Mercury in Organic Chemistry. 26.[1] Synthesis of Heterocycles via Intramolecular Solvomercuration of Aryl Acetylenes

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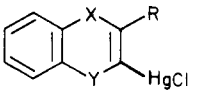
Abstract: A number of ortho substituted aryl acetylenes, o-$CH_3XC_6H_4YC{\equiv}CR$ (X = O, S, CO_2; Y = –, CO), have been observed to undergo facile intramolecular solvomercuration with mercuric acetate in acetic acid to afford the corresponding benzofuran, benzothiophene, isocoumarin, and chromone organomercuric chlorides,

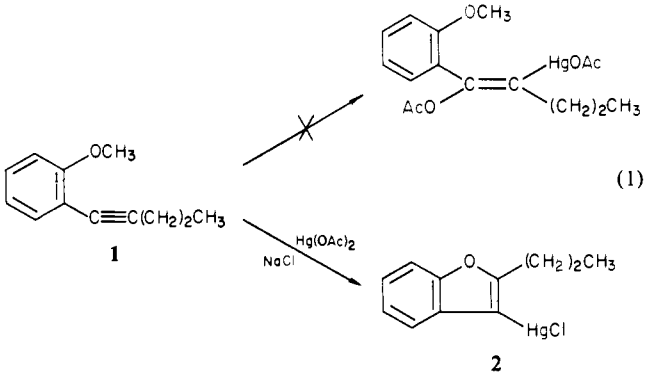


after aqueous sodium chloride workup. The aryl acetylenes m-$XC_6H_4YCH_2C{\equiv}CR$ (X = H, Y = O, R = CH_3; X = CH_3O, Y = CH_2, R = n-C_3H_7) undergo similar cyclizations to yield mercurated 2*H*-1-benzopyrans and 1,2-dihydronaphthalenes. The mercuration and subsequent carbonylation of o-$R^1OC_6H_4C{\equiv}CR^2$ [R^1 = Si(t-Bu)Me_2, R^2 = CH_3; R^1 = CH_3, R^2 = o-$C_6H_4OCH_3$] has provided a new approach to the coumarin and coumestan ring systems.

The solvomercuration–demercuration of olefins is an exceedingly valuable procedure in organic synthesis.[2-5] Analogous reactions of acetylenes have proven much less useful apparently due to the tendency of acetylenes to undergo polymercuration.[6-8] Only the chloro- and acetoxymercuration of acetylenes appear to be general reactions of real synthetic utility.[9] We now wish to report that the intramolecular solvomercuration of certain aryl acetylenes provides a valuable, general new approach to heterocyclic organomercurials useful in organic synthesis.

Results and Discussion

Benzofurans. In examining the acetoxymercuration of 1-*o*-anisyl-1-pentyne (**1**) we observed that, unlike the para isomer,[10] **1** does not undergo mercuric acetate addition to the carbon–carbon triple bond but instead undergoes intramolecular alkoxymercuration to afford the corresponding 3-(chloromercurio)-benzofuran **2** upon aqueous sodium chloride workup (eq 1). This



(1)

appears to be only the second example of the clean alkoxymercuration of an acetylene.[8] To optimize the yield of mercurated benzofuran, we have examined the effect of various mercuric salts, solvents, reaction times, and temperatures on the yield of **2**. The results are summarized in Table I. Best results were obtained using 1 equiv of mercuric acetate in acetic acid for 30 min at room temperature.

Table I. Reaction Conditions for the Mercuration of **1**

mercuric salt (equiv)	solvent	time, h	temp, °C	yield of **2**, %[a]
$Hg(OAc)_2$ (1)	CH_3CO_2H	4	0	31
$Hg(OAc)_2$ (1)	CH_3CO_2H	20	0	44
$Hg(OAc)_2$ (1)	CH_3CO_2H	0.25	25	64
$Hg(OAc)_2$ (1)	CH_3CO_2H	0.5	25	65–70
$Hg(OAc)_2$ (1)	CH_3CO_2H	4	25	52
$Hg(OAc)_2$ (2)	CH_3CO_2H	0.5	25	51
$Hg(OAc)_2$ (1)	CH_3OH	0.5	25	0
$Hg(OAc)_2$ (1)	CH_3NO_2	0.5	25	15
$Hg(O_2CCF_3)_2$ (1)	THF	10	0	37
$Hg(O_2CCF_3)_2$ (1)	THF	20	0	35
$Hg(O_2CCF_3)_2$ (1)	THF	0.25	25	51
$Hg(O_2CCF_3)_2$ (2)	THF	0.25	25	54
$Hg(O_2CCF_3)_2$ (1)	THF	20	25	48
$Hg(O_2CCF_3)_2$ (1)	CH_3CO_2H	0.33	25	48
$Hg(O_2CCF_3)_2$ (1)	CF_3CO_2H	0.5	25	0
$Hg(O_2CCF_3)_2$ (1)	CF_3CO_2H	20	25	0

[a] Isolated, recrystallized yield.

The scope of this mercurated benzofuran synthesis has been briefly examined using these standard conditions (entries 1–6, Table II). The reaction has proven general for a number of aryl-substituted derivatives bearing both electron-donating and electron-withdrawing substituents (entries 2 and 3). Additional carbon–carbon double bonds (entry 4) and aryl groups (entries 5 and 6) are also readily accommodated.

Other Heterocycles. Fortunately, this intramolecular solvomercuration approach to heterocyclic organomercurials is not limited to the preparation of mercurated benzofurans. Benzothiophenes can be prepared in a similar manner (entry 7, Table II). Introduction of a carbonyl group between the aromatic ring and the methoxy group affords the corresponding mercurated isocoumarin (entry 8, Table II). On the other hand, insertion of a methylene moiety in this position results in cyclization to the corresponding five-membered ring heterocycle (entry 9, Table II). This dramatic change in regioselectivity is presumably due to the electronic difference between the strong electron-withdrawing carbomethoxy group and the more electron-donating methoxymethyl group. Consistent with this idea is the observation that insertion of a carbonyl group between the acetylene moiety and the aromatic ring results in cyclization to the more remote acetylene carbon (entries 10 and 11, Table II). These reactions provide a novel

(1) "Mercury in Organic Chemistry. 25. Rhodium(I)-Catalyzed Alkenylation of Arylmercurials": Larock, R. C.; Narayanan, K. *J. Org. Chem.* **1983**, *48*, 4377.
(2) Chatt, J. *Chem. Rev.* **1951**, *48*, 7.
(3) Wright, G. F. *Ann. N.Y. Acad. Sci.* **1957**, *65*, 436.
(4) Zefirov, N. S. *Russ. Chem. Rev.* (*Engl. Transl.*) **1965**, *34*, 527.
(5) Kitching, W. *Organomet. Chem. Rev.* **1968**, *3*, 61.
(6) Larock, R. C. *Tetrahedron* **1982**, *38*, 1713.
(7) Hudrlik, P. F.; Hudrlik, A. M. *J. Org. Chem.* **1973**, *38*, 4254.
(8) During the course of the present investigation, Riediker and Schwartz reported a useful intramolecular alkoxymercuration process (Riediker, M.; Schwartz, J. *J. Am. Chem. Soc.* **1982**, *104*, 5842).
(9) Larock, R. C.; Liu, C.-L. *J. Org. Chem.* **1983**, *48*, 2151 and references therein.
(10) Spear, R. J.; Jensen, W. A. *Tetrahedron Lett.* **1977**, 4535.

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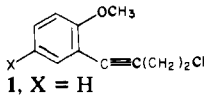
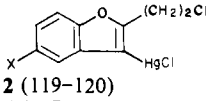
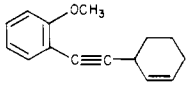
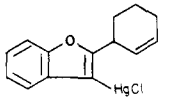
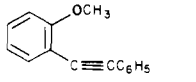
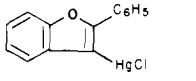
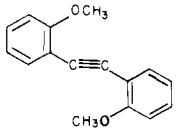
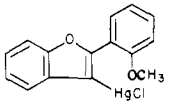
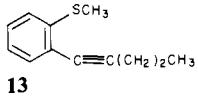
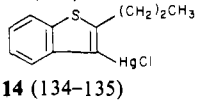
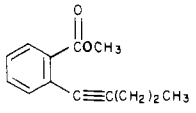
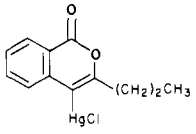
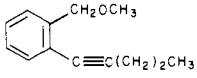
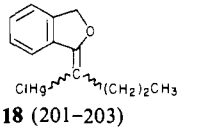
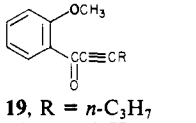
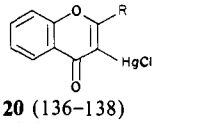
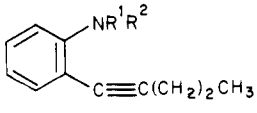
Table II. Synthesis of Heterocyclic Organomercurials via Mercuration of Aryl Acetylenes

entry	aryl acetylene	product (mp, °C)	isolated yield, %
			
1	**1**, X = H	**2** (119–120)	65–70
2	**3**, X = OCH_3	**4** (147–148)	60
3	**5**, X = NO_2	**6** (116–118)	45
			
4	**7**	**8** (123–125)	30
			
5	**9**	**10** (210–212)	59
			
6	**11**	**12** (205)	58
			
7	**13**	**14** (134–135)	66
			
8	**15**	**16** (195–197)	65
			
9	**17**	**18** (201–203)	38[a]
			
10	**19**, R = n-C_3H_7	**20** (136–138)	60
11	**21**, R = C_6H_5	**22** (254–255)	58

[a] Reaction run for 20 h.

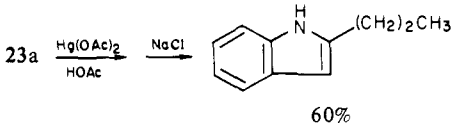
approach to 3-mercurated chromones, including flavone itself (**22**).

Indoles. The cyclization of nitrogen-containing aryl acetylenes to mercurated indoles proved frustrating. 2-(1-Pentynyl)aniline (**23a**) and several derivatives (**23b–d**) were prepared and subjected



23a, R^1 = H; R^2 = H
b, R^1 = H; R^2 = Ac
c, R^1 = CH_3; R^2 = CH_3
d, R^1 = CH_3; R^2 = Ac

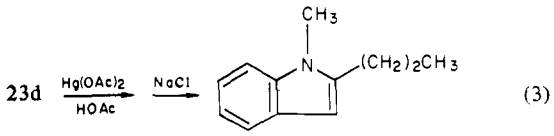
to mercuration under the usual conditions. While compound **23a** did indeed cyclize, the indole product contained no mercury (eq 2). Compound **23d** behaved similarly (eq 3). A variety of other



(2)

60%

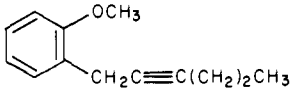
reaction conditions were examined on these substrates, but only the starting acetylenes or the mercury-free indoles could be isolated. Subsequent studies established that the anticipated heterocyclic mercurials were readily protodemercurated by the acetic acid present in the reaction mixture. Efforts to cyclize compounds **23b** and **23c** failed completely. In both cases the starting acetylenes were recovered after attempted mercuration.



(3)

46%

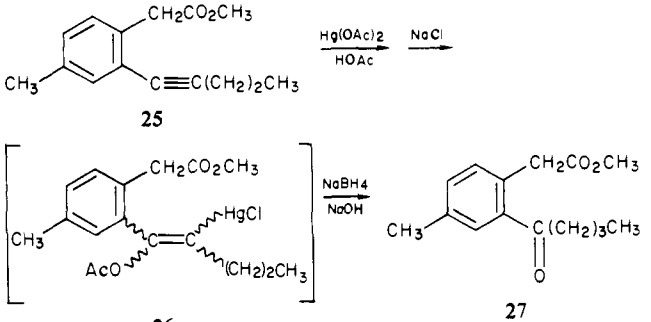
Failures. Several other aryl acetylenes failed to cyclize. 2-(2-Hexynyl)anisole (**24**) failed to react with either mercuric acetate



24

or mercuric trifluoroacetate under the usual conditions. This is a bit surprising, since 2-butyne is observed to readily add mercuric acetate to the triple bond under similar conditions. The aromatic ring apparently deactivates the acetylene toward such addition.

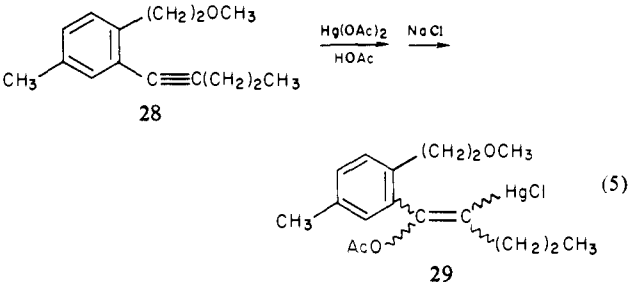
The acetylene **25** was observed to undergo reaction within 30 min with mercuric acetate in acetic acid (eq 4). While the



(4)

resulting mercurial was not isolated, alkaline sodium borohydride reduction afforded ketone **27**, providing evidence for the formation of mercurial **26** and not the desired cyclization product.

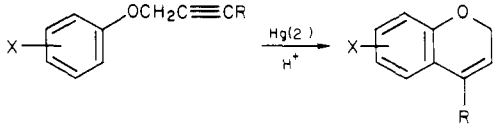
With acetylene **28**, the mercuration was sluggish, but after a 20-h reaction time the corresponding β-acetoxymercurial **29** could be isolated in 44% yield (eq 5). While six-membered ring het-



(5)

erocycles might have been expected from these reactions, it appears that cyclization cannot compete effectively with simple mercuric acetate addition to the triple bond.

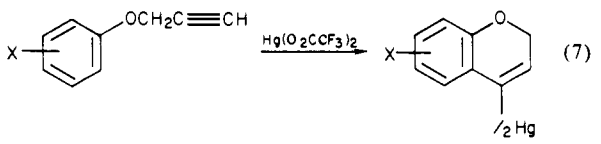
Benzopyrans and Dihydronaphthalenes. Several groups have reported that aryl propargylic ethers react with mercuric salts in strong acid to afford cyclized benzopyrans (eq 6).[11-13] Only with



(6)

(11) Thyagarajan, B. S.; Majumdar, K. C.; Bates, D. K. *J. Heterocycl. Chem.* **1975**, *12*, 59.

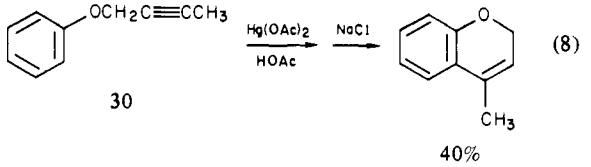
propargyl ethers themselves have organomercurials been isolated from these reactions (eq 7).[13] To account mechanistically for



(7)

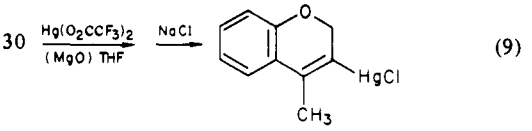
the unusual position of the mercury in these products, the authors proposed a complex rearrangement.

It appeared to us that these reactions must be proceeding by intramolecular electrophilic aromatic substitution by the mercury-complexed acetylene. To test this idea, we have examined the mercuration of 2-butynyl phenyl ether (**30**). Upon reaction with mercuric acetate in acetic acid, we isolated, as expected, 4-methyl-2*H*-1-benzopyran in 40% yield (eq 8). When the reaction



(8)

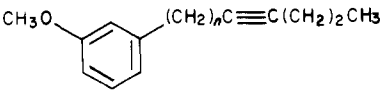
was run with mercuric trifluoroacetate, with or without 3 equiv of MgO, in tetrahydrofuran (THF), we were able to isolate the corresponding mercurial **31** instead in 33–40% yield (eq 9).



(9)

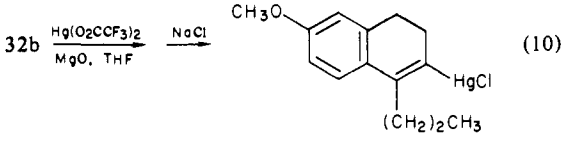
Attempts to cyclize phenyl tetrolate, $C_6H_5O_2CC{\equiv}CCH_3$, to the corresponding mercurated coumarin failed, however.

We have examined the feasibility of extending these cyclizations to mercurated carbocycles. Acetylenes **32a–c** were prepared and



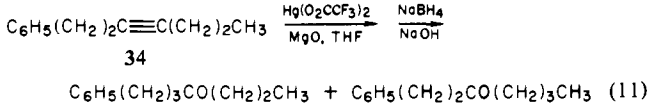
32a, $n = 1$
b, $n = 2$
c, $n = 3$

subjected to mercuration as described immediately above. While compounds **32a** and **32c** failed to react, compound **32b** afforded the corresponding mercurated 1,2-dihydronaphthalene **33** in 30% yield (eq 10). It was subsequently found that the methoxy group



(10)

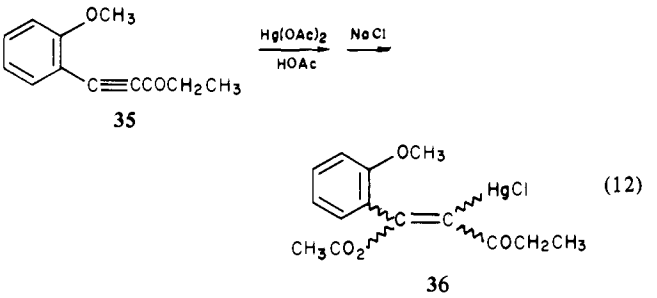
is vital to this cyclization. Attempts to cyclize 1-phenyl-3-heptyne (**34**), produced a mixture of two ketones after alkaline borohydride reduction, establishing that mercuration must be proceeding without participation of the aromatic ring (eq 11). These ketones



(11)

are presumably formed by reduction and hydrolysis of the corresponding β-(trifluoroacetoxy)mercurials. This carbocyclic synthesis thus appears limited to the preparation of relatively electron-rich mercurated 1,2-dihydronaphthalenes.

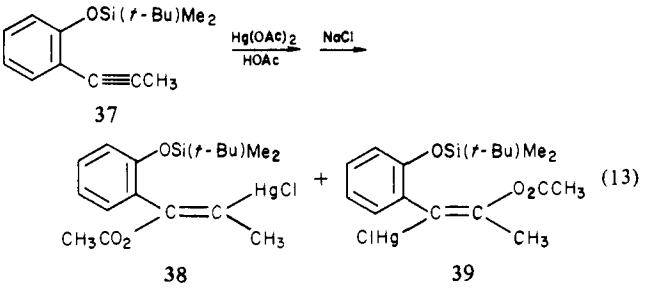
Coumarins. Through minor modifications in the substrates undergoing mercuration, we have also been able to prepare the coumarin ring system. Our objective was to effect β-acetoxymercury formation, rather than cyclization, on *o*-anisylacetylenes or derivatives. Our initial efforts focused on the mercuration of compound **35** (eq 12). Introduction of the ketone group ap-



(12)

parently disfavors cationic cyclization and results in β-acetoxymercurial formation, albeit in only 12% isolated yield. Because of the low yield, no further work was carried out on this system.

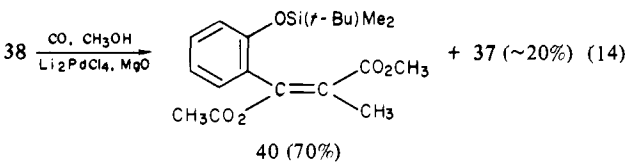
An alternate approach to the desired β-acetoxymercurials proved more successful. By employing a sterically bulky protecting group on oxygen, we have been able to block cyclization and effect exclusive β-acetoxymercury formation (eq 13). Two isomeric



(13)

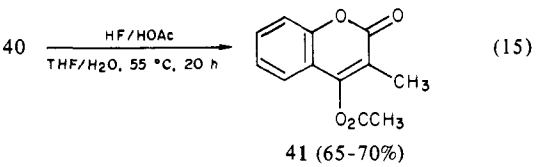
mercurials, **38** and **39**, were observed by NMR spectral analysis. After 30 min the ratio of **38** to **39** was 5:1, but the total yield was only 27%. After 20 h, the ratio was the same, but the yield had doubled. Finally, at 48 h the ratio was 12:1 and the mercurials could be isolated in 66% yield. The structures were assigned by comparing the NMR chemical shifts of the acetate and methyl protons with those reported by Uemura for the adduct of mercuric acetate and 1-phenylpropyne.[14] The major isomer could be isolated in pure form by column chromatography.

Carbonylation of this compound afforded a 70% yield of the corresponding methyl ester, plus approximately 20% of the starting acetylene (eq 14). Desilylation of **40** afforded the desired 4-



(14)

acetoxy-3-methylcoumarin in 65–70% yield (eq 15). Cyclization



(15)

thus confirms the stereo- and regiochemistry of the intermediate mercurial and affords a new route to coumarins.

Functionalization of the Organomercurials. For these mercuration reactions to really prove useful in organic synthesis, simple

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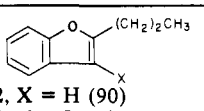
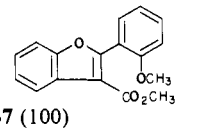
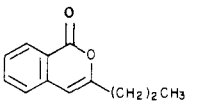
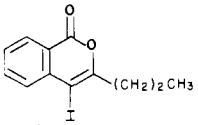
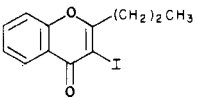
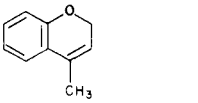
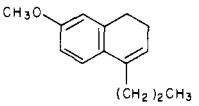
Table III. Functionalization of the Organomercurials

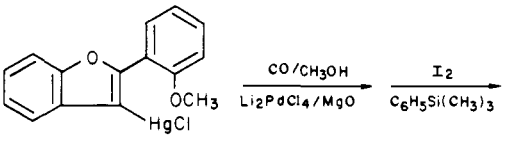
entry	organomercurial	reagent(s)	product (% yield)
			
1	**2**	$NaBH_4/NaOH$	**42**, X = H (90)
2	**2**	I_2	**43**, X = I (75)
3	**2**	$CO/CH_3OH/Li_2PdCl_4/MgO$	**44**, X = CO_2CH_3 (89)
4	**2**	$CH_3COCl/AlCl_3$	**45**, X = $COCH_3$, (75)
5	**2**	$H_2C{=}CHCO_2CH_3/Li_2PdCl_4$	**46**, X = $CH{=}CHCO_2CH_3$ (65)
			
6	**12**	$CO/CH_3OH/Li_2PdCl_4/MgO$	**47** (100)
			
7	**16**	$NaBH_4/NaOH$	**48** (75)[a]
			
8	**16**	I_2	**49** (82)[a]
			
9	**20**	I_2	**51** (93)
			
10	**31**	$NaBH_4/NaOH$	**52** (69)
			
11	**33**	$NaBH_4/NaOH$	**53** (70)[a]

[a] Crude yield; one peak by gas chromatographic analysis.

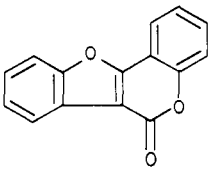
methods for the direct replacement of the mercury moiety by various functional groups are required. While a wide variety of such reactions are now known,[6] relatively few have been employed on heterocyclic mercurials. Thus, to establish the utility of these new organomercurials, we have briefly examined a number of synthetic transformations that may be of interest to the organic chemist. The results are summarized in Table III.

The majority of our work was carried out on 3-(chloromercurio)-2-*n*-propylbenzofuran (**2**). As seen in Table III, the mercury substituent is readily substituted by hydrogen, iodine, carbomethoxy, ketone, and acrylate groups. Alkaline sodium borohydride reduction proved particularly valuable as a means of establishing the structure of these new organomercurials, since the resulting hydrogen exhibited NMR chemical shifts which allowed easy characterization of the ring system.

Palladium-promoted carbonylation also proved to be a useful reaction. Thus, carbonylation, subsequent demethylation, and cyclization of organomercurial **3** provides a simple synthesis of the biologically interesting coumestan ring system in 90% yield (eq 16).



3



54 (16)

Conclusion. The mercuration of aryl acetylenes provides a broad range of naturally occurring, physiologically active heterocyclic ring systems, including benzofurans, benzothiophenes, isocoumarins, chromones, benzopyrans, 1,2-dihydronaphthalenes, coumarins, and coumestan. The ability to further functionalize intermediate organomercurials in many of these syntheses greatly expands the synthetic utility of these new heterocyclic approaches.

Experimental Section

Equipment. The infrared spectra were recorded on a Beckman IR-4250 infrared spectrophotometer or a Beckman Acculab 2 spectrophotometer, and the ^1H NMR spectra on a Varian Associates A-60 NMR, Hitachi Perkin-Elmer R-20B NMR, or a Varian Associates EM-360 NMR spectrometer. The mass spectra were obtained on an AEI MS-902 high-resolution mass spectrometer, while the GC/mass spectra were recorded on a Finnegan 4023 GC/MS data system. GLC analyses were performed on a Varian 3700 gas chromatograph with an attached Varian CDS-111 chromatography data system. Thin-layer chromatography was performed on Merck 60F-254 silica gel plates from MCB Manufacturing Chemists, Inc. Silica gel for column chromatography was purchased from Davison Chemical (60-200 mesh) and MCB Manufacturing Chemists, Inc. (230–400 mesh). Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc.

Reagents. All compounds were used directly as obtained commercially, unless otherwise indicated. The starting materials were purchased from Aldrich, except for 2-iodoanisole (Columbia Organics) and 1-pentyne (Farchan). Phenyltrimethylsilane was prepared in 67% yield by the reaction of phenylmagnesium bromide with trimethylchlorosilane. 1-Iodo-2-butyne was synthesized by bromination of 2-butyn-1-ol with phosphorus tribromide followed by reaction of the bromide with sodium iodide. Methyllithium was purchased from Alfa and titrated before use by the method of Watson and Eastham.[15] *n*-Butyllithium was also obtained from Alfa and titrated using 2,5-dimethoxybenzyl alcohol.[16] Mercuric acetate and acetic acid were used directly as obtained from Mallinckrodt and Fischer, respectively. Methanol was distilled from magnesium methoxide, acetonitrile and methylene chloride were distilled from phosphorus pentoxide, diethyl ether and tetrahydrofuran were distilled from calcium hydride, and *N,N*-dimethylformamide and pyridine were distilled from barium oxide before using. Magnesium oxide and lithium chloride were purchased from J. T. Baker. Palladium chloride was generously supplied by Johnson Matthey, Inc., and Engelhard Industries. Carbon monoxide was purchased from Matheson Gas Products.

Preparation of Aryl Iodides. The preparation of 2-iodo-4-methoxyanisole, 2-iodo-4-nitroanisole, and 2-iodothioanisole were carried out using the procedure of Ullmann.[17] The following preparation of **2-iodo-4-methoxyanisole** is representative. In a 250-mL Erlenmeyer flask was placed 7.66 g (50.0 mmol) of 2,5-dimethoxyaniline in 70 mL of water containing 7 mL of concentrated sulfuric acid. The solution was cooled to 0 °C and 3.5 g (50.7 mmol) of sodium nitrite in 15 mL of water was slowly added. The resulting mixture was stirred for 30 min, then added to a cold (~5 °C) solution of 15 g (90.4 mmol) of potassium iodide in 60 mL of water, and the stirring was continued for 2.5 h. The aqueous solution was extracted with 3 × 100 mL of ether, and the organic extracts were washed with 2 × 50 mL of 10% hydrochloric acid, 2 × 50 mL of saturated sodium bicarbonate, and 2 × 50 mL of a saturated sodium thiosulfate solution, dried ($MgSO_4$), and concentrated. Distillation of the concentrate provided 11.1 g (42 mmol, 84%) of 2-iodo-4-methoxyanisole: bp 98–101 °C (0.6 mmHg) [lit.[18] bp 157 °C (10 mmHg)]. The compound distills over as a pale yellow liquid but turns green upon standing. ^1H NMR ($CDCl_3$) δ 3.70 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 6.75–7.25 (m, 3 H, C_6H_3).

The following two aryl iodides were prepared in identical fashion. **2-Iodo-4-nitroanisole**: yield 71%; mp 93 °C (lit.[19] mp 96 °C); ^1H NMR ($CDCl_3$) δ 4.0 (s, 3 H, OCH_3), 6.95 (d, 1 H, J = 10 Hz, H-6), 8.35 (dd,

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1 H, J = 10, 3 Hz, H-5), 8.75 (d, 1 H, J = 3 Hz, H-3). **2-Iodothioanisole**: yield 92%; bp 154–156 °C (16 mmHg) [lit.[20] bp 173 °C (20 mmHg)]; ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3 H, SCH_3), 6.61–7.92 (m, 4 H, C_6H_4).

Methyl 2-Iodobenzoate. In a 100-mL round-bottom flask was placed 12.4 g (50 mmol) of 2-iodobenzoic acid in 20 mL of methanol containing 3 mL of concentrated sulfuric acid. The mixture was refluxed for 2 h, poured into 100 mL of water, and extracted with 3 × 50 mL of ether. The ether extracts were washed with 2 × 20 mL of water, 2 × 20 mL of 5% sodium bicarbonate, and 2 × 20 mL of brine, dried (Na_2SO_4), and concentrated. Distillation at 146–147 °C (16 mmHg) [lit.[21] bp 145–146 °C (16 mmHg)] provided 10.8 g (41 mmol, 82%) of methyl 2-iodobenzoate: ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3 H, OCH_3), 6.92–8.01 (m, 4 H, C_6H_4); IR (neat) 1720 (C=O) cm^{-1}.

***N*-Methyl-2-iodoaniline.** In a flame-dried 100-mL round-bottom flask, 2.25 g (10.3 mmol) of 2-iodoaniline was dissolved in 30 mL of dry tetrahydrofuran. The resulting solution was cooled to −78 °C under a nitrogen atmosphere, 6.25 mL of 1.6 M methyllithium (10 mmol) was added dropwise, and the resulting solution was stirred at −78 °C for 30 min. To the solution was added 1.90 g (15.1 mmol) of dimethyl sulfate and stirring was continued for 10 min at −78 °C. The solution was then warmed to room temperature and stirred for 2 h, followed by acidification with 10% hydrochloric acid. The reaction mixture was diluted with ether and the aqueous layer was removed. The ether extract was stirred with 30 mL of concentrated ammonium hydroxide for 30 min. The aqueous layer was removed, and the organic phase was washed with 20 mL of water and 30 mL of brine, dried ($MgSO_4$), and concentrated. Distillation at 101–105 °C (2.0 mmHg) [lit.[22] bp 108–110 °C (4.5 mmHg)] yielded 2.03 g (8.7 mmol, 87%) of *N*-methyl-2-iodoaniline: ^{1}H NMR ($CDCl_3$) δ 2.80 (s, 3 H, NCH_3), 4.0 (br s, 1 H, NH), 6.2–7.8 (m, 4 H, C_6H_4); IR (neat) 3410 (NH), 1590 (C=C) cm^{-1}; mass spectrum, m/z 232.970 23 (calcd for C_7H_8IN, 232.970 15).

***N*-Acetyl-*N*-methyl-2-iodoaniline.** In a dry 250-mL round-bottom flask, 2.1 g (9.0 mmol) of *N*-methyl-2-iodoaniline was dissolved in 50 mL of dry ether, and the solution was cooled to 0 °C. To the solution 0.931 g (9.2 mmol) of triethylamine was added followed by 0.725 g (9.2 mmol) of acetyl chloride. The reaction mixture was stirred at 0 °C for 30 min then warmed to room temperature and stirred overnight. The amine salts were removed by filtration, and the filtrate was diluted with ether and washed with 2 × 30 mL of water and 1 × 50 mL of brine, dried ($MgSO_4$), and concentrated to yield 2.45 g (8.91 mmol, ~100%) of essentially pure *N*-acetyl-*N*-methyl-2-iodoaniline: ^{1}H NMR ($CDCl_3$) δ 1.80 (s, 3 H, $NCOCH_3$), 3.20 (s, 3 H, NCH_3), 6.95–8.07 (m, 4 H, C_6H_4); IR (neat) 1665 (C=O), 1590 (C=C) cm^{-1}; mass spectrum ($M^+ - CH_3$), m/z 259.957 72 (calcd for C_8H_7INO, 259.957 24).

***N*-Acetyl-2-iodoaniline.** This compound was prepared as above starting from 2-iodoaniline: yield 76%; mp 109–110 °C (lit.[23] mp 109.5–110 °C); ^{1}H NMR ($CDCl_3$) δ 2.28 (s, 3 H, $NCOCH_3$), 6.81–8.40 (m, 5 H, C_6H_4 and NH); IR ($CHCl_3$) 3415 (NH), 1690 (C=O) cm^{-1}.

***N*,*N*-Dimethyl-2-iodoaniline.** In a 100-mL round-bottom flask were placed 8.64 g (39.5 mmol) of *o*-iodoaniline, 8.47 g (80 mmol) of sodium carbonate, and 15.2 g (120.6 mmol) of dimethyl sulfate in 50 mL of a 4:1 ethanol–water mixture. The contents of the flask were refluxed for 48 h. After the solution was cooled to room temperature, 30 mL of concentrated ammonium hydroxide was added to the mixture and stirring was continued for an additional 30 min at room temperature. The solution was extracted with 3 × 50 mL of ether, and the ether extracts were combined and washed with 1 × 50 mL of brine and 1 × 50 mL of water, dried ($MgSO_4$), and concentrated. Distillation of the concentrate provided 9.25 g (37.4 mmol, 95%) of the title compound: bp 125–128 °C (17 mmHg) [lit.[24] bp 116 °C (11 mmHg)]; ^{1}H NMR ($CDCl_3$) δ 2.75 [s, 6 H, $N(CH_3)_2$], 6.32–7.89 (m, 4 H, C_6H_4).

Methyl 2-Iodobenzyl Ether. In a flame-dried 100-mL round-bottom flask under an atmosphere of nitrogen was placed 1.87 g (7.99 mmol) of 2-iodobenzyl alcohol in 30 mL of dry tetrahydrofuran. The solution was cooled to −78 °C, and 5.0 mL of 1.6 M methyllithium was added. The solution was stirred for 30 min at −78 °C, then treated with 1.5 g (11.9 mmol) of dimethyl sulfate, and stirred at −78 °C for an additional 30 min. The cooling bath was removed, and the reaction mixture was warmed to room temperature and stirred overnight followed by acidification with 10% hydrochloric acid. The solution was extracted with ether and the ether was washed with 1 × 30 mL of concentrated ammonium hydroxide, 2 × 30 mL of water, and 1 × 50 mL of brine, dried ($MgSO_4$), and concentrated. The concentrate was distilled at 90–94 °C (2 mmHg) [lit.[25] bp 99–103 °C (4 mmHg)] to provide 1.4 g (5.65 mmol, 71%) of methyl 2-iodobenzyl ether: ^{1}H NMR ($CDCl_3$) δ 3.40 (s, 3 H, OCH_3), 4.38 (s, 2 H, CH_2O), 6.70–7.80 (m, 4 H, C_6H_4).

Methyl 2-Iodo-4-methylphenylacetate. The requisite acid was prepared by the thallation–iodination procedure developed by Taylor and McKillop.[26] In a dry 100-mL round-bottom flask were placed 10.74 g (19.76 mmol) of thallium trifluoroacetate [$Tl(TFA)_3$ was transferred to the flask in a glovebag] and 2.97 g (19.8 mmol) of *p*-tolylacetic acid in 20 mL of trifluoroacetic acid. The flask was degassed then stirred under an atmosphere of nitrogen for 48 h at room temperature. The reaction mixture was concentrated under reduced pressure followed by two coevaporations with 1,2-dichloroethane to provide 8.4 g (14.5 mmol, 73%) of crude 4-methyl-2-[bis(trifluoroacetoxy)thallium]phenylacetic acid. The crude thallium compound was suspended in 150 mL of water, then 14.9 g (90 mmol) of potassium iodide was added all at once, and the reaction mixture was refluxed for 5 h. After this time, 1.5 g (7.9 mmol) of sodium metabisulfite was added, and refluxing was continued for an additional 30 min. The reaction mixture was filtered through Celite while warm, and the Celite was washed with 200 mL of acetone. The aqueous acetone filtrate was extracted with 4 × 60 mL of ether, and the ether extracts were washed with 1 × 40 mL of saturated sodium thiosulfate and 1 × 40 mL of brine, dried ($MgSO_4$), and concentrated. The concentrate was recrystallized from hexanes to produce 3.37 g (12.21 mmol, 84%) of 2-iodo-4-methylphenylacetic acid: mp 137–139 °C; ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3 H, Ar CH_3), 3.81 (s, 2 H, Ar CH_2), 7.01–7.35 (m, 2 H, H-5, H-6), 7.72 (br s, 1 H, H-3), 11.48 (br s, 1 H, CO_2H); IR (Nujol) 3000 (br, CO_2H), 1695 (C=O) cm^{-1}; mass spectrum, m/z 275.965 53 (calcd for $C_9H_9IO_2$, 275.964 73).

The methyl ester was prepared as previously described for methyl 2-iodobenzoate: yield 100%; ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3 H, Ar CH_3), 3.71 (s, 3 H, OCH_3), 3.78 (s, 2 H, Ar CH_2), 7.15 (s, 2 H, H-5, H-6), 7.70 (br s, 1 H, H-3); IR (neat) 1730 (C=O), 1600 (C=C) cm^{-1}.

Methyl β-(2-Iodo-4-methylphenyl)ethyl Ether. The alcohol was prepared by the reduction of 2-iodo-4-methylphenylacetic acid using a modification of the procedure of Corey.[27] In a flame-dried 100-mL round-bottom flask, 3.26 g (11.81 mmol) of the acid was dissolved in 50 mL of dry ether, and the solution was cooled to 0 °C. To the solution, 6.1 g (47.3 mmol) of diisopropylethylamine was added, followed by 4.47 g (47.3 mmol) of methyl chloroformate, and the reaction mixture was stirred at 0 °C for 1 h, filtered, and concentrated. The concentrate was placed in a dry 250-mL round-bottom flask with 50 mL of dry tetrahydrofuran, then degassed, and cooled to 0 °C. To this solution 0.520 g (23.85 mmol) of lithium borohydride was added (nitrogen backflush) and the reaction was warmed to room temperature and stirred until the intermediate carbonate had disappeared as indicated by TLC analysis (~24 h). The reaction mixture was quenched by the addition of water followed by the dropwise addition of 10% hydrochloric acid and diluted with 50 mL of ether, and the aqueous layer was removed. The ether layer was washed with 2 × 30 mL of brine, dried ($MgSO_4$), and concentrated. The alcohol was isolated by column chromatography using hexanes–ethyl acetate (2:1) as the eluant to yield 2.38 g (9.1 mmol, 77%) of the desired alcohol (R_f 0.33): ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3 H, Ar CH_3), 2.57 (s, 1 H, OH), 2.92 (t, 2 H, J = 7 Hz, Ar CH_2), 3.80 (t, 2 H, J = 7 Hz, CH_2OH), 7.00–7.15 (m, 2 H, H-5, H-6), 7.70 (br s, 1 H, H-3); IR (neat) 3150–3550 (OH), 1600 (C=C) cm^{-1}; mass spectrum, m/z 261.985 59 (calcd for $C_9H_{11}IO$, 261.985 47).

The ether was prepared as follows. In a dry 100-mL round-bottom flask was placed 0.330 g (13.75 mmol) of sodium hydride (washed with hexanes and vacuum dried) in 25 mL of dry tetrahydrofuran. The flask was degassed and placed under an atmosphere of nitrogen. Then, 2.38 g (9.1 mmol) of the alcohol in 25 mL of dry tetrahydrofuran was added dropwise, and the mixture was stirred for 1.5 h. To the reaction mixture 2.0 g (15.87 mmol) of dimethyl sulfate was added, and the resulting mixture was stirred overnight at room temperature. The reaction was quenched by the addition of 10% hydrochloric acid and diluted with ether. After removal of the aqueous layer, the ether extract was stirred with 30 mL of concentrated ammonium hydroxide for 30 min. The organic phase was washed with 20 mL of water and 30 mL of brine, dried ($MgSO_4$), and concentrated. Column chromatography of the residue using hexanes–ethyl acetate (10:1) as the eluant provided 1.98 g (7.2 mmol, 79%) of the desired methyl ether (R_f 0.35): ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3 H, Ar CH_3), 2.91 (t, 2 H, J = 7 Hz, Ar CH_2), 3.38 (s, 3 H,

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OCH_3), 3.55 (t, 2 H, J = 7 Hz, CH_2O), 7.00–7.15 (m, 2 H, H-5, H-6), 7.70 (br s, 1 H, H-3); IR (neat) 3020 (C=CH), 1600 (C=C) cm^{-1}; mass spectrum, m/z 276.002 10 (calcd for $C_{10}H_{13}IO$, 276.001 12).

Preparation of Acetylenes. The majority of the acetylenes were prepared by the reaction of a cuprous acetylide with the appropriate aryl iodide under the conditions described by Castro.[28] The preparation of **2-(1-pentynyl)anisole (1)** is representative. In a 100-mL round-bottom flask under an atmosphere of nitrogen was placed 2.64 g (20.2 mmol) of cuprous *n*-propylacetylide in 75 mL of dry pyridine. To this mixture was added 4.66 g (19.9 mmol) of 2-iodoanisole, and the resulting mixture was refluxed for 15–20 h. The reaction mixture was diluted with water and ether and filtered through Celite, and the filter cake was washed several times with ether. The filtrate was separated, and the aqueous phase was extracted with 3 × 50 mL of ether. The combined etheral extracts and washings were washed successively 3 times each with 50 mL of 1% hydrochloric acid, 50 mL of 5% sodium bicarbonate, and 50 mL of water, dried ($MgSO_4$), and concentrated. The concentrate was distilled to provide 2.61 (15 mmol, 75%) of 2-(1-pentynyl)anisole (**1**): bp 95–100 °C (0.7 mmHg); ^1H NMR ($CDCl_3$) δ 1.0 (t, 3 H, J = 7 Hz, CH_3), 1.5 (m, 2 H, CH_2), 2.3 (t, 2 H, J = 7 Hz, C≡CCH_2), 3.8 (s, 3 H, OCH_3), 6.4–7.7 (m, 4 H, C_6H_4); IR (neat) 2230 (C≡C) cm^{-1}; mass spectrum, m/z 174.104 49 (calcd for $C_{12}H_{14}O$, 174.104 47).

The following acetylenes were prepared in an identical fashion. The acetylenes **3**, **5**, **13**, **17**, **23d**, **25**, and **28** were prepared with dry *N,N*-dimethylformamide as the solvent, and acetylene **9** was prepared with cuprous phenylacetylide instead of cuprous *n*-propylacetylide.

4-Methoxy-2-(1-pentynyl)anisole (3): yield 54%; bp 121–124 °C (0.6 mmHg); ^1H NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 6 Hz, CH_3), 1.62 (m, 2 H, CH_2), 2.45 (t, 2 H, J = 6 Hz, C≡CCH_2), 3.70 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 6.61–7.20 (m, 3 H, C_6H_3); IR (neat) 2210 (C≡C) cm^{-1}; mass spectrum, m/z 204.117 60 (calcd for $C_{13}H_{16}O_2$, 204.115 03).

4-Nitro-2-(1-pentynyl)anisole (5): yield 63%; mp 60–62 °C; ^1H NMR ($CDCl_3$) δ 1.05 (t, 3 H, J = 6 Hz, CH_3), 1.61 (m, 2 H, CH_2), 2.45 (t, 2 H, J = 7 Hz, C≡CCH_2), 4.00 (s, 3 H, OCH_3), 6.90–7.15 (m, 1 H, H-6), 8.10–8.31 (m, 2 H, H-5, H-3); IR ($CHCl_3$) 2220 (C≡C) cm^{-1}; mass spectrum, m/z 219.090 28 (calcd for $C_{12}H_{13}NO_3$, 219.089 55).

2-Methoxydiphenylacetylene (9): yield 53%; bp 120–122 °C (0.1 mmHg) [lit.[29] bp 144–145 °C (0.2 mmHg)]; ^1H NMR ($CDCl_3$) δ 3.80 (s, 3 H, OCH_3), 6.41–8.02 (m, 9 H, C_6H_4, C_6H_5); IR (neat) 2215 (C≡C) cm^{-1}; GC/MS, m/z (relative intensity) 208 (100, M^+), 131 (61).

Methyl 2-(1-Pentynyl)benzoate (15): yield 54%; by 180–182 °C (16 mmHg); ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 6 Hz, CH_3), 1.61 (m, 2 H, CH_2), 2.45 (t, 2 H, J = 7 Hz, C≡CCH_2), 3.90 (s, 3 H, OCH_3), 7.11–8.00 (m, 4 H, C_6H_4); IR (neat) 2240 (C≡C), 1730 (C=O) cm^{-1}; mass spectrum, m/z 202.098 61 (calcd for $C_{13}H_{14}O_2$, 202.099 38.

2-(1-Pentynyl)thioanisole (13): yield 70%; bp 177–180 °C (16 mmHg); ^1H NMR ($CDCl_3$) δ 1.05 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.38 (s, 3 H, SCH_3), 2.41 (t, 2 H, J = 7 Hz, C≡CCH_2), 6.91–7.59 (m, 4 H, C_6H_4); IR (neat) 2220 (C≡C) cm^{-1}; mass spectrum, m/z 190.081 73 (calcd for $C_{12}H_{14}S$, 190.081 63).

***N*-Acetyl-2-(1-pentynyl)aniline (23b)**: yield 37%; mp 63–65 °C; ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 6 Hz, CH_3), 1.63 (m, 2 H, CH_2), 2.20 (s, 3 H, $NCOCH_3$), 2.45 (t, 2 H, J = 7 Hz, C≡CCH_2), 6.79–8.42 (m, 5 H, C_6H_4, NH); IR (CCl_4) 3410 (NH), 2220 (C≡C), 1700 (C=O) cm^{-1}; mass spectrum, m/z 201.115 59 (calcd for $C_{13}H_{15}NO$, 201.115 37).

***N,N*-Dimethyl-2-(1-pentynyl)anillne (23c)**: yield 46%; isolated by column chromatography using hexanes–ethyl acetate (20:1), R_f 0.28; ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 6 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.45 (t, 2 H, J = 6 Hz, C≡CCH_2), 2.85 [s, 6 H, $N(CH_3)_2$], 6.59–7.40 (m, 4 H, C_6H_4); IR (neat) 2240 (C≡C) cm^{-1}; mass spectrum (M^+ – H), m/z 186.127 96 (calcd for $C_{13}H_{16}N$, 186.128 27). The reaction also produced **1-methyl-2-propylindole**: yield 30%; bp 170–174 °C (17 mmHg); ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.65 (t, 2 H, J = 7 Hz, C≡CCH_2), 3.55 (s, 3 H, NCH_3), 6.20 (s, 1 H, H-3), 6.79–7.55 (m, 4 H, C_6H_4); mass spectrum, m/z 173.119 97 (calcd for $C_{12}H_{15}N$, 173.120 45).

2-(1-Pentynyl)nitrobenzene: yield 53%; ^1H NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.41 (t, 2 H, J = 7 Hz, C≡CCH_2), 7.08–8.06 (m, 4 H, C_6H_4); IR (neat) 2230 (C≡C) cm^{-1}. This compound was reduced using the procedure of Schofield and Swain[30] for the reduction of 1-(2-nitrophenyl)-2-phenylacetylene to provide **2-(1-pentynyl)aniline (23a)**: yield 38%; bp 170–173 °C (17 mmHg); ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 6 Hz, CH_3), 1.59 (m, 2 H, CH_2), 2.40 (t, 2 H, J = 6 Hz, C≡CCH_2), 4.10 (br s, 2 H, NH_2), 6.39–7.29 (m, 4 H, C_6H_4); IR (neat) 3490 (NH), 3400 (NH), 2240 (C≡C) cm^{-1}; mass spectrum, m/z 159.104 43 (calcd for $C_{11}H_{13}N$, 159.104 80).

***N*-Acetyl-*N*-methyl-2-(1-pentynyl)aniline (23d)**: yield 29%; isolated by column chromatography using hexanes–ethyl acetate (2:1) as the eluant (R_f 0.25); ^1H NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 1.82 (s, 3 H, $NCOCH_3$), 2.42 (t, 2 H, J = 7 Hz, C≡CCH_2), 3.23 (s, 3 H, NCH_3), 6.91–7.62 (m, 4 H, C_6H_4); IR (neat) 2220 (C≡C), 1655 (C=O) cm^{-1}; mass spectrum, m/z 215.130 56 (calcd for $C_{14}H_{17}NO$, 215.131 02). This reaction also produced **1-acetyl-2-propylindole**: yield 32%; mp 68–71 °C; ^1H NMR ($CDCl_3$) δ 0.97 (t, 3 H, J = 7 Hz, CH_3), 1.65 (m, 2 H, CH_2), 2.73 (s, 3 H, $NCOCH_3$), 2.97 (t, 2 H, J = 7 Hz, C≡CCH_2), 6.40 (s, 1 H, H-3), 6.90–7.90 (m, 4 H, C_6H_4); IR (film) 1660 (C=O) cm^{-1}; mass spectrum, m/z 201.116 07 (calcd for $C_{13}H_{15}NO$, 201.115 37).

Methyl 2-(1-Pentynyl)benzyl Ether (17): yield 80%; isolated by column chromatography using hexanes–ethyl acetate (10:1) as the eluant (R_f 0.41); ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.42 (t, 2 H, J = 7 Hz, C≡CCH_2), 3.42 (s, 3 H, OCH_3), 4.52 (s, 2 H, CH_2O), 6.91–7.52 (m, 4 H, C_6H_4); IR (neat) 2240 (C≡C) cm^{-1}; mass spectrum, m/z 188.120 38 (calcd for $C_{13}H_{16}O$, 188.120 12).

Methyl 4-Methyl-2-(1-pentynyl)phenylacetate (25): yield 50%; isolated by column chromatography using hexanes–ethyl acetate (5:1) as the eluant (R_f 0.42); ^1H NMR ($CDCl_3$) δ 1.05 (t, 3 H, J = 7 Hz, CH_3), 1.62 (m, 2 H, CH_2), 2.30 (s, 3 H, Ar CH_3), 2.41 (t, 2 H, J = 7 Hz, C≡CCH_2), 3.70 (s, 3 H, OCH_3), 3.78 (s, 2 H, Ar CH_2), 7.04–7.41 (m, 3 H, C_6H_3); IR (neat) 2210 (C≡C), 1730 (C=O) cm^{-1}; mass spectrum, m/z 230.130 20 (calcd for $C_{15}H_{18}O_2$, 230.130 68).

Methyl β-[4-Methyl-2-(1-pentynyl)phenyl]ethyl Ether (28): yield 63%; isolated by column chromatography using hexanes–ethyl acetate (10:1) as the eluant (R_f 0.37); ^1H NMR ($CDCl_3$) δ 1.03 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.21 (s, 3 H, Ar CH_3), 2.36 (t, 2 H, J = 7 Hz, C≡CCH_2), 2.91 (t, 2 H, J = 7 Hz, Ar CH_2), 3.30 (s, 3 H, OCH_3), 3.55 (t, 2 H, J = 7 Hz, CH_2O), 6.89–7.25 (m, 3 H, C_6H_3); IR (neat) 2210 (C≡C) cm^{-1}; mass spectrum, m/z 216.151 31 (calcd for $C_{15}H_{20}O$, 216.151 42).

1-(3-Cyclohexenyl)-2-(2-anisyl)acetylene (7). In a flame-dried 50-mL round-bottom flask with a septum inlet was placed 3.0 g (10.3 mmol) of 1-(2-anisyl)-2,2-dibromoethylene (prepared from 2-anisaldehyde using the procedure of Rameriz, Desai, and McKelvie[31]) in 25 mL of dry tetrahydrofuran. The solution was cooled to −78 °C, and 10.8 mL of 2.2 M *n*-butyllithium (23.76 mmol) was added dropwise. The resulting solution was stirred at −78 °C for 1 h, then warmed to room temperature, and stirred for 45 min. The reaction mixture was cooled back down to −78 °C, and 2.45 g (15.2 mmol) of 3-bromocyclohexene and 1.0 g (5.25 mmol) of cuprous iodide were added. The solution was allowed to warm to room temperature and stirred overnight followed by acidification with 10% hydrochloric acid. The reaction mixture was extracted with 2 × 30 mL of ether, and the ether extracts were washed with 3 × 30 mL of saturated ammonium chloride, dried ($MgSO_4$), and concentrated. The crude residue was purified by column chromatography using hexanes–ethyl acetate (20:1) as the eluant to yield 1.10 g (5.19 mmol, 50%) of the desired acetylene (R_f 0.25): ^1H NMR ($CDCl_3$) δ 1.41–2.29 (m, 6 H, C_3H_6), 3.31 (m, 1 H, C≡CH), 3.80 (s, 3 H, OCH_3), 5.75 (s, 2 H, CH=CH), 6.59–7.48 (m, 4 H, C_6H_4); IR (neat) 2220 (C≡C) cm^{-1}; mass spectrum, m/z 212.120 36 (calcd for $C_{15}H_{16}O$, 212.120 12).

1,2-Bis(*o*-methoxyphenyl)acetylene (11). In a 100-mL round-bottom flask, 13.6 g (100 mmol) of 2-anisaldehyde and 1.38 g (21.2 mmol) of potassium cyanide were refluxed for 4 h in 25 mL of 50% ethanol. The reaction mixture was cooled to room temperature and placed in the freezer. The solid was filtered, washed with 50% ethanol, and recrystallized from ether to provide 5.74 g (21.1 mmol, 42%) of 2,2′-dimethoxybenzoin: mp 97–99 °C [lit.[32] mp 101.5 °C]; ^1H NMR ($CDCl_3$) δ 3.70 (s, 6 H, OCH_3), 4.45 (d, 1 H, J = 6 Hz, OH), 6.05 (d, 1 H, J = 6 Hz, CHO), 6.60–7.70 (m, 8 H, C_6H_4). In a 100-mL round-bottom flask fitted with a reflux condenser, 5.50 g (20.22 mmol) of the benzoin compound and 10.0 g (40.05 mmol) of copper(II) sulfate pentahydrate were refluxed in 12 mL of pyridine with 4 mL of water for approximately 2 h. After refluxing, the solution was allowed to cool and poured into 100 mL of water. The water was extracted with 3 × 75 mL of ether, and the ether extracts were washed with 1 × 25 mL of 10% hydrochloric acid and 2 × 25 mL of water, dried ($MgSO_4$), and concentrated. The solid residue was recrystallized from 80% ethanol to provide 3.48 g (12.89 mmol, 64%) of 2,2′-dimethoxybenzil: mp 128–129 °C [lit.[33] mp 128–129 °C]; ^1H NMR ($CDCl_3$) δ 3.6 (s, 3 H, OCH_3), 6.91–8.29 (m, 4 H, C_6H_4).

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The benzil derivative was refluxed for 60 h with 2.04 g (34.6 mmol) of 85% hydrazine hydrate in 12 mL of *n*-propyl alcohol to provide 1.92 g (6.44 mmol, 50%) of 2,2'-dimethoxybenzil dihydrazone: mp 232–234 °C (dec) [lit.[34] mp ~230 °C (dec)]; ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3 H, OCH_3), 5.25 (br s, 2 H, NH_2), 6.80–7.51 (m, 4 H, C_6H_4). The dihydrazone was refluxed with 3.43 g (15.84 mmol) of yellow mercuric oxide in 10 mL of xylenes for 2 h. The hot solution was filtered through Celite, and the Celite was washed with 30 mL of hot benzene. The filtrate was dried ($MgSO_4$) and the solvent was removed by vacuum. The crude solid was chromatographed through 10 g of silica gel with hexanes–ethyl acetate (4:1) as the eluant to isolate the crude acetylene (R_f 0.31). The solid was recrystallized from 85% ethanol to yield 0.252 g (1.06 mmol, 17%) of 1,2-bis(*o*-methoxyphenyl)acetylene (**11**): mp 124–126 °C [lit.[34] mp 126 °C]; ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3 H, OCH_3), 6.79–7.70 (m, 4 H, C_6H_4).

1-(2-Anisyl)-2-hexyn-1-one (19). In a flame-dried 100-mL round-bottom flask under a nitrogen atmosphere was added 2.07 g (30.4 mmol) of 1-pentyne in 45 mL of dry tetrahydrofuran. The solution was cooled to −78 °C, and 12.5 mL of 2.42 M *n*-butyllithium (30.3 mmol) was added dropwise. The reaction mixture was stirred at −78 °C for 10 min and at room temperature for 30 min. After cooling to −78 °C, a solution of 4.07 g (30.0 mmol) of 2-anisaldehyde in 15 mL of tetrahydrofuran was added dropwise. The reaction mixture was stirred at −78 °C for 10 min and at room temperature for 1 h, acidified with 10% hydrochloric acid, and extracted with 2 × 50 mL of ether. The organic layers were washed with 2 × 50 mL of saturated sodium bicarbonate and 2 × 50 mL of water, dried ($MgSO_4$), and concentrated to give 4.60 g (22.5 mmol, 75%) of the crude alcohol. The crude alcohol was treated with 6 mL of 4 M Jones reagent (24 mmol) in 30 mL of acetone at 0 °C for 30 min. The reaction mixture was poured into 200 mL of water and extracted with 2 × 100 mL of ether. The ether extracts were washed with 2 × 50 mL of water, 2 × 50 mL of saturated sodium bicarbonate, and 2 × 50 mL of brine, dried ($MgSO_4$), and concentrated. The crude concentrate was purified by column chromatography using hexanes–ethyl acetate (5:1) as the eluant to provide 4.25 g (21.04 mmol, 70% for two steps) of the desired acetylene **19** (R_f 0.30): ^{1}H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.41 (t, 2 H, J = 7 Hz, $C{\equiv}CCH_2$), 3.90 (s, 3 H, OCH_3), 6.87–8.18 (m, 4 H, C_6H_4); IR (neat) 2210 (C≡C), 1640 (C=O) cm^{-1}; mass spectrum, m/z 202.098 88 (calcd for $C_{13}H_{14}O_2$, 202.099 38).

1-(2-Anisyl)-3-phenyl-2-propyn-1-one (21). In a 25-mL round-bottom flask, 3.04 g (20.0 mmol) of 2-anisic acid and 3.60 g (30.3 mmol) of thionyl chloride were refluxed for 30 min. The excess thionyl chloride was then removed under vacuum. In a 100-mL round-bottom flask under nitrogen was added 2.68 g (20.0 mmol) of lithium iodide in 10 mL of dry ether to a suspension of 3.3 g (20.1 mmol) of cuprous phenylacetylide in 20 mL of dry ether. The acid chloride was added to this suspension via a double-ended needle, and the reaction mixture was stirred at room temperature for 1 h. To the mixture, 7 mL of hexamethylphosphoramide was added, and stirring was continued for 20 h. The reaction mixture was treated with 10% hydrochloric acid, poured into 100 mL of water, and extracted with 3 × 75 mL of ether. The ether extracts were washed with 2 × 50 mL of saturated ammonium chloride, 2 × 50 mL of saturated sodium bicarbonate, 1 × 50 mL of 5% sodium hydroxide, and 2 × 50 mL of water, dried ($MgSO_4$), and concentrated. Purification of the residue by column chromatography using hexanes–ethyl acetate (3:1) as the eluant provided 2.20 g (9.32 mmol, 47%) of the acetylene (R_f 0.30): ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3 H, OCH_3), 6.85–8.05 (m, 9 H, C_6H_4, C_6H_5); IR (neat) 2200 (C≡C), 1630 (C=O) cm^{-1}; mass spectrum, m/z 236.083 58 (calcd for $C_{16}H_{12}O_2$, 236.083 73).

1-(2-Anisyl)-2-hexyne (24). To a −78 °C solution of 1.70 (25.0 mmol) of 1-pentyne in 50 mL of dry tetrahydrofuran was slowly added 11.85 mL of 2.11 M *n*-butyllithium (25.0 mmol). The mixture was stirred at −78 °C for 10 min and at room temperature for 1 h. Then the solution was cooled back down to −78 °C and 4.40 g (21.9 mmol) of 2-methoxybenzyl bromide was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 2 days at room temperature. Ether was added and the mixture was then washed with 3 × 50 mL of brine, dried ($MgSO_4$), and concentrated. The concentrate was distilled to provide 3.52 g (18.7 mmol, 85%) of the acetylene **24**: bp 156–160 °C (16 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 6 Hz, CH_3), 1.52 (m, 2 H, CH_2), 2.2 (m, 2 H, $C{\equiv}CCH_2$), 3.48 (br s, 2 H, Ar CH_2), 3.81 (s, 3 H, OCH_3), 6.65–7.50 (m, 4 H, C_6H_4); IR (neat) 2220 (C≡C) cm^{-1}; mass spectrum, m/z 188.120 30 (calcd for $C_{13}H_{16}O$, 188.120 12).

1-(3-Anisyl)-2-hexyne (32a) was prepared in identical fashion: yield 38%; isolated by column chromatography using hexanes–ethyl acetate (10:1) as the eluant (R_f 0.46); ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_3), 1.55 (m, 2 H, CH_2), 2.23 (m, 2 H, $C{\equiv}CCH_2$), 3.54 (t, 2 H, J = 2 Hz, Ar CH_2), 3.80 (s, 3 H, OCH_3), 6.63–7.40 (m, 4 H, C_6H_4); IR (neat) 2220 (C≡C) cm^{-1}.

2-Butynyl Phenyl Ether (30). In a flame-dried 100-mL round-bottom flask was placed 0.240 g (10.0 mmol) of sodium hydride (washed with hexanes and vacuum dried) in 20 mL of dry tetrahydrofuran. To the suspension 0.940 g (10.0 mmol) of phenol was added under a nitrogen sweep, and the resulting mixture was stirred for 30 min. Then 1.80 g (10 mmol) of 1-iodo-2-butyne was added dropwise, and the reaction mixture was stirred overnight at room temperature, acidified with 10% hydrochloric acid, and extracted with 3 × 25 mL of ether. The ether extracts were washed with 40 mL of brine, 40 mL of 10% sodium hydroxide, 40 mL of saturated sodium bicarbonate, and 60 mL of brine, dried ($MgSO_4$), and concentrated. Purification of the residue by column chromatography yielded 1.44 g (9.86 mmol, 100%) of the desired ether **30** [hexanes–ethyl acetate (15:1), R_f 0.36]: ^{1}H NMR ($CDCl_3$) δ 1.82 (t, 3 H, J = 2 Hz, CH_3), 4.60 (q, 2 H, J = 2 Hz, CH_2), 6.75–7.47 (m, 5 H, C_6H_5); IR (neat) 2210 (C≡C) cm^{-1}; mass spectrum, m/z 146.073 32 (calcd for $C_{10}H_{10}O$, 146.073 17).

1-(3-Anisyl)-3-heptyne (32b). The acetylene was prepared using the procedure of Brown and co-workers[35] for the preparation of acetylenes from trialkylboranes. In a dry 100-mL round-bottom flask under nitrogen was placed 4 mL of 1 M borane–tetrahydrofuran (4 mmol) in 5 mL of dry tetrahydrofuran. The solution was cooled to 0 °C, and 1.60 g (11.94 mmol) of 3-methoxystyrene,[36] prepared from (3-methoxybenzyl)triphenylphosphonium bromide and aqueous formaldehyde,[37] in 5 mL of dry tetrahydrofuran was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 1 h. Then the solution was cooled back down to 0 °C, and 5 mmol of preformed 1-lithio-1-pentyne was added by a double-ended needle. The reaction mixture was warmed to room temperature and stirred for 2 h. Then the solution was cooled to −78 °C and 1.27 g (5.0 mmol) of iodine in 25 mL of dry tetrahydrofuran (or ether) was slowly added. The mixture was stirred at −78 °C for 30 min and at room temperature for 1 h. The crude reaction mixture was washed with 2 × 20 mL of 3 N sodium hydroxide (containing 1–2 mL of saturated sodium thiosulfate), and the aqueous washes were combined and reextracted with 25 mL of ether. The etheral layers were combined and treated with 12 mL of 3 N sodium hydroxide followed by 4 mL of 30% hydrogen peroxide. The resulting aqueous layer was saturated with potassium carbonate and removed. The organic phase was washed with 20 mL of saturated sodium bicarbonate and 30 mL of brine, dried ($MgSO_4$), and concentrated. The desired product was isolated by first distilling off the volatile components (1-iodo-1-pentyne) followed by column chromatography using hexanes–ethyl acetate (15:1) as the eluant (R_f 0.40): yield 0.580 g (2.87 mmol, 72% based on BH_3); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3 H, J = 6 Hz, CH_3), 1.48 (m, 2 H, CH_2), 2.00–2.46 (m, 4 H, $CH_2C{\equiv}CCH_2$), 2.65 (t, 2 H, J = 7 Hz, Ar CH_2), 3.78 (s, 3 H, OCH_3), 6.61–6.89 (m, 3 H, H-2, H-4, H-6), 7.12 (d, 1 H, J = 8 Hz, H-5); IR (neat) 2210 (C≡C) cm^{-1}; mass spectrum, m/z 202.135 51 (calcd for $C_{14}H_{18}O$, 202.135 77).

The acetylenes **32c** and **34** were prepared in the same manner starting with 3-allylanisole[38] and styrene, respectively. **1-(3-Anisyl)-4-octyne (32c)**: yield 86% based on BH_3; isolated by column chromatography using hexanes–ethyl acetate (15:1), R_f 0.42; ^{1}H, NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 7 Hz, CH_3), 1.15–1.90 (m, 4 H, CH_2), 1.99–2.32 (m, 4 H, $C{\equiv}CCH_2$), 2.68 (t, 2 H, J = 7 Hz, Ar CH_2), 3.77 (s, 3 H, OCH_3), 6.55–7.01 (m, 3 H, H-2, H-4, H-6), 7.50 (d, 1 H, J = 8 Hz, H-5); IR (neat) 2215 (C≡C) cm^{-1}.

1-Phenyl-3-heptyne (34): yield 100% based on BH_3; isolated by column chromatography using hexanes–ethyl acetate (20:1), R_f 0.45; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3 H, J = 7 Hz, CH_3), 1.50 (m, 2 H, CH_2), 1.97–2.44 (m, 4 H, $C{\equiv}CCH_2$), 2.79 (t, 2 H, J = 6 Hz, Ar CH_2), 7.26 (m, 5 H, C_6H_5); IR (neat) 2200 (C≡C) cm^{-1}.

1-(2-Anisyl)-1-hexyn-3-one (35). To a −78 °C solution of 3.0 g (10.27 mmol) of 1-(2-anisyl)-2,2-dibromoethylene in 25 mL of dry tetrahydrofuran was added 11.0 mL of 1.9 M *n*-butyllithium (20.9 mmol). The solution was stirred at −78 °C for 30 min and at room temperature for 1 h. Then the solution was cooled back down to −78 °C and 0.80 g (13.77 mmol) of freshly distilled propionaldehyde was added. The reaction mixture was allowed to slowly warm to room temperature and stirred overnight at room temperature followed by acidification with 10% hydrochloric acid and extraction with 2 × 30 mL of ether. The ether

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extracts were washed with saturated ammonium chloride, dried ($MgSO_4$), and concentrated to provide crude 1-(2-anisyl)-3-hydroxy-1-hexyne in 64% yield: ^1H NMR ($CDCl_3$) δ 1.05 (t, 3 H, J = 7 Hz, CH_3), 1.80 (m, 2 H, CH_2), 2.75 (br s, 1 H, OH), 3.88 (s, 3 H, OCH_3), 4.56 (t, 1 H, J = 7 Hz, CHOH), 6.75–7.59 (m, 4 H, C_6H_4). The alcohol was oxidized with Jones reagent in acetone to provide 0.936 g (4.98 mmol, 49% for the two steps) of the acetylenic ketone **35** after purification by column chromatography [hexanes–ethyl acetate (5:1), R_f 0.28]; ^1H NMR ($CDCl_3$) δ 1.21 (t, 3 H, J = 7 Hz, CH_3), 2.66 (q, 2 H, J = 7 Hz, CH_2), 3.88 (s, 3 H, OCH_3), 6.75–7.89 (m, 4 H, C_6H_4); IR (neat) 2200 (C≡C), 1670 (C=O) cm^{-1}; mass spectrum, m/z 188.083 64 (calcd for $C_{12}H_{12}O_2$, 188.083 73).

1-(2-[(*tert*-Butyldimethylsilyl)oxy]phenyl)-1-propyne (37). This compound was prepared by alkylation of the corresponding *gem*-dibromo olefin with dimethyl sulfate using the procedure described above: yield 68%; isolated by column chromatography using hexanes plus 2% ethyl acetate as the eluant (R_f 0.32); ^1H NMR ($CDCl_3$) δ 0.25 (s, 6 H, $SiCH_3$), 1.02 (s, 9 H, t-C_4H_9Si), 2.01 (s, 3 H, CH_3), 6.59–7.45 (m, 4 H, C_6H_4); IR (neat) 2240 (C≡C) cm^{-1}; mass spectrum, m/z 246.143 73 (calcd for $C_{15}H_{22}OSi$, 246.144 00).

Preparation of Organomercurials. Most of the acetylene mercuration reactions were performed under the same conditions. The following preparation of **3-(chloromercurio)-2-propylbenzofuran (2)** is representative. To a suspension of 0.637 g (2.0 mmol) of mercuric acetate in 6 mL of glacial acetic acid at room temperature was added 0.350 g (2.0 mmol) of 2-(1-pentynyl)anisole (**1**). The resulting solution was stirred at room temperature for 30 min, then poured into a saturated sodium chloride–ice mixture, and allowed to warm to room temperature. The solid was collected by filtration, washed with hexanes, and dissolved in hot chloroform. The chloroform solution was filtered through Celite, and the crude mercury compound was isolated by evaporation of the chloroform. The solid was recrystallized from 90% ethanol to yield 0.551 g (1.4 mmol, 70%) of 3-(chloromercurio)-2-propylbenzofuran (**2**): mp 119–120 °C; ^1H NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 7 Hz, CH_3), 1.73 (m, 2 H, CH_2), 2.84 (t, 2 H, J = 7 Hz, C=CCH_2), 7.09–7.70 (m, 4 H, C_6H_4); IR ($CHCl_3$) 3030 (C=CH), 1580 (C=C) cm^{-1}. Anal. Calcd for $C_{11}H_{11}ClHgO$: C, 33.43; H, 2.81; Hg, 50.75. Found: C, 33.47; H, 2.92; Hg, 50.93. The following mercurials were prepared in an identical fashion.

3-(Chloromercurio)-5-methoxy-2-propylbenzofuran (4): yield 60%; mp 147–148 °C; ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_3), 1.73 (m, 2 H, CH_2), 2.75 (t, 2 H, J = 7 Hz, C=CCH_2), 3.85 (s, 3 H, OCH_3), 6.80–7.20 (m, 3 H, C_6H_3); IR (Nujol) 3010 (C=CH), 1600 (C=C) cm^{-1}. Anal. Calcd for $C_{12}H_{13}ClHgO_2$: C, 33.89; H, 3.08; Hg, 47.17. Found: C, 33.63; H, 3.04; Hg, 47.31.

3-(Chloromercurio)-5-nitro-2-propylbenzofuran (6): yield 45%; mp 116–118 °C; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_3), 1.72 (m, 2 H, CH_2), 2.81 (t, 2 H, J = 7 Hz, C=CCH_2), 7.40 (d, 1 H, J = 10 Hz, H-7), 8.11 (dd, 1 H, J = 10, 3 Hz, H-6), 8.49 (d, 1 H, J = 3 Hz, H-4); IR (Nujol) 3080 (C=CH), 1570 (C=C), 1510 (NO_2) cm^{-1}. Anal. Calcd for $C_{11}H_{10}ClHgNO_3$: C, 30.01; H, 2.29; Hg, 45.56. Found: C, 30.22; H, 3.08; Hg, 45.32.

3-(Chloromercurio)-2-(3-cyclohexenyl)benzofuran (8): yield 30%; mp 123–125 °C; ^1H NMR ($CDCl_3$) δ 1.40–2.32 (m, 6 H, C_3H_6), 3.75 (m, 1 H, C=CCH), 6.08 (m, 2 H, HC=CH), 7.00–7.55 (m, 4 H, C_6H_4); IR (Nujol) 3060 (C=CH), 1600 (C=C), 1580 (C=C) cm^{-1}. Anal. Calcd for $C_{14}H_{13}ClHgO$: C, 38.81; H, 3.02; Hg, 46.29. Found: C, 38.53; H, 3.12; Hg, 46.37.

3-(Chloromercurio)-2-phenylbenzofuran (10): yield 59%; mp 205 °C (dec); ^1H NMR ($CDCl_3$) δ 6.89–7.80 (m, Ar); IR (Nujol) 3060 (C=CH), 3030 (C=CH), 1580 (C=C) cm^{-1}. Anal. Calcd for $C_{14}H_9ClHgO$: C, 39.17; H, 2.12; Hg, 46.73. Found: C, 39.26; H, 2.35; Hg, 46.94.

2-(2-Anisyl)-3-(chloromercurio)benzofuran (12): yield 58%; mp 205 °C; ^1H NMR ($CDCl_3$) δ 4.01 (s, 3 H, OCH_3), 6.89–8.02 (m, 8 H, C_6H_4); IR (Nujol) 3010 (C=CH), 1600 (C=C), 1580 (C=C) cm^{-1}. Anal. Calcd for $C_{15}H_{11}ClHgO_2$: C, 39.21; H, 2.41; Hg, 43.69. Found: C, 39.39; H, 2.52; Hg, 43.84.

3-(Chloromercurio)-2-propylbenzothiophene (14): yield 66%; mp 134–135 °C; ^1H NMR ($CDCl_3$) δ 0.99 (t, 3 H, J = 6 Hz, CH_3), 1.69 (m, 2 H, CH_2), 2.90 (t, 2 H, J = 7 Hz, C=CCH_2), 7.18–7.93 (m, 4 H, C_6H_4); IR (Nujol) 3015 (C=CH), 1600 (C=C), 1575 (C=C) cm^{-1}. Anal. Calcd for $C_{11}H_{11}ClHgS$: C, 32.12; H, 2.70; Hg, 48.77. Found: C, 32.06; H, 2.75; Hg, 48.88.

4-(Chloromercurio)-3-*n*-propylisocoumarin (16): yield 65%; mp 195–197 °C; ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_3), 1.69 (m, 2 H, CH_2), 2.65 (t, 2 H, J = 7 Hz, C=CCH_2), 7.10–8.19 (m, 4 H, C_6H_4); IR (Nujol) 3020 (C=CH), 1720 (C=O), 1610 (C=C) cm^{-1}. Anal. Calcd for $C_{12}H_{11}ClHgO_2$: C, 34.05; H, 2.62; Hg, 47.39. Found: C, 34.17; H, 2.75; Hg, 47.63.

Mercurial 18: reaction time, 20 h; yield 39%; mp 201–203 °C; ^1H NMR ($CDCl_3$) δ 1.04 (t, 3 H, J = 7 Hz, CH_3), 1.65 (m, 2 H, CH_2), 2.67 (t, 2 H, J = 7 Hz, C=CCH_2), 5.16 (s, 2 H, CH_2O), 6.82–7.70 (m, 4 H, C_6H_4); IR (Nujol) 3060 (C=CH), 1600 (C=C), 1550, 1500 cm^{-1}. Anal. Calcd for $C_{12}H_{13}ClHgO$: C, 35.22; H, 3.20; Hg, 49.01. Found: C, 34.98; H, 3.02; Hg, 49.27.

3-(Chloromercurio)-2-propylchromone (20): yield 60%; mp 136–138 °C; ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 7 Hz, CH_3), 1.89 (m, 2 H, CH_2), 2.70 (t, 2 H, J = 7 Hz, C=CCH_2), 7.02–8.21 (m, 4 H, C_6H_4); IR (Nujol) 3060 (C=CH), 1615 (C=O), 1600 (C=C), 1585 (C=C) cm^{-1}. Anal. Calcd for $C_{12}H_{11}HgO_2$: C, 34.05; H, 2.62; Hg, 47.39. Found: C, 33.84; H, 2.76; Hg, 47.16.

3-(Chloromercurio)flavone (22): yield 58%; mp 254–255 °C; ^1H NMR ($CDCl_3$) δ 7.19–8.25 (m, 9 H, Ar); IR (Nujol) 3070 (C=CH), 1615 (C=O, C=C), 1555 (C=C) cm^{-1}. Anal. Calcd for $C_{15}H_9ClHgO_2$: C, 39.38; H, 1.98; Hg, 43.88. Found: C, 39.43; H, 2.10; Hg, 43.90.

Vinylmercurial 29: reaction time, 20 h; yield 44%; mp 104–105 °C; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, J = 6 Hz, CH_3), 1.52 (m, 2 H, CH_2), 2.05 (s, 3 H, $COCH_3$), 2.23 (s, 3 H, Ar CH_3), 2.27 (t, 2 H, J = 7 Hz, C=CCH_2), 2.86 (t, 2 H, J = 7 Hz, Ar CH_2), 3.25 (s, 3 H, OCH_3), 3.55 (t, 2 H, J = 7 Hz, CH_2O), 6.93–7.21 (m, 3 H, C_6H_3); IR (Nujol) 3020 (C=CH), 1740 (C=O), 1650 (C=C) cm^{-1}. Anal. Calcd for $C_{17}H_{23}ClHgO_3$: C, 39.93; H, 4.53; Hg, 39.22. Found: C, 40.01; H, 4.64; Hg, 39.46.

Vinylmercurial 36: reaction time, 20 h; yield 12%; mp 126–128 °C; ^1H NMR ($CDCl_3$) δ 1.14 (t, 3 H, J = 7 Hz, CH_3), 2.19 (s, 3 H, $COCH_3$), 2.76 (q, 2 H, J = 7 Hz, CH_2), 3.90 (s, 3 H, OCH_3), 6.79–7.61 (m, 4 H, C_6H_4); IR (film) 3060 (C=CH), 1740 (C=O), 1665 (C=O), 1600 (C=C) cm^{-1}. Anal. Calcd for $C_{14}H_{15}ClHgO_4$: C, 34.79; H, 3.13; Hg, 41.50. Found: C, 34.28; H, 3.20; Hg, 41.12.

Vinylmercurials 38 plus 39: reaction time, 48 h; yield 66%; isolated by column chromatography using hexanes–ethyl acetate (5:1) as the eluant (both mercurials are thick oils). For **38**: ^1H NMR ($CDCl_3$) δ 0.24 (s, 6 H, $SiCH_3$), 1.03 (s, 9 H, t-C_4H_9Si), 2.02 (s, 3 H, $J_{^{199}Hg-CH_3}$ = 194 Hz, CH_3), 2.15 (s, 3 H, $COCH_3$), 6.69–7.48 (m, 4 H, C_6H_4). For **39**: ^1H NMR ($CDCl_3$) δ 0.24 (s, 6 H, $SiCH_3$), 1.03 (s, 9 H, t-C_4H_9Si), 1.91 (s, 3 H, $COCH_3$), 2.24 (s, 3 H, CH_3), 6.69–7.48 (m, 4 H, C_6H_4); IR (film) 3060, 3020 (C=CH), 1745 (C=O), 1600 (C=C) cm^{-1}. Anal. Calcd for $C_{17}H_{25}ClHgO_3Si$: C, 37.71; H, 4.65; Hg, 37.04. Found: C, 37.97; H, 4.74; Hg, 36.59.

3-(Chloromercurio)-4-methyl-2*H*-1-benzopyran (31). In a 25-mL round-bottom flask were placed 1.28 g (3.0 mmol) of mercuric trifluoroacetate and 0.360 g (9.0 mmol) of magnesium oxide in 6 mL of tetrahydrofuran. To the mixture was added 0.440 g (3.0 mmol) of 2-butynyl phenyl ether (**30**) in 3 mL of tetrahydrofuran. The reaction mixture was stirred at room temperature for 1 h, filtered through Celite, washed with 2 × 40 mL of brine, dried ($MgSO_4$), and concentrated. The concentrate was triturated with ether to give a yellowish solid, which was recrystallized from dichloromethane–hexanes at −78 °C to give 0.454 g (1.19 mmol, 40%) of mercurial **31**: mp 220 °C dec; ^1H NMR (Me_2SO-d_6) δ 2.21 (br s, 3 H, CH_3), 4.84 (br s, 2 H, CH_2), 6.60–7.26 (m, 4 H, C_6H_4); IR (Nujol) 3070 (C=CH), 3040, 1600 (C=C) cm^{-1}. Anal. Calcd for $C_{10}H_9ClHgO$: C, 31.49; H, 2.36; Hg, 52.64. Found: C, 31.63; H, 2.50; Hg, 52.49.

3-(Chloromercurio)-7-methoxy-4-propyl-1,2-dihydronaphthalene (33). In a 25-mL round-bottom flask were placed 0.430 g (1.0 mmol) of mercuric trifluoroacetate and 0.120 g (3.0 mmol) of magnesium oxide in 2 mL of tetrahydrofuran. To this mixture 0.20 g (1.0 mmol) of 1-(3-anisyl)-3-heptyne (**32b**) in 1 mL of tetrahydrofuran was added. The resulting mixture was stirred at room temperature for 10 h, filtered through Celite, washed with 2 × 40 mL of brine, dried ($MgSO_4$), and concentrated. The concentrate was purified by column chromatography using hexanes–ethyl acetate (10:1) as the eluant to provide 0.126 g (0.62 mmol, 62%) of the starting acetylene and 0.130 g (0.30 mmol, 30%) of mercurial **33** (R_f 0.20): mp 126–128 °C; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, J = 6 Hz, CH_3), 1.60 (m, 2 H, CH_2), 2.29–2.92 (m, 6 H, CH_2), 3.80 (s, 3 H, OCH_3), 6.61–6.82 (m, 2 H, H-6, H-8), 7.15 (d, 1 H, J = 8 Hz, H-5); IR (Nujol) 3030 (C=CH), 3000, 1605 (C=C), 1590 (C=C) cm^{-1}. Anal. Calcd for $C_{14}H_{17}ClHgO$: C, 38.45; H, 3.92; Hg, 45.87. Found: C, 38.36; H, 4.00; Hg, 45.74.

Reactions of Organomercurials: 2-Propylbenzofuran (42). This compound was prepared from mercurial **2** by using the conditions of Brown and Hammar[39] for the reduction of organomercurials. In a 25-mL round-bottom flask was placed 0.199 g (0.50 mmol) of **2** in 4 mL of a 1:1 tetrahydrofuran–water mixture. To this solution, 2 mL of 3 M sodium hydroxide and 4 mL of 0.5 M sodium borohydride in 3 M sodium hydroxide were added, and the resulting mixture was stirred for 1 h.

(39) Brown, H. C.; Hammar, W. J. *J. Am. Chem. Soc.* **1967**, *89*, 1522.

Sodium chloride was added to saturate the water layer and the mixture was filtered through Celite, extracted with 2 × 25 mL of ether, dried ($MgSO_4$), and concentrated. Bulb-to-bulb distillation of the concentrate at 125–130 °C (16 mmHg) provided 72 mg (0.45 mmol, 90%) of 2-propylbenzofuran (**42**) [lit.[40] bp 107–110 °C (12.5 mmHg)]: ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_3), 1.70 (m, 2 H, CH_2), 2.81 (t, 2 H, J = 7 Hz, C=CCH_2), 6.28 (s, 1 H, H-3), 7.01–7.60 (m, 4 H, C_6H_4); IR (neat) 3010, 1600 (C=C), 1550 (C=C) cm^{-1}; mass spectrum, m/z 160.088 88 (calcd for $C_{11}H_{12}O$, 160.088 82).

The following compounds were prepared in an identical manner in order to determine the structure of the cyclized compound. Only the pertinent spectral data will be listed here. **3-Propylisocoumarin** (**48**): ^1H NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 7 Hz, CH_3), 1.69 (m, 2 H, CH_2), 2.67 (t, 2 H, J = 7 Hz, C=CCH_2), 6.21 (s, 1 H, H-4), 7.11–8.20 (m, 4 H, C_6H_4); IR (neat) 1725 (C=O), 1655 (C=C), 1610 (C=C) cm^{-1}; GC/MS, m/z (relative intensity) 188 (48, M^+), 159 (15), 131 (59), 118 (100), 89 (100).

4-Methyl-2*H*-1-benzopyran (**52**): ^1H NMR ($CDCl_3$) δ 2.35 (br s, 3 H, CH_3), 4.63 (d, 2 H, J = 6 Hz, CH_2), 5.96 (t, 1 H, J = 6 Hz, H-3), 6.75–7.50 (m, 4 H, C_6H_4) (decoupling: irradiation at δ 4.63 causes 5.96 to collapse to a br s; irradiation at δ 5.96 causes 4.63 to collapse to a br s, but δ 2.35 remains the same; irradiation at δ 2.35 causes both 4.63 and 5.96 to sharpen, but their respective multiplicity remains the same); IR (neat) 1600 (C=C) cm^{-1}; GC/MS, m/z (relative intensity) 146 (70, M^+), 145 (77), 131 (100).

7-Methoxy-4-propyl-1,2-dihydronaphthalene (**53**): ^1H NMR ($CDCl_3$) δ 0.97 (t, 3 H, J = 6 Hz, CH_3), 1.62 (m, 2 H, CH_2), 2.29–2.94 (m, 6 H, CH_2), 3.79 (s, 3 H, OCH_3), 5.67 (br s, 1 H, H-3), 6.56–6.83 (m, 2 H, H-6, H-8), 7.16 (d, 1 H, J = 8.5 Hz, H-5); IR (neat) 1605 (C=C) cm^{-1}; GC/MS, m/z (relative intensity) 202 (50, M^+), 187 (5), 174 (54), 159 (100), 144 (31).

3-Iodo-2-propylbenzofuran (**43**). The iodination of **2** was performed using the procedure of Whitmore and Hanson[41] for the iodination of 2-(chloromercurio)phenol. In a 25-mL round-bottom flask was stirred 0.395 g (1.0 mmol) of **2** in 5 mL of chloroform. Then 0.254 g (1.0 mmol) of iodine in 5 mL of chloroform was added, and the resulting mixture was stirred for 3 h, filtered through Celite, washed with aqueous sodium iodide (5 g/40 mL of water), and dried (Na_2SO_4). Removal of the chloroform yielded a yellowish oil, which was purified by column chromatography using hexanes as the eluant to furnish 0.215 g (0.75 mmol, 75%) of the iodo compound (R_f 0.45): ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 7 Hz, CH_3), 1.80 (m, 2 H, CH_2), 2.89 (t, 2 H, J = 7 Hz, C=CCH_2), 7.20–7.62 (m, 4 H, C_6H_4); IR (neat) 3070 (C=CH), 1590 (C=C) cm^{-1}; mass spectrum, m/z 285.985 14 (calcd for $C_{11}H_{11}IO$, 285.985 47).

3-Iodo-2-propylchromone (**51**) was prepared using an identical procedure: yield 93%; isolated by column chromatography [hexanes–ethyl acetate (2:1), R_f 0.50]; ^1H NMR ($CDCl_3$) δ 0.99 (t, 3 H, J = 7 Hz, CH_3), 1.89 (m, 2 H, CH_2), 2.78 (t, 2 H, J = 7 Hz, C=CCH_2), 7.03–8.20 (m, 4 H, C_6H_4); IR (neat) 1615 (C=O), 1600 (C=C) cm^{-1}; mass spectrum, m/z 313.980 51 (calcd for $C_{12}H_{11}IO_2$, 313.980 38).

3-Acetyl-2-propylbenzofuran (**45**). The acylation of **2** was accomplished using the experimental procedure described by Larock and Bernhardt[42] for the acylation of alkenylmercurials. To a mixture of 0.135 g (1.0 mmol) of anhydrous aluminum trichloride and 0.080 g (1.0 mmol) of acetyl chloride in 10 mL of dry dichloromethane was added 0.395 g (1.0 mmol) of **2**. The resulting mixture was stirred at room temperature for 15 min, poured into 30 mL of water, and extracted with dichloromethane. The combined dichloromethane extracts were washed with 20 mL of 5% sodium bicarbonate, 20 mL of 3 M sodium thiosulfate, and 30 mL of water. All the aqueous layers were combined and reextracted with 2 × 30 mL of dichloromethane. The combined organic extracts were dried (Na_2SO_4) and concentrated. Bulb-to-bulb distillation produced 0.152 g (0.75 mmol, 75%) of the title compound: bp 123–127 °C (0.05 mmHg); ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_3), 1.69 (m, 2 H, CH_2), 2.61 (s, 3 H, $COCH_3$), 3.08 (t, 2 H, J = 7 Hz, C=CCH_2), 7.08–8.03 (m, 4 H, C_6H_4); IR (neat) 1675 (C=O), 1560 (C=C) cm^{-1}; mass spectrum, m/z 202.099 33 (calcd for $C_{13}H_{14}O_2$, 202.099 38). 2,4-DNP derivative: mp 165–167 °C; mass spectrum, m/z 382.126 27 (calcd for $C_{19}H_{18}N_4O_5$, 382.127 73).

Ester 46. This compound was prepared by using the procedure of Heck.[43] In a 25-mL round-bottom flask were stirred 0.395 g (1.0 mmol) of **2** and 0.354 g (4.1 mmol) of methyl acrylate in 7 mL of dry acetonitrile. After the mixture was stirred for a short time, a solution of lithium trichloropalladite (1 mmol) in 7 mL of dry acetonitrile was added, and the reaction mixture was stirred at room temperature for 24 h. Then ether and activated carbon were added, and the mixture was filtered through Celite. The filtrate was washed with 2 × 25 mL of saturated ammonium chloride, dried ($MgSO_4$), and concentrated. Bulb-to-bulb distillation at 200–205 °C (0.025 mmHg) provided 0.159 g (0.65 mmol, 65%) of the desired unsaturated ester **46**: ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_3), 1.79 (m, 2 H, CH_2), 2.92 (t, 2 H, J = 7 Hz, C=CCH_2), 3.90 (s, 3 H, OCH_3), 6.51 (d, 1 H, J = 17 Hz, C=CH), 7.09–7.62 (m, 4 H, C_6H_4), 7.85 (d, 1 H, J = 17 Hz, HC=C); IR (neat) 1720 (C=O), 1635 (C=C), 1580 (C=C) cm^{-1}; mass spectrum, m/z 244.109 74 (calcd for $C_{15}H_{16}O_3$, 244.109 95).

3-Carbomethoxy-2-propylbenzofuran (**44**). The preparation of this compound was accomplished using the procedure of Larock[44] for the carbonylation of organomercurials. In a 50-mL round-bottom flask were stirred 0.045 g (1.1 mmol) of anhydrous lithium chloride, 0.088 g (0.50 mmol) of palladium chloride, and 0.040 g (1.0 mmol) of magnesium oxide in 6 mL of dry methanol. After they were stirred for a short time, the contents of the flask were cooled to −78 °C. While the system was being flushed with carbon monoxide at −78 °C, 0.198 g (0.50 mmol) of **2** was added. A balloon filled with carbon monoxide was connected to the top of the flask, and the reaction mixture was allowed to slowly warm to room temperature and then stirred at room temperature overnight. Activated carbon was added and the reaction mixture was diluted with ether, filtered through Celite, washed with saturated ammonium chloride, dried ($MgSO_4$), and concentrated. The concentrate was purified by column chromatography using hexanes–ethyl acetate (10:1) as the eluant to provide 0.097 g (0.445 mmol, 89%) of 3-carbomethoxy-2-propylbenzofuran (**44**) (R_f 0.33): ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 7 Hz, CH_3), 1.71 (m, 2 H, CH_2), 3.02 (t, 2 H, J = 7 Hz, C=CCH_2), 3.89 (s, 3 H, OCH_3), 7.02–7.91 (m, 4 H, C_6H_4); IR (neat) 1715 (C=O), 1560 (C=C) cm^{-1}; mass spectrum, m/z 218.094 11 (calcd for $C_{13}H_{14}O_3$, 218.094 30).

The following esters were prepared in an identical fashion. **2-(2-Anisyl)-3-carbomethoxybenzofuran** (**47**): yield 100%; isolated by column chromatography using hexanes–ethyl acetate (4:1) as the eluant (R_f 0.30): ^1H NMR ($CDCl_3$) δ 3.75 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 6.91–7.75 (m, 7 H, Ar), 7.95–8.20 (m, 1 H, H-4); IR (neat) 1715 (C=O), 1600 (C=C) cm^{-1}; mass spectrum, m/z 282.088 38 (calcd for $C_{17}H_{14}O_4$, 282.089 21).

Vinyl ester 40: reaction time, 3 days; yield 70%; isolated by column chromatography using hexanes–ethyl acetate (5:1) as the eluant (R_f 0.40); ^1H NMR ($CDCl_3$) δ 0.18 (s, 6 H, $SiCH_3$), 0.98 (s, 9 H, t-C_4H_9Si), 1.94 (s, 3 H, CH_3), 2.14 (s, 3 H, $COCH_3$), 3.49 (s, 3 H, OCH_3), 6.67–7.30 (m, 4 H, C_6H_4); IR (neat) 1745 (C=O), 1720 (C=O), 1600 (C=C) cm^{-1}; mass spectrum (M^+ − t-C_4H_9), m/z 307.101 18 (calcd for $C_{15}H_{19}O_5Si$, 307.100 18).

6*H*-Benzofuro[3,2-*c*][1]-benzopyran-6-one (Coumestan) (**54**). The cyclization of 2-(2-anisyl)-3-carbomethoxybenzofuran (**47**) was performed under the conditions of Ho and Olah[45] for the demethylation of esters and ethers. In a 25-mL round-bottom flask, 0.130 g (0.87 mmol) of phenyltrimethylsilane, 0.080 g (0.28 mmol) of the ester, and 0.216 g (0.85 mmol) of iodine were heated at 110 °C for a period of 3 h. Then the reaction mixture was quenched by the addition of water and extracted with 2 × 50 mL of ether. The ether extracts were washed with 2 × 20 mL of glacial acetic acid, 2 × 20 mL of saturated sodium bicarbonate, and 1 × 50 mL of brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography using hexanes–ethyl acetate (4:1) as the eluant to give 0.059 g (0.25 mmol, 90%) of compound **54** (R_f 0.35): mp 179–181 °C [lit.[46] mp 181–182 °C]; ^1H NMR ($CDCl_3$) δ 7.09–7.88 (m, 7 H, Ar), 7.95–8.15 (m, 1 H, H-7); IR (film) 1735 (C=O), 1625 (C=C), 1600 (C=C) cm^{-1}. ^1H NMR and IR spectral data are identical with that reported in the literature.[46]

4-Acetoxy-3-methylcoumarin (**41**). In a 100-mL round-bottom flask was placed 0.325 g (0.89 mmol) of ester **40** in 6 mL of a mixture of 48% hydrofluoric acid/glacial acetic acid/tetrahydrofuran/water (1:3:1:1). The solution was heated at 55 °C for 20 h, diluted with water, and stirred with potassium carbonate for 1 h at room temperature. The reaction mixture was acidified with 10% hydrochloric acid and filtered through Celite, and the filtrate was extracted with 2 × 40 mL of ether. The ether extracts were washed with 20 mL of brine, 30 mL of dilute potassium hydroxide, 20 mL of saturated ammonium chloride, and 40 mL of water, dried ($MgSO_4$), and concentrated. Isolation of the desired compound by column chromatography [hexanes–ethyl acetate (2:1)] provided 0.138 g (0.633 mmol, 71%) of the coumarin **41**: mp 149–151 °C (lit.[47] mp 154

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°C); ^{1}H NMR ($CDCl_3$) δ 2.01 (s, 3 H, CH_3), 2.41 (s, 3 H, $COCH_3$), 7.03-7.46 (m, 4 H, C_6H_4); IR (Nujol) 1750 (C=O), 1700 (C=O), 1640 (C=C), 1600 (C=C) cm^{-1}; mass spectrum, m/z 218.058 20 (calcd for $C_{12}H_{10}O_4$, 218.057 91).

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A Model for the Cyanide Form of Oxidized Cytochrome Oxidase: An Iron(III)/Copper(II) Porphyrin Complex Displaying Ferromagnetic Coupling

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Abstract: The preparation and properties of the cyanide bridged Fe^{III}-Cu^{II} heterobinuclear complex of the ligand $\alpha,\alpha,\alpha,\alpha$-tetrakis(*o*-nicotinamidophenyl)porphyrin $[Fe(P)CNCu(N_4)](ClO_4)_2 \cdot 3H_2O$ are described. Bulk magnetic susceptibility, ESR, and Mössbauer data are interpreted in terms of weak ferromagnetic coupling between low-spin Fe(III) and Cu(II) ions, leading to an $S' = 1$ ground state with the $S' = 0$ level close in energy. A good description of the susceptibility and ESR line positions has been obtained by using the Hamiltonian $\mathcal{H} = -JS_1S_2 + J_D^{\alpha\beta}/[2\{S_1^{\alpha}S_2^{\beta} + S_1^{\beta}S_2^{\alpha}\}] + d(S_1xS_2) + [\mu_1\mu_2/r^3] - [3(\mu_1r)(\mu_2r)/r^5] + g_1\beta HS_1 + g_2\beta HS_2$ which incorporates isotropic, anisotropic, and asymmetric exchange, dipole-dipole, and Zeeman terms. The best-fit parameters are r(Fe-Cu distance) = 5 Å, d = 0.01 cm^{-1}, J = +0.25 cm^{-1}, J^{zz} = 0.006 cm^{-1}, K = 0.003 cm^{-1}, g_{Fe} = 3.6, 2.06, 1.19, and g_{Cu} = 2.15, 2.05, 2.05. A comparison is made of the properties of this complex and those of the a_3 sites of the cyanide-treated oxidized forms of bovine and bacterial cytochrome oxidases. While MCD and Mössbauer evidence for the natural oxidases have also indicated an $S' = 1$ ground state, their ESR silence compared to the present model system is explained in terms of the magnitudes of the zero-field splitting terms. The solvent-dependent properties of this complex are described. Solutions in 10% MeOH-$CHCl_3$, with and without 1 mol of 1-methylimidazole, show properties similar to the solid state. In CH_3CN and Me_2SO, little or no exchange coupling is evident, while in DMF an ESR silent species is formed. Possible structures consistent with these observations are presented.

An unequivocal description of the active site of cytochrome *c* oxidase still remains elusive despite the persistent attentions of many research groups who have probed the enzyme with a wide variety of sophisticated and modern techniques.[2] Four redox-active centers, cytochrome *a*,cytochrome a_3, Cu_a, and Cu_{a3} accept four electrons in the terminal stages of the respiratory chain and reduce oxygen to water. From the vast amount of available evidence the following picture, which appears to have general agreement, has emerged. In the oxidized resting state of the enzyme cytochrome *a*, which is low-spin Fe(III), and one of the Cu(II) ions Cu_a are both ESR detectable. The remaining high-spin cytochrome a_3 and Cu_{a3} are ESR silent, and on the basis of magnetic susceptibility[3,4] and MCD[4,5] results, it is generally believed that these are antiferromagnetically coupled to yield an $S' = 2$ spin state ($J > -200$ cm^{-1}). Reduction of oxygen is thought to occur at this center, as other external ligands such as CO, N_3^-, CN^-, NO, and S^{2-} are known to bind only to heme a_3 (and perhaps to Cu_{a3}). Indeed, the CN^--treated oxidized form of the enzyme has been well studied; the iron of heme a_3 is now forced low spin, but both it and the Cu_{a3} remain ESR undetectable.

Bulk magnetic susceptibility measurements of this form have been interpreted in terms of an antiferromagnetically coupled $S' = 0$ ground state with coupling constant $2J \leq -40$ cm^{-1}.[4] However, more recent MCD measurements[6] over the temperature range 1.5-200 K are totally at variance with this model and are consistent with strong ferromagnetic coupling between heme a_3-CN and $-Cu_{a3}$, leading to an $S' = 1$ ground state. This is further split by zero-field splitting leaving an $M_S = \pm 1$ ground state separated by >10 cm^{-1} from the $M_s = 0$ level. The lack of ESR signals is accounted for by forbidden $\Delta M_s = 2$ transitions within the $M_s = \pm 1$ levels. These results have been supported by a Mössbauer study[7] of an ^{57}Fe-enriched bacterial cytochrome oxidase from *Thermus thermophilus* which has been shown to have similar ESR and optical properties to the previously studied bovine enzyme. Low-temperature measurements in applied magnetic fields of the CN^--oxidized form of this enzyme indicate a paramagnetic ground state, again suggesting ferromagnetic coupling resulting in an $S' = 1$ system.

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