Electrophilic Reactions of Carbenoids. Synthesis of Fused Heterocyclic Systems via Intramolecular Nucleophilic Substitution of Carbenoids

Marek Topolski

Dittmer Laboratories of Chemistry, The Florida State University, Tallahassee, Florida 32306-3006

Received March 21, 1995[⊗]

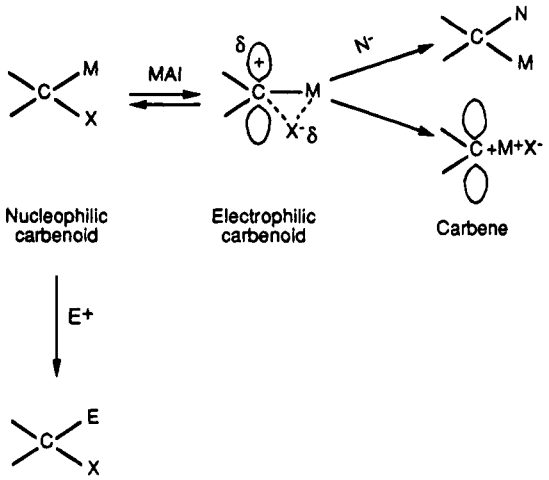
Intramolecular nucleophilic substitution of carbenoids with oxygen, nitrogen, and sulfur nucleophiles leading to the synthesis of fused heterocyclic compounds has been studied. For the purpose of this investigation styryl type gem-dihalides **4**, **8**, **18**, **20**, **28** containing a nucleophilic substituent in the ortho position of the aromatic ring have been synthesized. Carbenoids have been generated in those systems by the halogen–metal exchange reaction and shown to readily undergo intramolecular nucleophilic substitution by the properly located nucleophilic group (OH, SH, or NH_2). As a result a new synthetic route to benzofurans, thianaphthenes, and indoles has been established based on nucleophilic substitution of vinyl halides by an ortho substituent. The dramatic increase of reactivity of vinyl halides upon introduction of lithium has been explained as being due to metal-assisted ionization.

Introduction

Recently we have reported the results of our studies on the formation and reactions of chiral carbenoids in vinyl and cyclopropyl systems.[1] We were able to show that chiral carbenoids can be generated by either metalation (usually at ca. −70 °C) or halogen–metal exchange reactions (−100 °C) and that they can react with external nucleophiles yielding optically active products with overall inversion of configuration. In order to explain these findings we postulated a temperature profile for the behavior of carbenoids (Scheme 1). At very low temperatures (−100 °C and below) they behave as ordinary nucleophilic organolithiums and can react with a variety of electrophiles to give normal products expected for such reactions. At higher temperatures (ca. −80 °C) the process of metal-assisted ionization (MAI) takes place that leads to the weakening of carbon–halogen bond (assisted by lithium), and the nature of the carbenoid is changed from a nucleophilic organometallic reagent to an electrophilic species. During this process a positive charge is developed at the central carbon atom and a tight ion pair is produced with the leaving halide still blocking one enantioface of the substrate. We suggested that this very species can now undergo nucleophilic displacement reactions to form optically active products.

Our view of carbenoids, including the formation of the positive charge at the central carbon atom, finds support in ^{13}C NMR data of Seebach,[2] theoretical considerations by Schleyer,[3] and recent crystallographic analysis of a carbenoid published by Boche and co-workers.[4] Historically, the appellation "carbenoid" was suggested for the first time by Closs and Moss[5] who also indicated that it is this intermediate that is responsible for the observed electrophilic properties and not the carbene intermediate. The original definition of carbenoids as species bearing a metal atom and a halogen atom at the same carbon has recently been expanded to include α-oxygen substituted organolithium compounds.[6] Interestingly, α-metalated amines do not seem to follow the pattern.[7]

Scheme 1. Metal-Assisted Ionization



The chemistry of carbenoids has been thoroughly investigated and several excellent review articles have appeared.[8] Special emphasis has been laid on ambiphilic reactions of carbenoids,[9,10] especially reactions with

[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1995.

(1) (a) Topolski, M.; Walborsky, H. M. *J. Org. Chem.* **1994**, *59*, 5506. (b) Topolski, M.; Duraisamy, M.; Rachon, J.; Gawronski, J.; Gawronska, K.; Goedken, V.; Walborsky, H. M. *J. Org. Chem.* **1993**, *58*, 546. (c) Duraisamy, M.; Walborsky, H. M. *J. Am. Chem. Soc.* **1984**, *106*, 5035. (d) Walborsky, H. M.; Duraisamy, M. *Tetrahedron Lett.* **1985**, *26*, 2743. (e) Rachon, J.; Goedken, V.; Walborsky, H. M. *J. Am. Chem. Soc.* **1986**, *108*, 7435.

(2) (a) Seebach, D.; Siegel, H.; Mullen, K.; Hiltbrunner, K. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 784. (b) Seebach, D.; Gabriel, J.; Hassig, R. *Helv. Chim. Acta* **1980**, *63*, 2045. (c) Seebach, D.; Hassig, R.; Gabriel, J. *Helv. Chim. Acta* **1983**, *66*, 308.

(3) von Rague Schleyer, P.; Clark, T.; Kos, A. J.; Spitznagel, G. W.; Rohde, C.; Arad, D.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1984**, *106*, 6467.

(4) (a) Boche, G.; Marsch, M.; Muller, A.; Harms, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1032. (b) see also comments by Maercker, A. *Ibid.* **1993**, *32*, 1023.

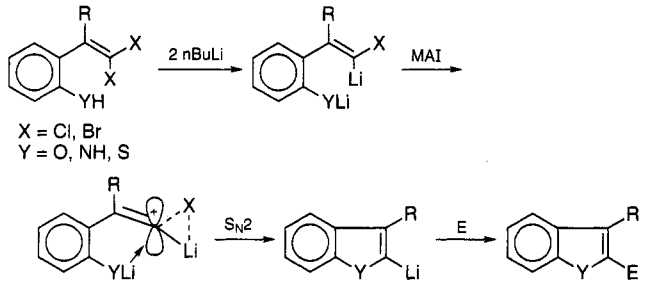
(5) (a) Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4042. (b) Moss, R. A.; Fan, H.; Gurumurthy, R.; Ho, G.-H. *J. Am. Chem. Soc.* **1991**, *113*, 1435.

(6) (a) Boche, G.; Opel, A.; Marsch, M.; Harms, K.; Haller, F.; Lohrenz, J. C. W.; Thummler, C.; Koch, W. *Chem. Ber.* **1992**, *125*, 1265. (b) Boche, G.; Bosold, F.; Lohrenz, J. C. W.; Opel, A.; Zulauf, P. *Chem. Ber.* **1993**, *126*, 1873. (c) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933.

(7) Boche, G.; Marsch, M.; Harbach, J.; Harms, K.; Ledig, B.; Schubert, F.; Lohrenz, J. C. W.; Ahlbrecht, H. *Chem. Ber.* **1993**, *126*, 1887.

0022-3263/95/1960-5588$09.00/0

Scheme 2. Synthesis of Heterocyclic Systems Using Carbenoids Chemistry

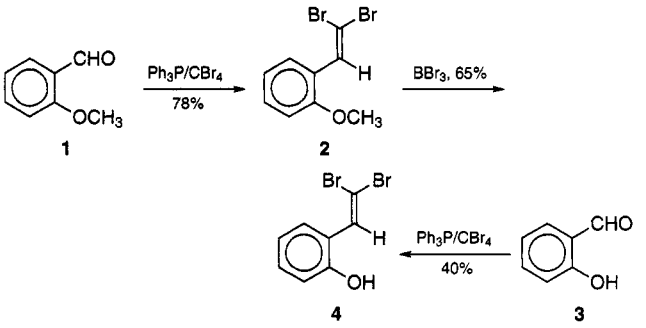


excess of organolithium reagent as an external nucleophile.[1,9a,10c,11]

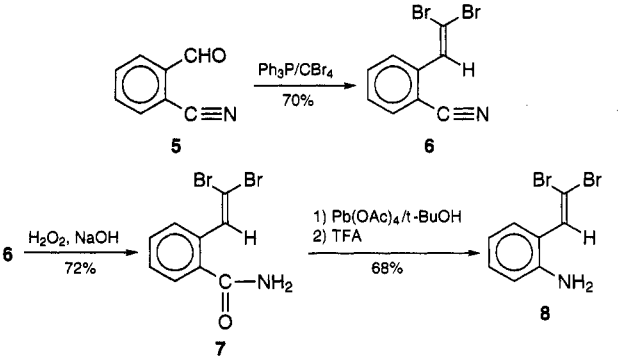
In continuation of our research on carbenoids and their electrophilic reactions we sought synthetically useful applications for our new concept of activating otherwise unreactive halides toward nucleophilic substitutions. Our attention has been focussed on the intramolecular version of these substitutions that should lead to new ring closure reactions. The systems we have designed bear a vinyl halide unit attached to an aromatic ring having an ortho substituent. Reactions of oxygen (OH), sulfur (SH), and nitrogen (NH_2) nucleophiles with vinyl carbenoids would be realized in this way and new synthetic routes to fused heterocycles should result (Scheme 2). Since the unsaturation is already introduced in the substrate no follow-up procedures (such as dehydrogenations or reductions, so common in heterocyclic synthesis) would be necessary to obtain the aromatic system. Moreover, lithiated heterocycles formed by the nucleophilic substitution of carbenoids should be trapped by electrophiles different than the proton, thus opening possibilities for further functionalizations. Dihalides were used rather than monohalides for two reasons: to avoid geometrical isomers in the starting materials and also to be able to use the lithium–halogen exchange reaction[12] for the generation of carbenoids instead of metalation.[13] The former method is usually considered preferable.

A plethora of methods exists for the preparation of benzofurans, thianaphthenes, and indoles.[14] It may seem difficult to even think about yet another approach. However, virtually none of those methods is based on nucleophilic substitution of a vinyl halide by an ortho substituent in an appropriate substrate. Most probably such approaches would have been considered ill-conceived

Scheme 3



Scheme 4



or at least not likely to give acceptable yields due to the well known resistance of vinyl halides toward nucleophilic substitution and solvolysis.[15] Metal-assisted ionization, which is known to dramatically increase the reactivity of vinyl halides, makes this approach feasible.

In this paper we wish to report the results of our studies on the synthesis of fused heterocyclic systems via intramolecular nucleophilic substitution of carbenoids.

Results and Discussion

At first we focused our attention on the synthesis of parent, unsubstituted heterocyclic systems. For this purpose compound **4** (oxygen nucleophile, precursor to benzofuran) and **8** (nitrogen nucleophile, precursor to indole) had to be synthesized. Synthesis of **4** was achieved by a two-step procedure in which *o*-methoxybenzaldehyde (**1**) was first converted to dibromoalkene **2** by the reaction with carbon tetrabromide and triphenylphosphine in methylene chloride at room temperature for 1 h[16] (78%) followed by deprotection with BBr_3 in methylene chloride (65%) (Scheme 3). Alternatively, direct preparation of **4** from salicylaldehyde (**3**) is also feasible, though the yield is only modest (40%).

Synthesis of the amine **8** (depicted in the Scheme 4 below) starts from *o*-cyanobenzaldehyde (**5**) which was converted with carbon tetrabromide–triphenylphosphine to dibromoalkene **6** in 70% yield. Transformation of **6** to **7** was achieved with sodium hydroxide and hydrogen peroxide in alcohol.[17] The amide **7** was obtained in 72% yield. The Hoffmann rearrangement of **7** was found to

(8) (a) Kirmse, W. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1. (b) Kobrich, G. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 473. (c) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383. (d) Taylor, K. G. *Tetrahedron* **1982**, *38*, 2751. (e) Siegel, H. *Topics Curr. Chem.* **1982**, *106*, 55. (f) Brinker, U. D. *Methoden der Organischen Chemie* (Houben Weyl); Georg Thieme Verlag: Stuttgart, New York, 1989; Vol. E19b.

(9) (a) Kobrich, G.; Fischer, R. H. *Chem. Ber.* **1968**, *101*, 3208. (b) Seebach, D. *Chem. Ber.* **1972**, *105*, 487. (c) Taylor, K. G.; Chaney, J. *J. Am. Chem. Soc.* **1976**, *98*, 4158. (d) Kitatani, K.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1975**, *97*, 949. (e) Smithers, R. H. *J. Org. Chem.* **1983**, *48*, 2095. (f) Tarhouni, R., Kirschleger, B.; Rambaud, M.; Villieras, J. *Tetrahedron Lett.* **1984**, 835.

(10) (a) Gunther, H.; Bothner-By, A. A. *Chem. Ber.* **1963**, *96*, 3112. (b) Duhamel, L.; Poirier, J. M. *J. Org. Chem.* **1979**, *44*, 3585. (c) Kitatani, K.; Yamamoto, H.; Hiyama, T.; Nozaki, H. *Bull.Chem. Soc. Jpn.* **1977**, *50*, 2158. (d) Charreau, P.; Julia, M.; Verpeaux, J. N. *Bull. Soc. Chim. Fr.* **1990**, *127*, 275.

(11) (a) Kobrich, G.; Ansari, F. *Chem. Ber.* **1967**, *100*, 2011. (b) Nelson, D. J. *J. Org. Chem.* **1984**, *49*, 2059.

(12) (a) Gilman, H.; Jacoby, L. *J. Org. Chem.* **1938**, *3*, 108. (b) Wittig, G.; Packels, U. *Chem. Ber.* **1938**, *71*, 1903.

(13) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: New York, 1974.

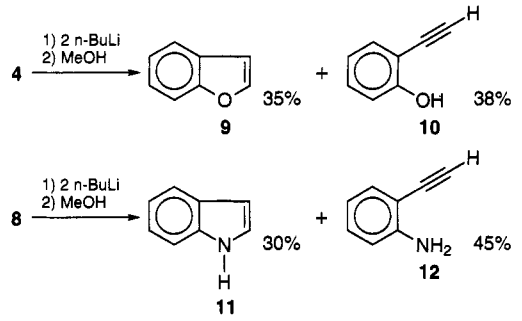
(14) *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R.; Rees, C., Ed.; Pergamon Press: Oxford, 1984; Vol. 4.

(15) (a) Roberts, J. D.; Chambers, V. C. *J. Am. Chem. Soc.* **1951**, *73*, 5034. (b) von Ragué Schleyer, P.; Sliwinski, W. F.; Van Dine, G. W.; Schollkopf, U.; Paust, J.; Fellenberger, K. *J. Am. Chem. Soc.* **1972**, *4*, 125.

(16) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

(17) (a) Noller, C. R. *Organic Syntheses*; Wiley: New York, 1943; Coll. Vol. 2, p 586. (b) MacIsaac, J. E., Jr.; Ball, R. E.; Behrman, E. J. *J. Org. Chem.* **1971**, *36*, 3048. (c) Wiberg, K. B. *J. Am. Chem. Soc.* **1953**, *75*, 3961.

Scheme 5



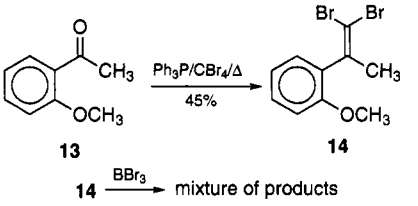
be somewhat difficult. Thus the classical hypobromite approach[18] led to a complicated mixture of products. Also hypervalent iodine reagents[19] would not produce the desired compound. Finally, lead tetraacetate proved to be the reagent of choice.[20] The conversion of **7** to **8** was accomplished in 68% yield by refluxing the substrate with equimolar amount of lead tetraacetate in *tert*-butyl alcohol for 1.5 h followed by cleavage of the intermediate carbamate with trifluoroacetic acid.

The hydroxy compound **4** and the amine **8** were now reacted with 2 equiv of *n*-butyllithium at −100 °C and allowed to cyclize at −70 °C (Scheme 5). Two products were isolated in each case: the expected fused heterocycle (**9** or **11**, respectively) and ortho substituted phenylacetylene (**10** or **12**).

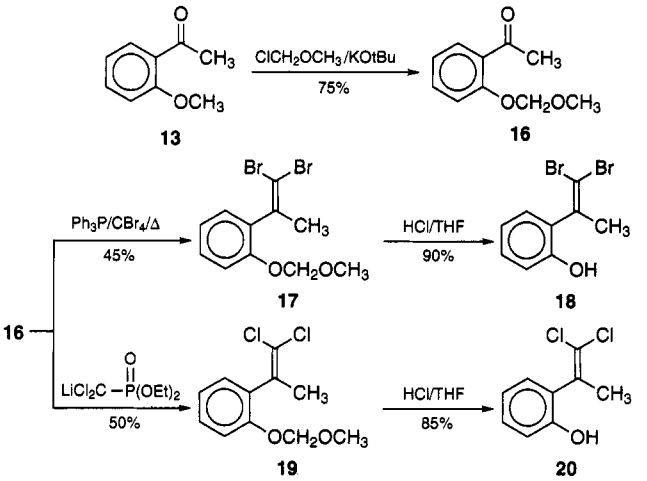
In both cases, after initial proton abstraction from the ortho substituent, the organolithium reagent can either replace bromine to give the desired carbenoid or attack β hydrogen which leads to the formation of the side product phenylacetylene derivative. The ratio of indole **11** to *o*-(aminophenyl)acetylene (**12**) (2:3) was found to be virtually the same with *n*-butyllithium and *tert*-butyllithium (2 h at −100 °C). The organolithium reagent is tentatively assumed to replace the more hindered bromine atom due to the chelating effect[21] of the deprotonated ortho substituent in the phenyl ring. In this way the stereochemistry of the carbenoid is that required for the nucleophilic substitution reaction to take place with inversion of configuration[1] (compare Scheme 2). The heterocyclic rings are formed as expected, but the yields are only modest, as a result of the competitive elimination reaction.

At this point we turned our attention to systems in which the hydrogen atom is replaced with another substituent, for instance methyl, and the elimination is impossible. In the oxygen series syntheses of both the dibromo compound **18** and the dichloro compound **20** were carried out in order to compare the behavior of the appropriate bromo and chlorocarbenoids in the cyclization reaction. *o*-Hydroxyacetophenone **15** was chosen as an easily available starting material. At first several unsuccessful attempts were made to convert this compound to either **18** or **20** directly, that is without protection of the phenolic oxygen. Also unsuccessful were approaches to use acetyl or *tert*-butyldimethylsilyl protective groups, in the latter case apparently due to a steric effect. When a small methyl group was used as a protection, the conversion to the dibromoolefin **13** was achieved in 45% yield. Quite unexpectedly, however (compare cleavage of **2** to **4**, Scheme 3) attempts to cleave the methyl ether were all in vain (Scheme 6).

Scheme 6



Scheme 7



Finally, the methoxymethyl group was selected as a suitable protection and employed in the synthesis of both **18** and **20** (Scheme 7).

o-Hydroxyacetophenone (**15**) was converted to the protected compound **16** by the action of potassium *tert*-butoxide and chloromethyl methyl ether in THF in 75% yield. The conversion of **16** to the dibromoolefin **17** was achieved in 41% yield by refluxing it overnight with carbon tetrabromide and triphenylphosphine in toluene.[22] Horner olefination with diethyl lithiodichloromethanephosphonate[23] gave rise to the formation of the dichloroolefin **19** (50% yield). Deprotection was easily achieved with hydrochloric acid in THF to give **18** and **20** in 90% and 85% yield, respectively.

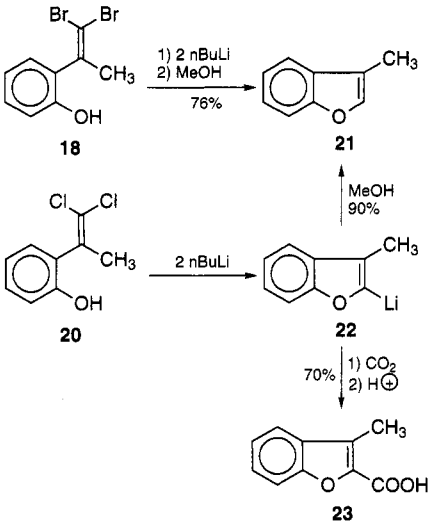
Cyclization of the dibromoolefin **18** proceeded smoothly with *n*-butyllithium in THF at −70 °C to give 3-methylbenzofuran **21** (76%) (Scheme 8).

Under the same conditions (*n*-butyllithium, 70 °C, 2 h), the dichloroolefin **20** reacted very slowly and only small amounts of the desired product could be isolated, along with the unreacted starting material. Fortunately, *tert*-butyllithium proved to be much more effective though 5 h at −100 °C were required to obtain an excellent yield of **21**. Alternatively, the intermediate 2-benzofuryllithium **22** was trapped with carbon dioxide to give 70% yield of the acid **23**.

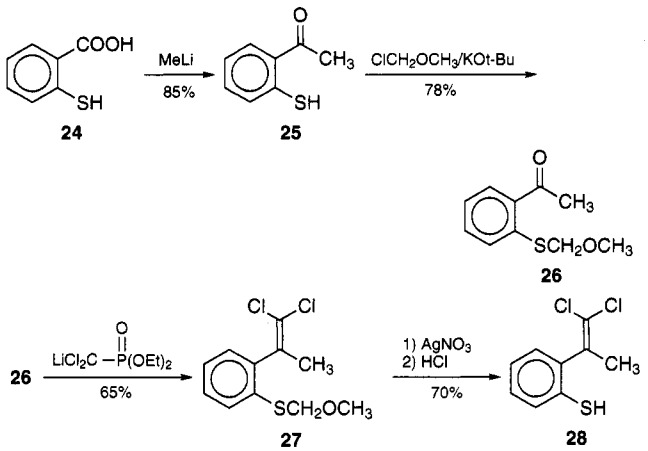
In order to further investigate the intramolecular nucleophilic substitution of carbenoids leading to het-

(18) Wallis, E. S.; Lane, J. F. *Org. React.* **1946**, *3*, 267.
(19) (a) Lazbin, M.; Koser, G. F. *J. Org. Chem.* **1986**, *51*, 2669. (b) Lazbin, M.; Koser, G. F. *Ibid* **1987**, *52*, 476. (c) Radhakrishna, A. S.; Rao, C. G.; Varna, R. K.; Singh, B. B.; Bhatnagan, S. P. *Synthesis* **1983**, 538. (d) Loudon, G. M.; Radhakrishna, A. S.; Almond, M. R.; Blodgett, J. K.; Boutin, R. H. *J. Org. Chem.* **1984**, *49*, 4272. (e) Boutin, R. H.; Loudon, G. M. *Ibid* **1984**, *49*, 4277. (f) Wasielewski, C.; Topolski, M.; Dembkowski, L. *J. Prakt. Chem.* **1989**, *331*, 507.
(20) Baumgarten, H. E.; Smith, H. L.; Staklis, A. *J. Org. Chem.* **1975**, *40*, 3554.
(21) Mahler, H.; Braun, M. *Tetrahedron Lett.* **1987**, *28*, 5145. (b) Harada, T.; Katsuhira, T.; Oku, A. *J. Org. Chem.* **1992**, *57*, 5805.
(22) Posner, G. H.; Loomis, G. L.; Sawaya, H. S. *Tetrahedron Lett.* **1975**, 1373.
(23) Seyferth, D.; Marmor, R. S. *J. Organomet. Chem.* **1973**, *59*, 237.

Scheme 8



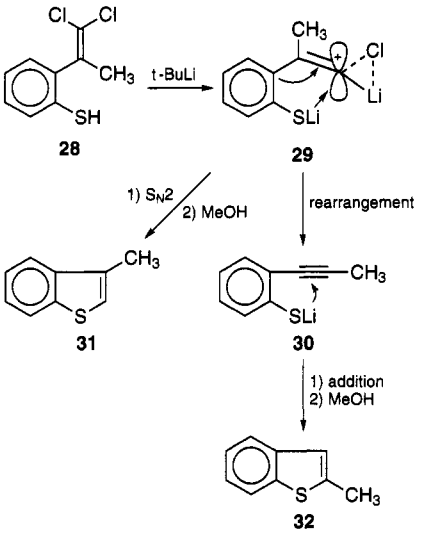
Scheme 9



erocyclic compounds, a system containing a sulfur nucleophile (compound **28**) was designed and synthesized. The synthesis of **28** is depicted in the Scheme 9.

The preparation starts with thiosalicylic acid **24** which was reacted with large excess of methyllithium to afford *o*-mercaptoacetophenone (**25**) in 85% yield. Since this compound could not be converted to either dichloroolefin **28** or dibromo derivative directly, a suitable protection was sought. Again, the methoxymethyl group was found to be the best choice, though some unexpected problems (described below) were encountered. The protected ketone **26** was obtain from **25** in 78% yield by S-alkylation with chloromethyl methyl ether/potassium *tert*-butoxide in THF. Several fruitless attempts were made to convert **26** to an appropriate dibromo compound. On the other hand Horner olefination of **26** with lithiodichloromethanephosphonate afforded the dichloro derivative **27** in 65%. At this point, with a bundle of literature procedures available, the deprotection of **27** was approached. Concentrated HCl in THF, HBr in AcOH,[24] BF_3 etherate in AcOH,[25] and trifluoroacetic acid were tested and one by one they failed to produce **28**[26] though some kind of a cleavage reaction was always observed. Finally, silver nitrate[27] (which attacks sulfur rather than oxygen) in ethanol followed by the decomposition of the intermediate silver derivative with hydrochloric acid, smoothly removed the protective group to give the desired product **28** in 70% yield.

Scheme 10



The cyclization reaction of **28** with *tert*-butyllithium is depicted in the Scheme 10. *n*-Butyllithium was tried as well but it did not give satisfactory results.

The reaction in this case produced a mixture of two isomeric products: 3-methylthianaphthene (**31**) and 2-methylthianaphthene (**32**) (ratio **31** to **32**, 3:2). Possibly, competition exists between nucleophilic substitution leading to the anticipated 3-methylthianaphthene (**31**) and Fritsch–Buttenburg–Wiechell rearrangement[28] of the carbenoid **29**. The latter reaction, which also requires a trans relationship between the migrating group and the leaving group[29] would conceivably be greatly accelerated by the negatively charged sulfur. The resulting ortho-substituted phenylpropyne **30** would then undergo cyclization to give **32**.

Summary

In order to gain further insight into nucleophilic substitutions on carbenoid species and find useful synthetic applications for those reactions, vinyl dihalides **4**, **8**, **18**, **20**, **28** have been synthesized. Carbenoids have been generated from those vinyl halides and have been shown to undergo intramolecular substitution reaction with oxygen, nitrogen, and sulfur nucleophiles present as ortho substituents in aromatic rings. The cyclization reactions give rise to the formation of the corresponding heterocyclic systems: benzofurans, thianaphthenes, and indoles. Not only are the parent heterocyclic compounds formed by this entirely new approach but it is possible to further functionalize the initially formed lithiated heterocycles as well (formation of the acid **23**). Some limitations to this new approach have been found,

(24) Brownlee, P. J. E.; Cox, M. E.; Handford, B. O.; Marsden, J. C.; Young, G. T. *J. Chem. Soc.* **1964**, 3832.
(25) Hiskey, R. G.; Sparrow, J. T. *J. Org. Chem.* **1970**, *35*, 215.
(26) In the author's opinion these results are not very surprising after all. In all those cases the initial attack of the acidic reagent occurs at oxygen leaving behind SCH_2^+ species that can undergo a variety of reactions, with the formation of a free thiol being perhaps the least likely one, especially under anhydrous conditions. Clearly it is advisable to choose a reagent attacking sulfur (thiophilic reagent such as silver nitrate) rather than oxygen.
(27) Holland, G. F.; Cohen, L. A. *J. Am. Chem. Soc.* **1958**, *80*, 3765.
(28) (a) Kobrich, G.; Trapp, H.; Hornke, I. *Tetrahedron Lett.* **1964**, 1131. (b) Kobrich, G.; Trapp, H.; Hornke, I. *Chem. Ber.* **1967**, *100*, 961. (c) Kobrich, G.; Ansari, F. *Ibid.* **1967**, *100*, 2011.
(29) (a) Bothner-By, A. A. *J. Am. Chem. Soc.* **1955**, *77*, 3293. (b) Curtin, D. Y.; Flynn, E. W.; Nystrom, R. F. *J. Am. Chem. Soc.* **1958**, *80*, 4599. (c) Kobrich, G.; Trapp, H. *Chem. Ber.* **1966**, *99*, 680.

too: elimination of acetylenes in compounds **4** and **8** and isomers formation in the case of the sulfur compound **28**, which is presumbly due to the competitive Fritsch–Buttenburg–Wiechell rearrangement.

Experimental Section

All reagents were purchased from Aldrich. Bulk solvents were distilled before use. All melting points and boiling points are uncorrected. All the reactions were carried out under dry argon atmosphere. ^{1}H NMR spectra were recorded at 300 MHz using $CDCl_3$ as solvent unless noted otherwise, with Me_4-Si and $CHCl_3$ (7.27 ppm) as internal standards. ^{13}C NMR spectra were recorded at 75 MHz. Column chromatography was carried out by using silica gel (70–230 mesh) (Merck). Radial chromatography separations were performed with Merck silica gel 60 PF_{254}. Microanalysis were performed by Beller Laboratories, Gottingen, Germany.

1,1-Dibromo-2-(*o*-methoxyphenyl)ethene (2). *o*-Methoxybenzaldehyde (**1**) (1.36 g, 10 mmol) was added dropwise with stirring and external cooling to a previously prepared solution of triphenylphosphine (10.48 g, 40 mmol) and carbon tetrabromide (6.62 g, 20 mmol) in methylene chloride (100 mL). The reaction mixture was subsequently stirred at room temperature for 1 h and quenched with ice. The organic layer was then separated and dried, and the solvent was removed under reduced pressure. The remaining solid product was extracted three times with boiling ether (100 mL), and the combined ethereal extracts were evaporated to dryness. Pure 1,1-dibromo-2-(*o*-methoxyphenyl)ethene (**2**) was obtained as an oil by using column chromatography (pentane–ether 4:1). Yield 2.28 g, 78%. ^{1}H NMR δ 3.83 (s, 3H), 6.87 (d, J = 8.4 Hz, 1H), 6.96 (dd, J = 7.8, Hz, J = 7.8 Hz, 1H), 7.32 (m, 1H), 7.60 (s, 1H), 7.68 (d, J = 6.6 Hz). ^{13}C NMR δ 55.42, 89.70, 110.70, 120.34, 124.63, 129.32, 130.11, 133.13, 156.88. MS (PCI) 291 (M + 1, 100%), 293 (M + 3, 89%). Anal. Calcd for $C_9H_8Br_2O$: C, 37.02; H, 2.77. Found: C, 37.15; H, 2.78.

1,1-Dibromo-2-(*o*-hydroxyphenyl)ethene (4). Cleavage of Methyl Ether of 2. To the solution of 1,1-dibromo-2-(*o*-methoxyphenyl)ethene (**2**) (1.11 g, 3.8 mmol) was added BBr_3 (4 mL of 1 M solution in CH_2Cl_2) at 0 °C. The cooling bath was then removed, and the reaction mixture was stirred for 3 h at room temperature and quenched with water. The organic phase was then separated and dried, and the solvent was removed under reduced pressure. Pure 1,1-dibromo-2-(*o*-hydroxyphenyl)ethene (**4**) was obtained by using column chromatography with pentane–ether 4:1 as an eluent. Yield 682 mg, 65%. MP 54–57 °C. IR 3273 cm^{-1}. ^{1}H NMR δ 6.82 (d, J = 8.1 Hz; 1H), 6.95 (dd, J = 8.4 Hz, J = 8.4 Hz; 1H), 7.24 (m, 1H), 7.52 (m, 1H), 7.56 (s, 1H). ^{13}C NMR 92.08, 115.89, 120.82, 123.05, 129.37, 130.22, 132.57, 152.74. MS (PCI) 277 (M + 1, 58%) 279 (M + 3, 100%). Anal. Calcd for $C_8H_6Br_2O$: C, 34.57; H, 2.18. Found: C, 34.63; H, 2.26.

1,1-Dibromo-2-(*o*-hydroxyphenyl)ethane (4). Direct Preparation from Salicylaldehyde (3). To the solution of triphenylphosphine (5.24 g, 20 mmol) and CBr_4 (3.31 g, 10 mmol) in CH_2Cl_2 was added salicylaldehyde **3** (0.61 g, 5 mmol) as a solution in CH_2Cl_2 (5 mL). Temperature was maintained at around 0 °C (ice bath) during the addition. When the addition was completed, the cooling bath was removed and the reaction mixture was additionally stirred for 1 h at room temperature. It was then quenched with water and worked-up as described in the preparation of **2**. Purification by column chromatography afforded pure 1,1-dibromo-2-(*o*-hydroxyphenyl)ethene (**4**). Yield 555 mg, 40%. Mp 54–57 °C.

1,1-Dibromo-2-(*o*-cyanophenyl)ethene (6). The procedure, previously described for the preparation of **2** and **4** in the oxygen series was followed exactly starting from *o*-cyanobenzaldehyde (**5**) (2.62 g, 20 mmol). The crude product was purified by column chromatography (eluent: pentane–ether 9:1). Yield 4.02 g, 70%. Mp 83–84 °C. IR 2222 cm^{-1}. ^{1}H NMR δ 7.46 (m, 1H), 7.64 (m, 1H), 7.71 (d, J = 8.7 Hz; 1H), 7.72 (s, 1H), 7.86 (m, 1H). ^{13}C NMR 95.46, 112.23, 128.73, 128.88, 129.17, 132.77, 133.19, 133.39, 139.08. MS (PCI) 286 (M + 1, 53%), 288 (M + 3, 100%). Anal. Calcd for $C_9H_5Br_2N$: C, 37.67; H, 1.76. Found: C, 37.96; H, 1.93.

1,1-Dibromo-2-(*o*-carboxamidophenyl)ethene (7). Sodium hydroxide (1 mL of 6 N solution) was added to the solution of 1,1-dibromo-2-(*o*-cyanophenyl)ethene (**6**) (574 mg, 2 mmol) in a mixture of ethanol (15 mL) and hydrogen peroxide (10 mL of 30% solution), and the reaction mixture was stirred at room temperature for 4 h. It was then quenched by adding 5% HCl to pH = 3. Ether (50 mL) was then added, and the reaction mixture was washed with brine. The organic layer was then separated, and the water phase was extracted with ether (50 mL). The combined organic layer was dried, and the solvents were removed under reduced pressure. The solid residue was purified by using column chromatography ($CHCl_3$–ethanol 5:1). Yield 2.04 g, 72%. Mp 102–103 °C. IR 3336, 3189, 1655 cm^{-1}. ^{1}H NMR δ 5.85 (s, broad, 2H), 7.42 (dd, J = 7.5 Hz, J = 7.5 Hz; 1H), 7.50 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 1.5 Hz; 1H), 7.63 (m, 2H), 7.84 (s, 1H). ^{13}C NMR 91.99, 127.95, 128.71, 129.99, 130.88, 134.02, 134.63, 136.36, 170.67. MS (PCI) 304 (M + 1, 53%), 306 (M + 3, 100%). Anal. Calcd for $C_9H_7Br_2NO$: C, 35.56; H, 2.33. Found: C, 35.79; H, 2.36.

1,1-Dibromo-2-(*o*-aminophenyl)ethene (8). To a solution of the amide **7** (3.05 g, 10 mmol) in *tert*-butyl alcohol (25 mL) was added lead tetraacetate (4.43 g, 10 mmol), and the reaction mixture was stirred and boiled under reflux for 1.5 h. It was then cooled to ambient temperature and filtered through a short pad of Celite. The solvent was removed under reduced pressure, and the residue was dissolved in trifluoroacetic acid (25 mL). The reaction mixture was kept at room temperature for 1 h and then evaporated to dryness. 2 N Sodium hydroxide (10 mL) was subsequently added, and the product was extracted with ether (3 × 50 mL). The combined organic layers were dried, and the solvent was removed under reduced pressure. The oily residue was chromatographed on silica gel (eluent: pentane–AcOEt 9:1) to afford pure amine **8**. Yield 1.88 g, 68%. IR 3444, 3362, 1612 cm^{-1}. ^{1}H NMR δ 3.90 (s, broad, 2H), 6.75 (d, J = 8.4 Hz; 1 H), 6.82 (dd, J = 7.5 Hz, J = 7.5 Hz; 1H), 7.18 (m, 1H), 7.32 (d, J = 7.8 Hz; 1H), 7.37 (s, 1H). ^{13}C NMR 93.02, 116.23, 118.97, 122.32, 129.42, 129.89, 134.21, 143.26. MS (PCI) 276 (M + 1, 70%), 278 (M + 3, 100%). HRMS calcd for $C_8H_7N^{79}Br_2$ 274.8945, found 274.9002 (M, 51%); calcd for $C_8H_7N^{79}Br^{81}Br$ 276.8925, found 276.8994 (M + 2, 100%), calcd for $C_8H_7N^{81}Br_2$ 278.8905, found 278.8979 (M + 4, 49%).

Reaction 1,1-Dibromo-2-(o-hydroxyphenyl)ethene 4 with *n*-Butyllithium. Formation of Benzofuran 9. To the solution of 1,1-dibromo-2-(*o*-hydroxyphenyl)ethene (**4**) (590 mg, 2.12 mmol) in THF (15 mL) was added *n*-butyllithium (4.33 mL of 1.5 M solution, 6.5 mmol) at −100 °C. The reaction mixture was then stirred at −70 °C for 2 h and quenched with MeOH. Pentane (25 mL) was added next, and the solution was washed with water (20 mL). The two phases were then worked-up separately. The organic layer was dried, and the solvent was removed under reduced pressure. The residue was purified by using radial chromatography (elution with pentane) to afford pure benzofuran **9**. Yield 85 mg, 35%. IR identical with that of an authentic sample (commercial). ^{1}H NMR δ 6.78 (d, J = 1.5 Hz; 1H), 7.27 (m, 2H), 7.52 (d, J = 8.1 Hz, 1H), 7.61 (d, J = 10.5 Hz; 1H), 7.62 (s, 1H). ^{13}C NMR 106.61, 111.48, 121.30, 122.84, 124.35, 127.57, 145.08, 155.24. MS (PCI) 119 (M + 1). The aqueous phase was acidified with 5% HCl to pH = 1 and extracted with ether (3 × 25 mL). The ethereal layer was then separated, dried, and evaporated to dryness. The residue was purified by using radial chromatography (pentane–ether 9:1) to give pure (*o*-hydroxyphenyl)-acetylene (**10**).[30] Yield 95 mg, 38%. IR 3484, 3279, 2100 cm^{-1}. ^{1}H NMR δ 3.46 (s, 1H), 5.77 (s, 1H), 6.92 (m, 2H), 7.28 (m, 1H), 7.38 (m, 1H). ^{13}C NMR 78.33, 84.24, 108.44, 114.99, 120.48, 131.12, 132.24, 157.75.

Reaction of 1,1-Dibromo-2-(o-aminophenyl)ethene (8) with *n*-Butyllithium. Formation of Indole 11. Compound **8** (200 mg, 0.72 mmol) was reacted with *n*-butyllithium (1.5 mmol, 1 mL of 1.5 M solution in hexanes) under the same conditions as described above for its oxygen analogue **4**. The crude product was separated by using radial chromatography. Elution with 3% NEt_3 in hexane gave two major products:

(30) Prey, V.; Berbalk, H. *Monatsh. Chem.* **1951**, *82*, 990.

Indole **11** (identical with an authentic sample, commercial). Yield 25 mg, 30%. Mp 51–53 °C. ^{1}H NMR δ 6.58 (m, 1H), 7.15 (dd, J = 9 Hz, J = 7.5 Hz; 1H), 7.23 (m, 2H), 7.42 (d, J = 8.4 Hz; 1H), 7.67 (d, J = 7.8 Hz; 1H), 8.18 (s, broad, 1H). ^{13}C NMR 102.69, 111.11, 119.95, 120.87, 122.13, 124.26, 128.04, 136.00. MS (PCI) 118 (M + 1).

(*o*-Aminophenyl)acetylene **12**.[31] Yield 38 mg, 45%. IR 3457, 3365, 3266, 2092 cm^{-1}. ^{1}H NMR δ 3.38 (s, 1H), 4.22 (s, broad, 2H), 6.68 (m, 2H), 7.14 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 1.5 Hz; 1H), 7.32 (dd, J = 7.5 Hz, J = 1.5 Hz; 1H). ^{13}C NMR 80.65, 82.34, 106.76, 114.43, 117.91, 130.28, 132.80, 148.79. MS (PCI) 118 (M + 1).

Compound **8** was also reacted with *tert*-butyllithium (3 equiv) at −100 °C for 2 h. The same two major products were found in virtually the same ratio.

1,1-Dibromo-2-(*o*-methoxyphenyl)propene (14). *o*-Methoxyacetophenone (**13**) (1.5 g, 10 mmol) was added to the solution of triphenylphosphine (10.48 g, 40 mmol) and CBr_4 (6.62 g, 20 mmol) in toluene (100 mL), and the reaction mixture was refluxed overnight with vigorous stirring. Most of the solvent was then distilled under reduced pressure. The residual solid material was subsequently extracted with boiling hexane (3 × 100 mL), and the combined hexane extracts were evaporated under reduced pressure. The crude product was purified by column chromatography (pentane–ether 4:1). Yield 1.38 g, 45%. ^{1}H NMR δ 2.12 (s, 3H), 3.83 (s, 3H), 6.93 (ddd, J = 15.6 Hz, J = 7.8 Hz, J = 1.2 Hz; 2H), 7.09 (dd, J = 7.8 Hz, J = 1.9 Hz; 1H), 7.30 (m, 1H). ^{13}C NMR 24.42, 55.52, 88.18, 111.41, 120.73, 129.33, 129.41, 131.26, 141.38, 155.88. MS (PCI) 305 (M + 1, 58%) 307 (M + 3, 100%). Anal. Calcd for $C_{10}H_{10}Br_2O$: C, 39.25; H, 3.30. Found: C, 39.43; H, 3.33.

Attempts to Cleave the Methyl Ether of 1,1-Dibromo-2-(*o*-methylphenyl)propene (14) with BBr_3. Several attempts were made to react 1,1-dibromo-2-(*o*-methoxyphenyl)-propene (**14**) with a 1 M solution of BBr_3 in CH_2Cl_2. At −70 °C no reaction was observed, whereas at room temperature a complicated mixture of products was obtained with the desired phenol **18** being only a minor component. Attempts to isolate **18** in a pure form by column chromatography failed.

***o*-(Methoxymethoxy)acetophenone (16).** To the suspension of potassium *tert*-butoxide (6.16 g, 55 mmol) in THF (100 mL) was added *o*-hydroxyacetophenone (**15**) (7.1 g, 52 mmol) and the reaction mixture was stirred for 15 min. Subsequently chloromethyl methyl ether (4.53 mL, 60 mmol) was added dropwise with stirring, and the reaction mixture was additionally stirred for 2 h. Water (50 mL) was then added and the product was extracted with pentane (3 × 50 mL). The combined organic layers were then washed with 10% NaOH (50 mL) and brine (50 mL). Upon removal of solvent a liquid product was obtained which was purified by using Kugelrohr distillation. Yield 7.02 g, 75%. Bp 145–150 °C/0.2 mmHg. IR 1667 cm^{-1}. ^{1}H NMR δ 2.64 (s, 3H), 3.52 (s, 3H) 5.28 (s, 2H), 7.05 (dd, J = 7.5 Hz, J = 7.5 Hz; 1H), 7.18 (d, J = 9 Hz; 1H), 7.44 (m, 1H), 7.71 (dd, J = 7.5 Hz, J = 1.8 Hz; 1H). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.64; H, 6.73. Found: C, 66.90; H, 6.88.

1,1-Dibromo-2-[*o*-(methoxymethoxy)phenyl]propene (17). This product was prepared from *o*-(methoxymethoxy)-acetophenone (**16**) (3.6 g, 20 mmol), triphenylphosphine (20.96 g, 80 mmol), and CBr_4 (13.24 g, 40 mmol) according to the procedure previously described for 1,1-dibromo-2-(*o*-methoxyphenyl)propene (**14**) (see above). Column chromatography (pentane–ether 4:1) afforded pure compound **17**. Yield 2.75 g, 41%. Mp 46–48 °C. ^{1}H NMR δ 2.14 (s, 3H), 3.49 (s, 3H), 5.19 (s, 2H), 7.01 (dd, J = 7.5 Hz, J = 7.5 Hz; 1H), 7.08 (m, 2H), 7.27 (m, 1H). ^{13}C NMR 24.58, 56.04, 88.24, 94.66, 115.15, 122.02, 129.28, 129.40, 132.16, 141.34, 153.41. MS (PCI) 334 (M, 7%), 336 (M + 2, 9%), 303 (56%). 305 (100%). Anal. Calcd for $C_{11}H_{12}Br_2O_2$: C, 39.31; H, 3.61. Found: C, 39.30; H, 3.72.

1,1-Dibromo-2-(*o*-hydroxyphenyl)propene 18. 1,1-Dibromo-2-(O-methoxymethyl-o-hydroxy)phenyl propene **17** (2.69 g, 8 mmol) was dissolved in THF (75 mL), and concentrated HCl (25 mL) was added with external cooling (ice). The reaction mixture was stirred for 3 h at room temperature (TLC control). It was then diluted with pentane (100 mL) and washed with brine (50 mL). The organic layer was dried and evaporated to dryness. The remaining solid material was purified by using column chromatography (eluent pentane–ether 4:1). Yield 2.10 g, 90%. Mp 86–88 °C. IR 3365 cm^{-1}. ^{1}H NMR δ 2.17 (s, 3H), 5.80 (s, broad, 1H), 6.93 (m, 2H), 7.05 (dd, J = 7.5 Hz, J = 1.8 Hz; 1H), 7.23 (m, 1H). ^{13}C NMR 24.90, 90.07, 116.39, 121.20, 128.53, 128.97, 129.79, 139.96, 151.28. MS (PCI) 291 (M + 1, 56%), 293 (M + 3, 100%). Anal. Calcd for $C_9H_8Br_2O$: C, 37.02; H, 2.77. Found: C, 37.19; H, 2.86.

1,1-Dichloro-2-[*o*-(methoxymethoxy)phenyl]propene (19). To the solution of diethyl trichloromethanephosphonate[32] (2.8 g, 11 mmol) in THF (25 mL) was added *n*-butyllithium (11 mmol, 7.33 mL of 1.5 M solution in hexanes), and the reaction mixture was stirred for 15 min at −90 °C. *o*-(Methoxymethoxy)acetophenone (**16**) (1.8 g, 10 mmol) was then added at the same temperature. After the addition had been completed, the cooling bath was removed and the reaction mixture was stirred overnight at room temperature. It was then diluted with pentane (50 mL) and washed with brine (20 mL). The organic phase was dried, and the solvent was removed under reduced pressure. The oily residue was then purified by using column chromatography (eluent: pentane–ether 9:1). Yield 1.23 g, 50%. ^{1}H NMR δ 2.14 (s, 3H), 3.48 (s, 3H), 5.19 (s, 2H), 7.01 (m, 1H), 7.13 (m, 2H), 7.27 (m, 1H). ^{13}C NMR 21.75, 55.99, 94.63, 115.07, 117.53, 121.99, 129.43, 129.55, 130.24, 133.89, 153.81. MS (PCI) 246 (M, 9%) 215 (100%). Anal. Calcd for $C_{11}H_{12}Cl_2O_2$: C, 53.46; H, 4.90. Found: C, 53.89; H, 4.99.

1,1-Dichloro-2-(*o*-hydroxyphenyl)propene (20). 1,1-Dichloro-2-[*o*-(methoxymethoxy)phenyl]propene (**19**) was hydrolyzed with HCl in THF following the procedure previously described for its dibromo analogue **17**. Purification by column chromatography (pentane–ether 9:1) afforded pure product **20**. Yield 85%. Mp 55–57 °C. IR 3319 cm^{-1}. ^{1}H NMR δ 2.17 (s, 3H), 4.80 (s, broad, 1H), 6.93 (m, 2H), 7.07 (dd, J = 7.5 Hz, J = 1.8 Hz; 1H), 7.23 (m, 1H). ^{13}C NMR 21.99, 116.27, 119.17, 121.13, 126.89, 128.91, 129.79, 132.39, 151.72. MS 203 (M + 1, 100%). Anal. Calcd for $C_9H_8Cl_2O$: C, 53.23; H, 3.98. Found: C, 53.52; H, 6.28.

3-Methylbenzofuran (21). Preparation from 1,1-Dibromo-2-(*o*-hydroxyphenyl)propene (18). To the solution of 1,1-dibromo-2-(*o*-hydroxyphenyl)propene (**18**) (0.58 g, 2 mmol) in THF (15 mL) was added *n*-butyllithium (4.1 mmol, 2.73 mL of 1.5 M solution in hexanes) at −100 °C. The reaction mixture was stirred for 30 min at that temperature and then for 2 h at −70 °C. It was then quenched with MeOH, diluted with pentane (50 mL), and washed with brine (20 mL). The organic phase was dried and the solvent was removed under reduced pressure. Purification by radial chromatography (elution with pentane) gave pure 3-methylbenzofuran (**21**).[33] Yield 200 mg, 76%. ^{1}H NMR δ 2.25 (d, J = 0.9 Hz; 3H), 7.27 (m, 2H), 7.44 (m, 2H), 7.53 (m, 2H). ^{13}C NMR 7.57, 111.42, 115.74, 119.52, 122.34, 124.21, 129.22, 141.57, 155.58. MS (PCI) 133 (M + 1, 100%). The NMR spectra reported here are identical with those found in literature.[33b,c]

3-Methylbenzofuran (21). Preparation from 1,1-Dichloro-2-(*o*-hydroxyphenyl)propene (20). To the solution of 1,1-dichloro-2-(*o*-hydroxyphenyl)propene (**20**) (404 mg, 2 mmol) in THF (15 mL) was added *tert*-butyllithium (6 mmol, 4.8 mL of 1.25 M solution in pentane) at −100 °C. The reaction mixture was stirred for 5 h at the same temperature and quenched with MeOH. The reaction mixture was diluted with pentane (50 mL) and washed with water (20 mL). The organic phase was then dried, and the solvent was removed under reduced pressure. The residue was purified by using radical chromatography (eluent: pentane) to give 238 mg, 90% yield of 3-methylbenzofuran (**21**).

(31) Schofield, K.; Swain, T. *J. Chem. Soc.* **1949**, 2393.

(32) Kosolapoff, G. M. *J. Am. Chem. Soc.* **1947**, *69*, 1002.

(33) (a) Fleming, I.; Woolias, M. *J. Chem. Perkin Trans. 1* **1979**, 829. (b) Okuyama, T.; Fueno, T. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1263. (c) Platzer, N.; Basselier, J.-J.; Demerseman, P. *Bull. Soc. Chim. Fr.* **1974**, 905.

3-Methylbenzofuran-2-carboxylic Acid (23). 1,1-Dichloro-2-(*o*-hydroxyphenyl)propene (**20**) was reacted with *tert*-butyllithium under the same conditions as described above for the preparation of 3-methylbenzofuran (**21**). Instead of quenching with MeOH, however, the reaction mixture was allowed to reach −70 °C (after 5 h at −100 °C), and a stream of dry CO_2 was passed through for 1 h. The reaction mixture was then allowed to reach room temperature, and it was quenched with water. The water phase was separated, additionally extracted with ether (20 mL), and acidified with 5% HCl (pH = 1). The product was extracted with ether (3 × 25 mL), the organic extracts were dried and evaporated to dryness. The oily residue was kept overnight in vacuum (0.2 mmHg) to remove most of the byproduct 2,2-dimethylpropanoic acid. It was then triturated with pentane, and the solid product was purified by using radial chromatography (chloroform−ethanol 4:1). Yield 245 mg, 70%. Mp 187−189 °C; lit. 188.5−189.5 °C.[34] IR 3377, 1675 cm^{-1}. ^1H NMR δ 2.64 (s, 3H), 7.34 (dd, J = 12 Hz, J = 12 Hz; 1H), 7.53 (m, 2H), 7.65 (d, J = 12 Hz; 1H). MS (PCI) 177 (M + 1, 100%).

***o*-Mercaptoacetophenone (25).** To the solution of thiosalicylic acid (**24**) (6.16 g, 40 mmol) in THF (200 mL) was added methyllithium (160 mmol, 107 mL of 1.5 M solution in ether) at 0 °C (caution!). The reaction mixture was stirred overnight at room temperature and it was quenched with water (caution, remains of methyllithium may react violently!) and then saturated NH_4Cl solution. The organic phase was separated and subsequently washed with 5% $NaHCO_3$ and brine. It was then dried and the solvent was evaporated. The oil residue was distilled under reduced pressure (Kugelrohr) to give *o*-mercaptoacetophenone (**25**).[35] Yield 5.2 g, 85%. IR 2531, 1569 cm^{-1}. ^1H NMR δ 2.63 (s, 3H), 4.47 (s, 1H), 7.25 (m, 3H), 7.90 (d, J = 9 Hz; 1H).

***o*-(Methoxymethylthio)acetophenone (26).** The procedure previously described for O-alkylation of *o*-hydroxyacetophenone with chloromethyl methyl ether (see preparation of **16**) was extracted followed starting from *o*-mercaptoacetophenone (**25**) (3.5 g, 23 mmol). The crude product was purified by using Kugelrohr distillation. Yield 3.52 g, 78%. bp 170−175 °C. This product crytallized on standing and was purified by recrystallization (ether−pentane). Mp 39−41 °C. IR 1665 cm^{-1}. ^1H NMR δ 2.62 (s, 3H), 3.45 (s, 3H), 4.97 (s, 2H), 7.25 (m, 1H), 7.45 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 1.8 Hz; 1H) 7.77 (m, 2H). ^{13}C NMR 28.50, 56.09, 76.09, 125.11, 128.45, 130.24, 132.37, 136.83, 139.42, 200.17. MS (PCI) 196 (M, 5%), 165 (100%). Anal. Calcd for $C_{10}H_{12}O_2S$: C, 61.19; H, 6.17. Found: C, 61.06; H, 6.28.

1,1-Dichloro-2-*o*-methoxymethylthio)phenyl]propene (27). This compound was prepared by employing the Horner type protocol used for the synthesis of the oxygen analogue **19** (see above). Starting from *o*-(methoxymethylthio)-acetophenone (**26**) (1.7 g, 8.7 mmol) and three times excess of both diethyl trichloromethanephosphonate and *n*-butyllithium, 65% yield of **27** was realized, after column chromatography (pentane−ether 9:1). ^1H NMR δ 2.15 (s, 3H), 3.43 (s, 3H), 4.97 (dd, J = 11.4 Hz, J = 6.6 Hz; 2H), 7.08 (dd, J = 7.5 Hz, J = 1.2 Hz; 1H), 7.27 (m, 2H), 7.62 (dd, J = 11.4 Hz, J = 1.5 Hz). ^{13}C NMR δ 21.98, 55.99, 77.17, 118.70, 127.06, 128.30, 128.78, 130.52, 134.33 135.68, 141.35. MS (PCI) 263 (M + 1, 17%), 231 (100%). Anal. Calcd for $C_{11}H_{12}Cl_2SO$: C, 50.20; H, 4.61. Found C, 50.33; H, 4.56.

1,1-Dichloro-2-(*o*-mercaptophenyl)propene (28). To the solution of silver nitrate (170 mg, 1 mmol) in EtOH (25 mL) was added 1,1-dichloro-2-[*o*-(methoxymethylthio)phenyl]-propene (**27**) (263 mg, 1 mmol), and the reaction mixture was kept in dark at room temperature overnight. White solid of a silver derivative precipitated during this time. The solid was filtered, washed with EtOH and ether, and dried. It was then suspended in pentane (25 mL), and 6 N HCl (25 mL) was added with vigorous stirring. The stirring was continued for additional 2 h, and the pentane layer was separated. Virtually pure product **28** was obtained upon removal of the solvent. Final purification was achieved by using radial chromatography (elution with pentane). Yield 152 mg, 70%. IR 2565 cm^{-1}. ^1H NMR δ 2.15 (s, 3H), 3.91 (s, 1H), 7.07 (m, 1H), 7.18 (m, 2H), 7.34 (m, 1H). ^{13}C NMR 21.28, 119.30, 126.31, 128.48, 128.62, 129.79, 130.43, 135.49, 139.53. MS (PCI) 219 (M + 1, 50%), 183 (100%). Anal. Calcd for $C_9H_8Cl_2S$ C, 49.33; H, 3.69. Found: C, 49.98; H, 3.87.

Mixture of 3-Methyl- and 2-Methylthianaphthenes 31 and 32. Reaction of 1,1-Dichloro-2-(*o*-mercaptophenyl)-propene 28 with *tert*-Butyllithium. To the solution of 1,1-dichloro-2-(*o*-mercaptophenyl)propene (**28**) (140 mg, 0.64 mmol) in THF (10 mL) cooled to −100 °C was added *tert*-butyllithium (1.67 mL, 2 mmol of 1.2 M solution in pentane). The reaction mixture was allowed to reach −70 °C, at which temperature it was maintained for additional 3 h. It was then quenched with MeOH and washed with water (15 mL). The water layer, after acidification yielded 20% of unreacted starting material **28**. The original organic phase was dried, and the solvent was removed under reduced pressure. The residue was found (NMR, TLC) to consist mainly of the mixture of **31** and **32** along with some minor impurities. Careful radial chromatography with cyclohexane as an eluent allowed to isolate pure 3:2 mixture of the positional isomers **31**[36] and **32**.[37] Yield 57 mg, 60%. All attempts to separate this mixture by chromatographic methods (including GC-MS conditions) failed. The products **31** and **32** were identified by comparing the ^1H and ^{13}C NMR spectra of the mixture with literature data for pure samples.[33c,38] ^1H NMR δ 2.45 (d, J = 0.9 Hz; 3H, 3-methyl isomer), 2.59 (d, J = 1.2 Hz; 3H, 2-methyl isomer) 6.98 (d, J = 1.2 Hz; 1H, 2-methyl isomer), 7.08 (d, J = 1.2 Hz; 1H 3-methyl isomer), 7.22−7.44 (m, 2H, both isomers), 7.65 (d, J = 7.2 Hz; 1H, 2-methyl isomer), 7.70−7.80 (m, 1H, both isomers), 7.86 (dd, J = 6.9 Hz, J = 1.2 Hz; 1H, 3-methyl isomer). ^{13}C NMR 13.62 (3-methyl isomer), 15.85 (2-methyl isomer); the following peaks correspond to C4, C5, C6, C7 carbons of both isomers, C2 carbon of 3-methyl isomer and C3 carbon of 2-methyl isomer: 121.61, 121.73, 121.84, 122.12, 122.67, 122.91, 123.49, 123.96, 124.22 (broad, presumably two unseparated peaks); 132.30 (C3, 3-methyl isomer); signals at 139.89, 139.92, 140.52, 140.71, 141.06 correspond to C3a and C7a carbons for both isomers and C2 carbon for 2-methyl isomer. MS (PCI) 149 (M + 1, 100%).

Acknowledgment. This work was supported by a grant from the National Science Foundation for which we are grateful. The author is greatly indebted to professor Harry M. Walborsky for his support, encouragement, and valuable discussions.

JO950542C

(34) Tanaka, S. *J. Am. Chem. Soc.* **1951**, *73*, 872.
(35) Tanaka, H.; Yokoyama, A. *Chem. Pharm. Bull.* **1962**, *10*, 13.
(36) Dickinson, R. P.; Iddon, B. *J. Chem. Soc. C* **1968**, 2733.
(37) Cherry, W. H.; Craig, J. T.; Porter, Q. N. *Aust. J. Chem.* **1979**, *32*, 133.
(38) (a) Clark, P. D.; Ewing, D. F.; Scrowston, R. M. *Org. Magn. Reson.* **1976**, *8*, 252. (b) Takahashi, K.; Kanda, T.; Matsuki, Y. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 768.