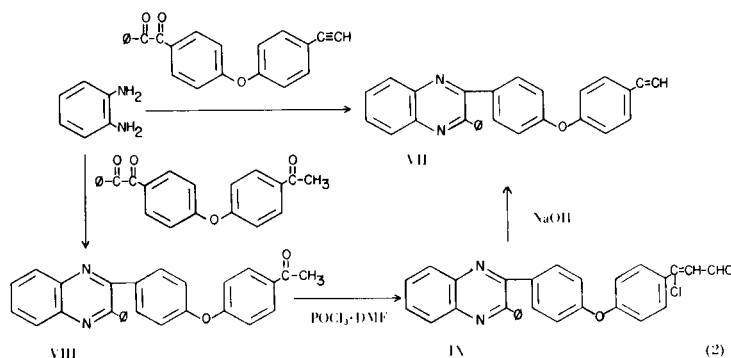


FIGURE 5. HIGH PRESSURE LIQUID CHROMATOGRAMS OF THE THERMALLY INDUCED REACTION PRODUCT OF VII

Scheme 2



(4-acetylphenoxy)phenylene]-3-phenylquinoxaline (VIII, mass spectrum in Figure 3). Compound VIII was treated with the Vilsmeier reagent in dry DMF to provide 4-(3-phenylquinoxalinyloxy)phenyl- β -chlorocinnamaldehyde (IX) (mass spectrum in Figure 3). Compound IX in dioxane was treated with aqueous sodium hydroxide to yield VII as a glassy orange solid which melted at 62-65°, resolidified, and remelted at 131-133°. An analytically pure sample was obtained by recrystallization from cyclohexane (mass spectrum in Figure 3).

The DSC curve of VII in Figure 4 shows a melting endotherm peaking at 136°, followed by a broad strong exotherm from ~175° to ~350° (peaks at 278°). Upon

rerunning the same sample, no major thermal changes were observed. The infrared spectrum of VII showed a C \equiv C-H stretch at 3.02 μ and C=C at 4.7 μ which disappeared upon heating to 350° in nitrogen indicating the strong exotherm in the DSC curve was due to reaction of the acetylene groups. The thermally induced reaction of an acetylene group is very complex. Two different dimers and a third, cyclobutadiene which is unstable, as well as several other species such as benzene and cyclooctatetrene may be formed. Of the two possible stable dimers shown in Eq. 3, compound X would be predicted based upon a consideration of an ionic mechanism. Although compound XI is generally formed *via* a chemical reaction (*e.g.*,

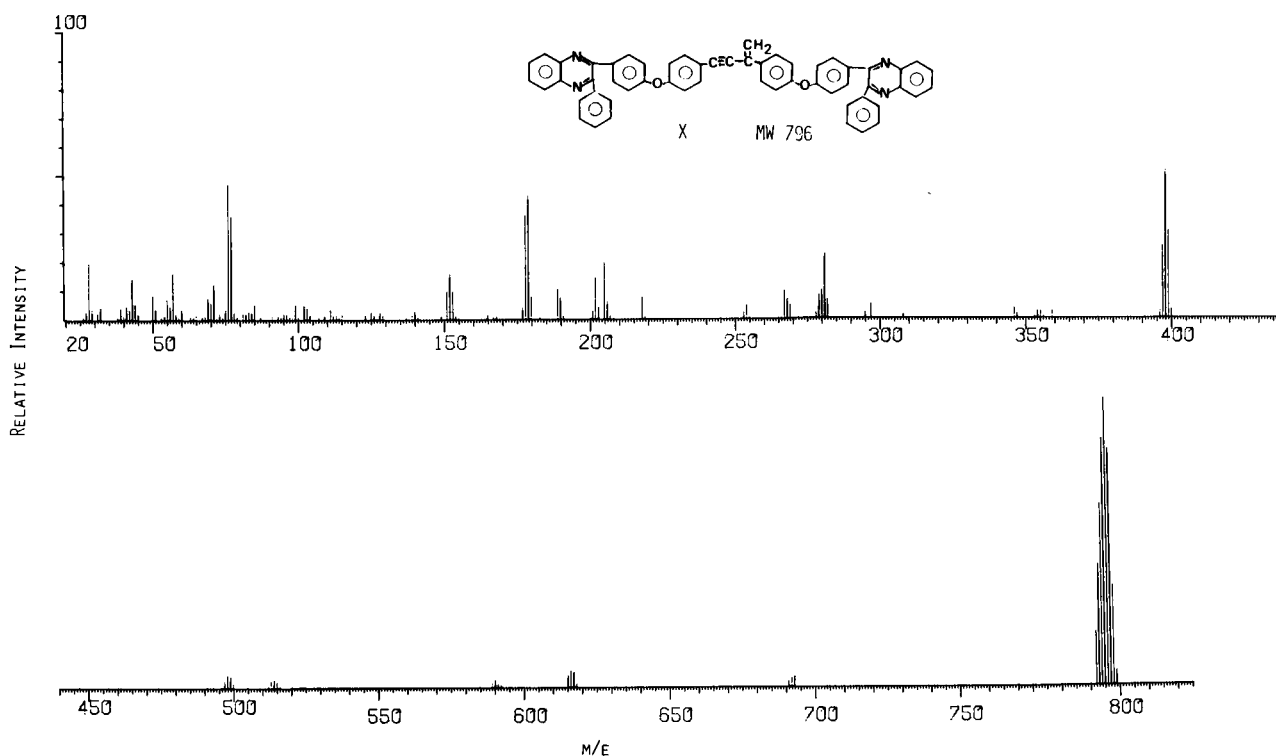
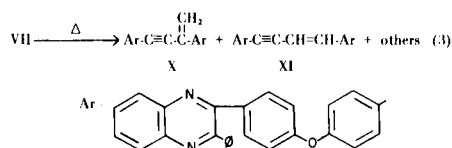


FIGURE 6. MASS SPECTRUM OF COMPOUND X



cuprous chloride and ammonium chloride), the possibility of formation by a thermal reaction must be considered.

For polymer work, it was of interest to know the minimum temperature for reaction of the acetylene group, the effect of higher temperature upon the product, and the identity of the major component in the product. Samples of VII were separately heated for 0.5 hour at 195°, 247°, 298°, and 350° under nitrogen and each product was analyzed by HPLC. The chromatograms were obtained under essentially identical conditions and are shown in Figure 5. Compound VII failed to undergo any substantial reaction at 195°. After 247°, a substantial amount of unreacted VII, one major and four minor components were observed. The chromatogram of the 298° product showed a small amount of VII, one major, and five minor components. One major and four minor components are present in the chromatogram of the 350° product. No unreacted VII was detected. The major component formed at 247°, 298°, and 350° exhibited essentially the same retention time. A preparative separation by HPLC on this component was performed from the 350° product for analysis by mass spectroscopy (Figure 6). The fragmentation pattern and infrared spectrum were consistent with that expected for the dimer, compound X, from addition of one acetylene with another. Attempts to isolate and identify the minor components were beyond the scope of this program.

EXPERIMENTAL

All melting points are uncorrected. ^1H -nmr spectra were recorded on a Varian A60-A instrument using TMS as internal standard. Chemical shifts are given in δ (ppm). Infrared spectra were recorded on a Digilab FTS-15 spectrophotometer. High pressure liquid chromatography was performed with a Waters Associates Model ALC 202/R401 instrument with a Model 6000 Solvent Delivery System using a Zorbax-Sil column and a 254 nm fixed wavelength ultraviolet detector. Chromatographic conditions were optimized to obtain maximum resolution for the most complex mixture. These conditions were then employed for all separations. However, small differences in retention time were observed due primarily to changes in the activity of the column and demixing of the mobile phase.

A Finnigan Model 3300 Quadrupole Mass Spectrometer equipped with a Model 6000 Data System was used to obtain the electron-impact spectra of each compound. Samples were introduced into the ion source with a programmable temperature solid inlet probe. Each spectra was obtained by heating the sample at 2°/minute from the ion source temperature (100°) to a temperature where enough sample was vaporized to generate a usable spectrum. Heating to 200° was generally sufficient. Each 70 ev

spectra was obtained by repeatedly scanning the 10-1000 amu mass range over a 15 second period while the sample was heated. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

4-Phenoxybenzil (II).

A solution of diphenyl ether (340 g., 2.0 moles) and phenylacetyl chloride (140 g., 0.91 mole) in methylene chloride (150 ml.) was added dropwise during 2 hours to a stirred slurry of anhydrous aluminum chloride (140 g., 1.1 moles) in methylene chloride (450 ml.) at ambient temperature. After stirring overnight, the dark red reaction mixture was poured into a stirred mixture of ice and hydrochloric acid. The organic phase was separated, washed thoroughly with water and saturated sodium chloride solution, dried over calcium sulfate, and concentrated to dryness. The white residue was thoroughly washed with two 400 ml. portions of cold cyclohexane to yield 4-phenylacetylphenoxybenzene (I) as a white solid (223 g., 85% yield), m.p. 83-85.5°. Recrystallization from cyclohexane (2 l.) provided white crystals (191 g., 86% recovery), m.p. 87-88°. Compound I (191 g., 0.66 mole) and selenium dioxide (73.5 g., 0.66 mole) in glacial acetic acid (800 ml.) were refluxed overnight. The black reaction mixture was filtered hot and the cooled yellow filtrate poured into cold water (2 l.) to precipitate a yellow gum. The gum was washed thoroughly with hot water and taken up in methylene chloride. After drying over calcium sulfate, the solution was concentrated to dryness to provide 4-phenoxybenzil (II) as a yellow solid (192 g., 96% yield), m.p. 43-44°. Recrystallization from ethanol provided yellow crystals, m.p. 45-46.5°, [lit. m.p. 65.0-65.7° (4)].

Anal. Calcd. for $\text{C}_{20}\text{H}_{14}\text{O}_3$: C, 79.45; H, 4.67. Found: C, 79.38; H, 4.61.

4-Acetylphenoxybenzil (III).

A solution of II (60.4 g., 0.2 mole) and acetyl chloride (16.4 g., 0.21 mole) in methylene chloride (250 ml.) was added dropwise during 2.5 hours to a stirred slurry of anhydrous aluminum chloride (93.1 g., 0.7 mole) in methylene chloride (200 ml.) at ambient temperature. The dark purple reaction mixture was stirred overnight and poured into a stirred mixture of ice and hydrochloric acid. The organic phase was separated, washed thoroughly with water and saturated sodium chloride solution, dried over calcium sulfate, and concentrated to dryness. The residual yellow solid (67.4 g., 98% yield), m.p. 55-59°, was dissolved in methanol (700 ml.) and the hot methanol solution placed in an ice bath. Yellow crystals (53 g.) formed which melted at 59-61°, resolidified, and remelted at 93-94°. When the methanol solution was cooled slowly, near-white crystals of 4-acetylphenoxybenzil (III) formed, m.p. 93-94°.

Anal. Calcd. for $\text{C}_{22}\text{H}_{16}\text{O}_4$: C, 76.73; H, 4.68. Found: C, 76.82; H, 4.73.

4-Phenylglyoxalylphenoxy- β -chlorocinnamaldehyde (IV).

Compound III (10.3 g., 0.03 mole) in dry DMF (45 ml.) was added dropwise during 0.5 hour at ambient temperature to a stirred solution of the Vilsmeier reagent [prepared by the dropwise addition of redistilled phosphorus oxychloride (8.3 ml., 0.09 mole) to dry DMF (35 ml.) at 5° followed by stirring at ambient temperature for 2 hours]. The reaction mixture was stirred overnight and the orange solution poured into cold, aqueous sodium acetate (30 g. in 200 ml. of water) to yield a yellow gum. The yellow gum was extracted with methylene chloride, washed thoroughly with water followed by saturated sodium chloride, dried over calcium sulfate, and concentrated to dryness to yield an orange gum (10.3 g., 88% yield). Extraction twice with boiling cyclohexane (250

ml.) yielded an insoluble orange gum (6.7 g.) and clear yellow solution. Upon cooling, the yellow solution provided pale yellow crystals (3.0 g., 29% yield), m.p. 82-84°, of 4-phenylglyoxalylphenoxy- β -chlorocinnamaldehyde (IV); pmr (deuteriochloroform): δ 6.84 (d, 1H, -CHO), δ 7.2-8.5(m), 10.64 (d, 1H, -C=CH-).

Anal. Calcd. for C₂₃H₁₅ClO₄: C, 70.68; H, 3.87; Cl, 9.07. Found: C, 70.53; H, 3.85; Cl, 8.88.

The cyclohexane insoluble orange gum was dissolved in dioxane, treated with charcoal, filtered, and quenched in water to provide a yellow gum which was dried at 60° over phosphorus pentoxide *in vacuo*. The resulting glassy orange solid softened at 79°, partially melted at 87-91°, and cleared at 93°; pmr (deuteriochloroform): δ 7.2-8.3 (m), δ 8.65 (s, 1H).

Anal. Calcd. for C₂₃H₁₅ClO₄: C, 70.68; H, 3.87; Cl, 9.07. Found: C, 70.46; H, 3.81; Cl, 8.73.

4-Ethynylphenoxybenzil (VI).

A solution of the yellow crystals of III (3.0 g., 0.0077 mole) in dioxane (30 ml.) was added to a solution of sodium hydroxide (3.0 g., 0.075 mole) in water (30 ml.). The brown reaction mixture was stirred at 55-60° for 2 hours followed by pouring into cold water (200 ml.). The orange aqueous solution was extracted twice with methylene chloride (150 ml.) and the methylene chloride solution washed with water, dried over calcium sulfate, and concentrated to dryness to yield 4-ethynylphenoxybenzil (IV) as a yellow oil (0.5 g., 20% yield).

Anal. Calcd. for C₂₂H₁₄O₃: C, 80.97; H, 4.32. Found: C, 80.69; H, 4.44.

The aqueous phase was acidified with dilute hydrochloric acid to provide a yellow solid (1.4 g.) which was extracted with boiling benzene (100 ml.). The benzene solution was concentrated to dryness to yield 4-ethynylphenoxybenzoic acid as a yellow solid (1.0 g.), m.p. 161-163° (introduced into preheated bath at 150°); ir (nujol mull): 3.01 μ (C \equiv C-H), 3.80 and 3.94 μ (doublet, OH), 4.73 μ (C \equiv C), 5.85 μ (C=O); mass spectrum, m/e (relative abundance): 239(23), 238(100, M⁺), 221(29), 192(13), 166(10), 165(50), 164(15), 163(10), 139(10), 118(10), 101(15), 89(21), 75(35), 65(17), 63(21), 51(31), 50(19), 39(25), 28(19).

2-[4-(4-Ethynylphenoxy)phenylene]-3-phenylquinoxaline (VII).

A solution of VI (0.8636 g., 0.0027 mole) and 1,2-diaminobenzene (0.2866 g., 0.0027 mole) in ethanol (100 ml.) was refluxed for 0.5 hour. The yellow solution was poured into cold water (100 ml.) and extracted with methylene chloride. The methylene chloride was evaporated to leave VII as a glassy yellow solid (1.00 g., 94% yield) which melted at 61-65°, resolidified, and remelted at 132-134°. After standing for several days, the yellow solid sintered at 126° and melted at 132-134°. Recrystallization from cyclohexane provided a yellow solid, m.p. 132-134°.

Anal. Calcd. for C₂₈H₁₈ON₂: C, 84.40; H, 4.55; N, 7.03. Found: C, 84.24; H, 4.65; N, 6.97.

2-[4-(4-Acetylphenoxy)phenylene]-3-phenylquinoxaline (VIII).

A solution of III (5.16 g., 0.015 mole) and 1,2-diaminobenzene (1.62 g., 0.015 mole) in ethanol (100 ml.) was refluxed for 1 hour. The resulting hot yellow solution was treated with charcoal, filtered, and concentrated to dryness to provide a glassy yellow solid (6.0 g., 97% yield), m.p. 62-64°. A 1.0 g. portion was recrystallized from cyclohexane (50 ml.) to yield VIII as pale yellow crystals, m.p. 146.5-147.5°.

Anal. Calcd. for C₂₈H₂₀N₂O₂: C, 80.75; H, 4.84; N, 6.73. Found: C, 80.67; H, 4.90; N, 6.66.

4-(3-Phenylquinoxalinyloxy)- β -chlorocinnamaldehyde (IX).

A solution of VIII (4.3 g., 0.010 mole) in dry DMF (40 ml.) was added to a solution of the Vilsmeier reagent (9.0 ml. of phosphorus oxychloride and 30 ml. of DMF) and stirred overnight at ambient temperature under nitrogen. The orange solution was poured into aqueous sodium acetate (30 g. in 250 ml. of water) to precipitate a yellow solid which was thoroughly washed with water and dried over phosphorus pentoxide *in vacuo*. The resulting yellow solid (4.5 g.), m.p. 71-75° (DMF still present), was extracted twice with boiling cyclohexane (150 ml.) to provide an insoluble yellow solid (2.8 g.), m.p. 146-148°, and yellow solution. The solution was concentrated to 50 ml. and cooled to provide IX as pale yellow crystals (1.4 g., 30% yield), m.p. 171-173°.

Anal. Calcd. for C₂₉H₁₉ClN₂O₂: C, 75.24; H, 4.14; N, 6.05; Cl, 7.66. Found: C, 75.30; H, 4.27; N, 5.93; Cl, 7.58.

The insoluble yellow solid exhibited an ir and mass spectrum essentially identical to that of the yellow crystals of IX.

2-[4-(4-Ethynylphenoxy)phenylene]-3-phenylquinoxaline (VII).

A solution of IX (0.93 g., 0.002 mole) in dioxane (10 ml.) was added to a stirred solution of sodium hydroxide (2.0 g., 0.05 mole) in water (15 ml.) and the reaction mixture stirred at 55-63° for 2 hours. The dark orange solution was poured into cold water (100 ml.) and extracted with methylene chloride. The methylene chloride solution was washed thoroughly with water, dried over calcium sulfate, and concentrated to dryness to provide a glassy orange solid (0.53 g., 68% yield) which melted at 62-65°, resolidified, and remelted at 131-133°. An analytically pure sample, m.p. 132-134°, was obtained by recrystallizing from cyclohexane.

Thermal Reaction of VII.

Small portions (~20 mg.) of VII were heated in the DSC at a rate of 20°/minute in a nitrogen atmosphere and held for 0.5 hour at 195, 247, 298, and 350°. Each sample was then analyzed by HPLC (see Figure 5) and the major component in the 350° product isolated and analyzed by mass spectroscopy and ir.

Reaction of 4-Phenoxybenzil with Sodium Hydroxide.

A solution of 4-phenoxybenzil (2.0 g., 0.0066 mole) in dioxane (25 ml.) was added to a solution of sodium hydroxide (2.0 g., 0.05 mole) in water (20 ml.) and the reaction mixture stirred under the conditions indicated in Table I. The reaction mixture was then poured into cold water (250 ml.) and filtered to provide the starting material, 4-phenoxybenzil, as a yellow oil. The filtrate was acidified with dilute hydrochloric acid to provide a white solid which was recrystallized from cyclohexane to afford 4-phenoxybenzil as white crystals, m.p. 158-159° [lit. m.p. 161° (5)]; mass spectrum: M⁺, 214.

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