Preparation of Hydrocarbons. Bicyclo[3.2.1]octene (2) and bicyclo[3.2.1]octadiene (1) were prepared according to the procedure reported by Moore.[25] Bicyclo[3.2.2]nonatriene (6) was prepared from cycloheptatriene as described by Grutzner and Winstein.[16] Bicyclo[3.2.2]nonadiene (5) was synthesized from bicyclo[3.2.2]non-6-en-2-one (11).[26] Ketone 11 was reacted sequentially with $NaBH_4$, TosCl, and *t*-BuOK/18-crown-6-ether in THF at 25 °C. All the hydrocarbons were purified by preparative GLPC.

Acidity Measurements. The procedures devised by Streitwieser[27] were used in which a weighed amount of a polyarylmethane, whose pK_a and anionic extinction coefficient had been determined, was added at 20 °C to CHA containing cesium cyclohexylamide. The UV spectrum of the resulting solution was recorded, a weighed amount of a GLPC purified hydrocarbon of unknown pK_a was added, and the spectrum was recorded. The polyarylmethanes (pK_a's in parentheses)[13] used for the acidity determinations are listed below with the pK_a value measured for hydrocarbons **1**, **2**, **5**, and **6** prior to statistical correction.

Diene 1: triphenylmethane (31.45), pK_a 32.0 ± 0.3; *p*-biphenyldiphenylmethane (30.2), pK_a 31.4 ± 0.3.

Diene 5: tri-*p*-tolylmethane (33.0), pK_a 34.1 ± 0.3; *o*-biphenylphenylmethane (33.5), pK_a 34.5 ± 0.3.

Triene 6: triphenylmethane (31.45), pK_a 32.1 ± 0.3; tri-*p*-tolylmethane (33.0), pK_a 32.0 ± 0.3; *p*-biphenyldiphenylmethane (30.2), pK_a 31.9 ± 0.3.

Octene 2: *p*-biphenylmethane (39.0), $pK_a > 40.5$.

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Registry No. 1, 4096-95-1; 1 anion, 87508-61-0; 2, 823-02-9; 5, 14993-07-8; 5 anion, 87481-57-0; 6, 16216-91-4; 6 anion, 87462-59-7; 1,3-cyclopentadiene anion, 87507-94-6.

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Nucleophilic Aromatic Substitutions of Unactivated Aryl Halides by Methyl Selenide Anions. Synthesis and Selective Dealkylations of Aryl Alkyl Selenides

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Lithium methyl selenide, easily prepared from powdered gray selenium and MeLi, reacts with unactivated aryl halides, in DMF, to afford the aryl methyl selenides as a result of a nucleophilic aromatic substitution. The aryl methyl selenides are rapidly dealkylated in the reaction medium by MeSeLi to give the aryl selenide anions. Addition of an alkyl halide or of cyanogen iodide gives rise to the formation of aryl alkyl selenides or aryl selenocyanates in good yields. From competitive experiments, carried out on compounds of the type ArClSeR and ArClSR, it has been shown that an RSe group is as efficient as an RS group in activating the nucleophilic aromatic substitution of a chlorine atom by MeS or MeSe anions in DMF. (Alkylthio)phenyl and alkoxyphenyl alkyl selenides can be selectively dealkylated by nucleophilic aliphatic substitution with MeSNa or MeSeLi in DMF or by electron transfer with sodium in HMPA. In the first case the easiness with which the dealkylation occurs follows the order ArSeMe > ArOMe > ArSMe, whereas in the second case the order is ArSeR > ArSR > ArOR. The synthetic utility of these reactions is exemplified and discussed.

In previous papers we have reported that alkanethiolate and alkoxy anions easily react with unactivated aryl chlorides or bromides to give the products of nucleophilic aromatic substitutions. These reactions are made possible by the use of HMPA as the solvent. More recently, however, we have found that similar results can be obtained also in DMF, thus avoiding the use of the carcinogenic HMPA.[1] Thus very simple and useful procedures have been developed for the synthesis of aryl alkyl ethers,[2] thioethers,[1,3] phenols,[2] aromatic thiols,[1,4] and aryl thiocyanates[5] from aryl halides, as well as for the synthesis of alkoxyphenols,[2] alkoxyaryl alkyl sulfides,[1,6] alkoxythiophenols,[1,7] (alkylthio)phenols,[1,7] hydroxythiophenols,[1,7] poly(alkylthio)benzenes,[1,8] and polymercaptobenzenes[1,9] from polychlorobenzenes.

We now report that similar nucleophilic aromatic substitutions of unactivated aryl halides can be effected also by the alkyl selenide anions. These reactions thus represent a convenient synthesis of aryl alkyl selenides **2** from

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unactivated aryl halides **1** (eq 1).

$$\underset{\mathbf{1}}{ArX} + RSe^- \rightarrow \underset{\mathbf{2}}{ArSeR} + X^- \quad (1)$$

Because of the simple procedure employed and of the high yields obtained the method now described compares favorably with other syntheses described in the literature[10] and can give a contribution to the growing synthetic applications of organoselenium compounds.[11]

Results and Discussion

Several methods are described in the literature for the synthesis of alkyl selenide anions. Most of these methods consist of the alkylation of the selenide anion which can be prepared by the reduction of elemental selenium with various reducing agents.[12] We have found that the easiest and cleanest way to obtain an alkyl selenide anion is the reaction of alkyllithium compounds with elemental selenium in THF, which gives rise to a milky suspension of the lithium alkyl selenide which can be directly used for further reactions. Throughout this paper we have only used lithium methyl selenide, but this method can very likely be applied to the synthesis of other alkyl or aryl selenide anions.

When a solution of chlorobenzene (**3a**, 0.01 mol) in DMF was added to the suspension of MeSeLi (0.03 mol) in THF and the temperature was raised to 120 °C, so that all the THF distilled off from the reaction mixture, the chlorine atom was displaced by the methyl selenide anion to give the phenyl methyl selenide (**4**). This compound, however, was rapidly dealkylated by the MeSe anion to give the phenyl selenide anion **5** (Scheme I). Similar results were

Scheme I

$$MeLi + Se \rightarrow MeSeLi$$

$$\underset{\mathbf{3a},\ X = Cl}{\underset{\mathbf{3b},\ X = Br}{C_6H_5X}} + MeSeLi \rightarrow LiX + \underset{\mathbf{4}}{C_6H_5SeMe}$$

$$\underset{\mathbf{4}}{C_6H_5SeMe} + MeSeLi \rightarrow Me_2Se + \underset{\mathbf{5}}{C_6H_5SeLi}$$

$$\mathbf{5} + MeI \rightarrow LiI + \mathbf{4}$$

obtained by using bromobenzene **3b**. Addition of methyl iodide to the final reaction mixture afforded **4** in about 50% yield. Thus, two consecutive reactions are going on, i.e., a nucleophilic aromatic substitution on the unactivated halogenobenzene by the strongly nucleophilic methyl selenide anion,[13] followed by a nucleophilic aliphatic substitution on the aryl methyl selenide to give the dealkylation product. The latter reaction seems to be much faster than the nucleophilic aromatic substitution. In fact, if the course of the reaction is monitored by treating small aliquots of the reaction mixture with excess ethyl iodide, one finds that, even at the early stages, the C_6H_5SeMe is only present in traces, the major reaction product (more than 95%) being C_6H_5SeEt. Similar results are obtained also in reactions in which chlorobenzene was used in large excess with respect to MeSeLi. Thus, the course of this reaction is similar to that of chlorobenzene with sodium methanethiolate[1,4] with the difference that in the latter case the two consecutive reactions, i.e., the formation of thioanisole and its dealkylation to thiophenol, have comparable rates, and complete dealkylation can be obtained only by using an excess of MeSNa and with prolonged reaction times. As has been shown in the case of the reactions of alkanethiolate anions with aryl halides,[3,4] we suggest that also in the present case the displacement of the chlorine atom by the lithium methyl selenide occurs with the classical S_NAr mechanism and that the dealkylation of the aryl methyl selenide occurs with an S_N2 mechanism. The different behavior shown by the two reactions can be attributed to the fact that on the one hand the methyl selenide is a stronger nucleophile than the methanethiolate anion and on the other hand the C_6H_5SeMe is more reactive than the C_6H_5SMe in the S_N2-type dealkylation reactions carried out in DMF. This latter point will be discussed in more detail below.

When the *o*-, *m*-, and *p*-dichlorobenzenes (**6a–c**) are treated with an excess of MeSeLi in DMF, the reaction takes place easily to afford the chlorophenyl methyl selenides **7a–c** which are completely dealkylated to the chlorophenyl selenide anions **8a–c**. The bis(methylselenyl)benzenes **9a–c** or their dealkylation products, which in principle could be formed from **7a–c**, were not formed at all (Scheme II). Good yields of chlorophenyl

Scheme II[a]

$$\underset{\mathbf{6a-c}}{C_6H_4Cl_2} \xrightarrow[DMF]{MeSeLi} \underset{\mathbf{7a-c}}{C_6H_4ClSeMe} \underset{MeI}{\overset{MeSeLi}{\rightleftharpoons}} \underset{\mathbf{8a-c}}{C_6H_4ClSe^-}$$

$$\underset{\mathbf{9a-c}}{C_6H_4(SeMe)_2} \qquad \underset{\mathbf{10}}{p\text{-}C_6H_4ClSeEt} \qquad \underset{\mathbf{11}}{p\text{-}C_6H_4ClSeCHMe_2}$$

$$\underset{\mathbf{7c}}{p\text{-}C_6H_4ClSeMe} \xrightarrow[DMF]{MeSNa} \underset{\mathbf{8c}}{p\text{-}C_6H_4ClSe^-} \xrightarrow{EtI} \mathbf{10}$$

$$\underset{\mathbf{12}}{p\text{-}C_6H_4ClSMe} \xrightarrow[DMF]{MeSeLi} p\text{-}C_6H_4ClS^- +$$

$$\underset{\mathbf{13}}{p\text{-}C_6H_4(Se^-)SMe} \xrightarrow{MeI} \mathbf{12} + \underset{\mathbf{14}}{p\text{-}C_6H_4(SeMe)SMe}$$

[a] **a**, ortho; **b**, meta; **c**, para

methyl selenides **7a–c** were obtained by adding MeI to the final reaction mixtures. Similarly, treatment of the reaction mixture from **6c** with EtI or Me_2CHI afforded good yields of *p*-chlorophenyl ethyl (**10**) and isopropyl selenide (**11**), respectively. Even if the nucleophile is changed, the only reaction given by the chlorophenyl methyl selenides is the nucleophilic aliphatic substitution at the methyl group. Thus, the reaction of the *p*-chlorophenyl methyl selenide **7c** with methanethiolate anions in DMF afforded only the *p*-chlorophenyl selenide anion (**8c**), which on treatment with EtI gave **10** in 81% yield (Scheme II). In the chlorophenyl methyl selenides **7a–c**, therefore, the attack of the MeSe and MeS anion at the carbon atom of the methyl group is much faster than the attack at the aromatic carbon atom holding the chlorine atom. On the contrary, in the chlorophenyl methyl sulfides, obtained from the reactions of **6a–c** with sodium methanethiolate, the two reactions have comparable rates, and a mixture of the chlorothiophenols and of the bis(methylthio)benzenes is obtained.[1,4] Similar results were obtained by using MeSeLi as the nucleophile. In fact, when *p*-chlorophenyl methyl sulfide **12** was treated with lithium methyl selenide in DMF, a mixture of *p*-chlorothiophenol

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and of *p*-(methylthio)phenyl selenide anion (**13**) was obtained. On treatment with methyl iodide the starting product **12** and *p*-(methylthio)phenyl methyl selenide (**14**) were obtained in 50% and 27% yields, respectively (Scheme II). This different behavior between the selenides **7** and the sulfides **12** toward MeSe and MeS anions is certainly due to the fact that in ArSeMe the dealkylation is faster than in ArSMe (see below). In addition, the observed different reactivity between **7** and **12** could also be due to the fact that an RSe substituent is less efficient than an RS group in activating the nucleophilic aromatic substitution of the chlorine atom. No information is available in the literature about this point, and the results described so far do not allow one to draw any conclusion about the importance of this factor. Useful information can be obtained by using as substrates the chlorophenyl isopropyl sulfides and selenides in which the nucleophilic aliphatic substitution is made much more difficult by the presence of the secondary alkyl group. Indeed, when the *o*-, *m*- and *p*-chlorophenyl isopropyl sulfides (**15a–c**) were treated with an excess of MeSeLi, the only reaction observed was the displacement of the chlorine atom to give (isopropylthio)phenyl methyl selenides **16a–c** which were rapidly demethylated to give the anions **17a–c**. Treatment of the reaction mixtures with methyl iodide gave good yields of the products **16a–c** (Scheme III). This reactivity

Scheme III

$$C_6H_4ClSCHMe_2 \xrightarrow[DMF]{MeSeLi}$$
15a–c

$$C_6H_4(SeMe)SCHMe_2 \underset{MeI}{\overset{MeSeLi}{\rightleftharpoons}} C_6H_4(Se^-)SCHMe_2$$
16a–c **17a–c**

$$17c + Me_2CHI \rightarrow p\text{-}C_6H_4(SeCHMe_2)SCHMe_2$$
18

$$p\text{-}C_6H_4ClSeCHMe_2 \xrightarrow[DMF]{MeSeLi}$$
11

$$p\text{-}C_6H_4(SeMe)SeCHMe_2 \underset{MeI}{\overset{MeSeLi}{\rightleftharpoons}} p\text{-}C_6H_4(Se^-)SeCHMe_2$$
19 **20**

$$11 \xrightarrow[DMF]{MeSeLi} p\text{-}C_6H_4ClSe^- \xrightarrow{MeI} p\text{-}C_6H_4ClSeMe$$
8c **7c**

$$20 + Me_2CHI \rightarrow p\text{-}C_6H_4(SeCHMe_2)_2$$
21

$$11 \xrightarrow[DMF]{MeSNa} p\text{-}C_6H_4(SMe)SeCHMe_2 \underset{MeI}{\overset{MeSNa}{\rightleftharpoons}}$$
22

$$p\text{-}C_6H_4(S^-)SeCHMe_2$$
23

is similar to that observed in the reactions of compounds **15a–c** with sodium methanethiolate.[1,4] In the case of the reaction of **15c** with MeSeLi the final reaction mixture was also treated with Me_2CHI and *p*-(isopropylthio)phenyl isopropyl selenide (**18**) was obtained in 73% yield.

The reaction of the *p*-chlorophenyl isopropyl selenide (**11**) with an excess of MeSeLi, after treatment with MeI, afforded a mixture of *p*-(methylselenyl)phenyl isopropyl selenide (**19**, 77%) and of *p*-chlorophenyl methyl selenide (**7c**, 8%), deriving from the anions **20** and **8c** (Scheme III). Thus, even in the case of the isopropyl derivatives the dealkylation reaction by the methyl selenide anion cannot be completely suppressed. The major reaction product, however, is **19**. The formation of this compound indicates that the alkylselenyl substituent does not deactivate the nucleophilic aromatic substitution of the chlorine atom. This is the first example in which two chlorine atoms are consecutively displaced to give a bis(alkylselenyl)benzene; the whole of the results described above indicates that this reaction can be effected only if the first alkylselenium group which is introduced does not contain a primary alkyl group.[14] If the reaction mixture of **11** and MeSeLi is treated with Me_2CHI, bis(isopropylselenyl)benzene (**21**) is obtained in 75% yield. The reaction of **11** with sodium methanethiolate gave rise to *p*-(methylthio)phenyl isopropyl selenide (**22**) together with small amounts of its dealkylation product **23**; treatment of the final reaction mixture with methyl iodide afforded **22** in 86% yield. This result once again indicates that the alkylselenium substituent does not deactivate the displacement of the chlorine atom and at the same time that, as expected, the MeS anion is less efficient than the MeSe anion in effecting the S_N2 reaction.

The results described above do not give any clear answer about the difference between the alkylselenium and alkylthio substituents in the activation of the nucleophilic aromatic substitution of the chlorine atom by the MeSe and MeS anion. In order to gain more convincing evidences about this problem, experiments have been carried out in which an equimolecular mixture of **15c** and **11** is allowed to react with an insufficient quantity of the nucleophile, and the ratios of the products formed, after treatment with methyl iodide, have been measured by GLC. In these competitive experiments the ratios **16c**/**19** and *p*-$C_6H_4(SMe)SCHMe_2$/**22** are assumed to give directly the values of the relative reaction rates of **15c** and **11** with $MeSe^-$ and MeS^-, respectively. In both cases it was found that the ratios of the products formed was 1 ± 0.3, demonstrating that the *p*-$C_6H_4ClSeCHMe_2$ and the *p*-$C_6H_4ClSCHMe_2$ present a substantially similar reactivity toward the MeSe or the MeS anions. From these experiments it emerges that an alkylselenium group is as efficient as an alkylthio group in activating the displacement of a chlorine atom from the para position by a MeS or a MeSe anion in DMF.

It is thus clear that the different reactivity observed between the chlorophenyl methyl selenides and the chlorophenyl methyl sulfides (Scheme II) in their reactions with MeSe and MeS anions is mainly due to the fact that in the selenium compounds the dealkylation occurs more easily than in the corresponding sulfur compounds.

The reaction with MeSeLi in DMF has been extended to other aromatic halides such as the bromo- and chlorobiphenyls, the chloroquinoline, and the bromonaphthalene. In every case the reactions could not be stopped at the stage of the aryl methyl selenide because of their fast demethylation. It was therefore preferred to work with an excess of MeSeLi so that all the starting aryl halides could be converted into the corresponding aryl selenide anions. This procedure therefore represents a very convenient one-pot synthesis of aryl selenide anions starting from elemental selenium and unactivated aryl halides. The aryl selenide anions thus obtained can be directly used for further reactions. They can be oxidized (by air or iodine) to give the diselenides or can be alkylated by simply adding an alkylating agent to their solution in DMF. In most cases we have treated the final reaction mixture with methyl iodide, and the aryl methyl selenides have been isolated in good yields. Similar good results were obtained in the examples in which the alkylation was effected with ethyl or isopropyl iodides. In two cases the aryl selenide anion was treated with cyanogen iodide, and the corresponding aryl selenocyanates have been isolated in good yields. All these results are collected in Table I.

(14) The use of $Me_2CHSeLi$ should allow one to effect the one-pot synthesis of poly(alkylselenyl)benzenes from polychlorobenzenes. These reactions are presently under investigation.

Table I. Reactions of Aryl Halides (0.01 mol) with Excess MeSeLi in DMF at 120 °C

starting halide	equiv of MeSeLi	reaction time,[a] h	alkylating agent	product	% yield[b]
C_6H_5Cl	3	48	MeI	C_6H_5SeMe	45
C_6H_5Br	3	48	MeI	C_6H_5SeMe	52
o-$C_6H_4Cl_2$	4	16	MeI	o-$C_6H_4ClSeMe$	87
m-$C_6H_4Cl_2$	4	8	MeI	m-$C_6H_4ClSeMe$	86
p-$C_6H_4Cl_2$	4	8	MeI	p-$C_6H_4ClSeMe$	72
p-$C_6H_4Cl_2$	4	8	EtI	p-$C_6H_4ClSeEt$	81
p-$C_6H_4Cl_2$	4	8	Me_2CHI	p-$C_6H_4ClSeCHMe_2$	76
p-$C_6H_4ClSeMe$[c]	3	8	EtI	p-$C_6H_4ClSeEt$	83
p-C_6H_4ClSMe	3	16	MeI	p-C_6H_4ClSMe and	50
				p-$C_6H_4(SeMe)SMe$	27
o-$C_6H_4ClSCHMe_2$	3	25	MeI	o-$C_6H_4(SeMe)SCHMe_2$	87
m-$C_6H_4ClSCHMe_2$	3	20	MeI	m-$C_6H_4(SeMe)SCHMe_2$	87
p-$C_6H_4ClSCHMe_2$	3	20	MeI	p-$C_6H_4(SeMe)SCHMe_2$	75
p-$C_6H_4ClSCHMe_2$	3	20	Me_2CHI	p-$C_6H_4(SeCHMe_2)SCHMe_2$	73
p-$C_6H_4ClSeCHMe_2$[d]	3	14	MeI	p-$C_6H_4(SeMe)SeCHMe_2$ and	77
				p-$C_6H_4ClSeMe$	8
p-$C_6H_4ClSeCHMe_2$	3	14	Me_2CHI	p-$C_6H_4(SeCHMe_2)_2$ and	75
				p-$C_6H_4ClSeCHMe_2$	10
o-C_6H_4PhCl	3	36	MeI	o-$C_6H_4PhSeMe$	63
m-C_6H_4PhBr	3	24	MeI	m-$C_6H_4PhSeMe$	87
p-C_6H_4PhBr	3	6	MeI	p-$C_6H_4PhSeMe$	76
2-$C_{10}H_7Br$	3	23	MeI	2-$C_{10}H_7SeMe$	83
4-chloroquinoline	3	3.5	MeI	4-C_9H_6NSeMe	60
p-C_6H_4PhBr	3	6	ICN[e]	p-$C_6H_4PhSeCN$	76
2-$C_{10}H_7Br$	3	23	ICN[e]	2-$C_{10}H_7SeCN$	75

[a] The progress of the reaction was monitored by TLC and/or GLC. [b] Based on isolated products after column chromatography and calculated from the amount of aryl halide employed. [c] The same reaction carried out with MeSNa afforded, after 10 h, an 81% yield of the p-$C_6H_4ClSeEt$. [d] The same reaction carried out with MeSNa afforded, after 16 h, an 86% yield of the p-$C_6H_4(SMe)SeCHMe_2$ (**22**). [e] The reaction with ICN required 4 h.

Scheme IV

$$p\text{-}C_6H_4(SeMe)SeCHMe_2 \xrightarrow[DMF]{MeSNa} \underset{\mathbf{19}}{}$$

$$p\text{-}C_6H_4(Se^-)(SeCHMe_2) \xrightarrow{Me_2CHI} \underset{\mathbf{21}}{p\text{-}C_6H_4(SeCHMe_2)_2}$$
$$\mathbf{20}$$

$$p\text{-}C_6H_4(SR)SeR \xrightarrow[DMF]{MeSNa} p\text{-}C_6H_4(SR)Se^- \xrightarrow[\text{or MeI}]{EtI}$$
$$\mathbf{14},\ R = Me \qquad \mathbf{13},\ R = Me$$
$$\mathbf{24},\ R = Et \qquad \mathbf{25},\ R = Et$$

$$p\text{-}C_6H_4(SR)SeR_1$$
$$\mathbf{26},\ R = Me;\ R_1 = Et$$
$$\mathbf{27},\ R = Et;\ R_1 = Me$$

$$p\text{-}C_6H_4(OMe)SeMe \xrightarrow[DMF]{MeSNa} \underset{\mathbf{29}}{p\text{-}C_6H_4(OMe)Se^-} \xrightarrow{EtI}$$
$$\mathbf{28}$$

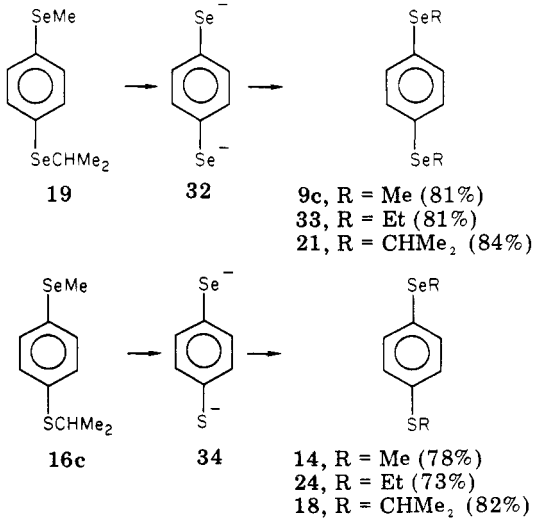
$$p\text{-}C_6H_4(OMe)SeEt$$
$$\mathbf{30}$$

Thus, the present method can be considered of general validity and can be applied to the synthesis of the aryl diselenides, aryl alkyl selenides, (alkylthio)aryl alkyl selenides, (alkylselenyl)aryl alkyl selenides, and arylselenocyanates as well as of any other selenium compound which can be obtained from the aryl selenide anions. This synthesis is therefore very versatile and extremely simple, and it presents several advantages over other existing methods. The only limitation we have observed is that of the synthesis of compounds of the type Ar(SeR)SeR′ or Ar(SR)SeR′ in which both R and R′ are primary alkyl groups. These compounds, which cannot be obtained by means of two consecutive nucleophilic aromatic substitutions, can, however, be prepared in good yields by means of the selective dealkylation procedures which are described below.

Interesting results were obtained from the reactions of bis(alkylselenyl)benzenes, (alkylthio)phenyl alkyl selenides, and alkoxyphenyl alkyl selenides with dealkylating agents. These investigations were limited to the para isomers, but it is reasonable to assume that similar results can be obtained with the ortho and meta isomers also. Two dealkylation reactions have been examined: the reaction with sodium methanethiolate in DMF, which gives rise to the dealkylation products through an S_N2 process,[1,4,7] and the reaction with sodium in HMPA, which gives the dealkylation products through an electron-transfer process.[7,9,15]

When the bis(alkylselenyl)benzene **19** was treated with sodium methanethiolate, the reaction occurred selectively at the primary alkyl group to give the anion **20**; treatment of the reaction mixture with isopropyl iodide afforded bis(isopropylselenyl)benzene (**21**) in 75% yield (Scheme IV). This result is in agreement with the S_N2 nature of

Scheme V



the reaction and is identical with that observed in the corresponding (methylthio)phenyl isopropyl sulfide.[4b] The

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same reaction applied to *p*-(methylthio)phenyl methyl selenide (**14**) and *p*-(ethylthio)phenyl ethyl selenide (**24**) (both prepared in good yield from **16c**, as described below) selectively occurred at the alkyl group linked to the selenium atom to give the anions **13** and **25**, which on treatment with ethyl iodide or methyl iodide, respectively, afforded **26** (94%) or **27** (85%) (Scheme IV). In compounds **14** and **24** two electrophilic centers are available for the nucleophilic attack by the thiolate anion: the methyl or ethyl carbon atom linked to selenium and that linked to sulfur. Under the experimental conditions employed, the attack occurs selectively at the SeR group. Moreover, when *p*-methoxyphenyl methyl selenide (**28**) was treated with MeSNa, the reaction occurred selectively at the SeMe group to give the anion **29**; treatment with ethyl iodide gave **30** in 93% yield (Scheme IV). In previous papers[1,7] we have shown that in the methoxythioanisoles the reaction with thiolate anions occurred selectively at the methoxy group. All these results indicate therefore that these intramolecular competitive nucleophilic substitution reactions are very selective and that the easiness with which the dealkylation occurs follows the order ArSeMe > ArOMe > ArSMe. We cannot find a straightforward interpretation for this reactivity sequence, and it is likely the result of several factors. An important role in determining the observed leaving ability of the three ArX anions is certainly played by the reaction medium employed. However, the qualitative results available so far do not justify further speculation about this problem. Obviously, this order cannot be respected if the nature of the alkyl groups is changed. Thus, for instance, in the reaction of *p*-(methylthio)phenyl isopropyl selenide (**22**) with MeSNa (Scheme III) the ArS anion is displaced more easily than the ArSe anion because the sulfur atom is linked to a methyl group whereas the selenium atom is linked to the secondary isopropyl group. As indicated by the results reported in Schemes II and III, the same selectivity is also observed when the nucleophilic substitution is effected by the MeSeLi; this is clearly demonstrated by the reactions of **12**, **15a–c**, and **11** with an excess of lithium methyl selenide. Moreover, MeSeLi is a more powerful nucleophile than the MeSNa.[13] Thus MeSeLi in DMF can be used for the dealkylation of aryl methyl or aryl ethyl ethers, thioethers, and selenoethers with several synthetic advantages over the sodium or lithium alkanethiolates.

The dealkylation of the bis(alkylselenyl)benzenes and of the (alkylthio)phenyl alkyl selenides can also be effected by electron transfer. These reactions are carried out in HMPA[16] with sodium and very likely proceed through the intermediate formation of the radical anions **31**, as has been suggested in the case of the aryl alkyl sulfides.[7,9,15] The radical anions **31** selectively fragment at the alkyl selenium bond to give the aryl selenide anions (eq 2); the

$$\underset{}{\mathrm{ArSeR}} + \mathrm{Na} \rightarrow \underset{\mathbf{31}}{[\mathrm{ArSeR}]^{-}\cdot\mathrm{Na}^{+}} \rightarrow \mathrm{ArSeNa} + \mathrm{R}\cdot \quad (2)$$

alternative fragmentation to give an alkyl selenide anion and an aryl radical was not observed in the cases we have investigated so far. Interestingly, when the bis(alkylselenyl)benzene **19** was treated with excess sodium, both the SeR groups suffered fragmentation to give the dianion **32** (Scheme V). Thus, this behavior is similar to that already observed in the case of the poly(alkylthio)benzenes, which, on treatment with sodium, gave rise to the fragmentation of all the alkylthio groups to afford good yields of the corresponding polymercaptobenzenes.[1,9] Similarly, *p*-(isopropylthio)phenyl methyl selenide (**16c**) reacted with sodium to afford the anion **34** (Scheme V) in which both the SeR and the SR groups have been dealkylated. This reaction thus opened the way to the synthesis of the bis(alkylselenyl)benzenes and of the (alkylthio)phenyl alkyl selenides in which the two alkyl groups are equal. In fact, by addition of methyl, ethyl, or isopropyl iodide to the reaction mixtures containing the dianions **32** and **34**, compounds **9c**, **33**, and **21** and compounds **14**, **24**, and **18** were obtained in good yields. Reaction yields are reported in parentheses in Scheme V. These reactions are particularly useful for the synthesis of the methyl and ethyl derivatives (**9c**, **33**, **14** and **24**) which, for the reasons discussed above, cannot be obtained directly from the *p*-dichlorobenzene by means of two consecutive nucleophilic substitutions.

These dealkylation reactions can also be effected under less drastic conditions. Instead of addition of the sodium to the solution of **19** and **16c** in HMPA, the sodium is first allowed to dissolve in HMPA, and then **19** and **16c** are added to the resulting solution. As it has already been observed in the case of bis(alkylthio)benzenes,[15] under these experimental conditions the reaction stops at the stage of the monodealkylation. In the case of compound **19** this process is not selective, and a mixture of the *p*-$C_6H_4(SeCHMe_2)Se^-$ and *p*-$C_6H_4(SeMe)Se^-$, in almost equal amounts, is obtained. On the contrary, the reaction of **16c** gives rise exclusively to the *p*-$C_6H_4(SCHMe_2)Se^-$ anion, indicating that the alkyl–selenium bond is more easily broken than the alkyl–sulfur bond. In previous works we have shown that in molecules containing an alkoxy and a thioalkoxy group the reaction occurs selectively at the SR group, the fragmentation of the oxygen alkyl bond requiring more drastic conditions.[1,7,15] Thus it can be concluded that in these fragmentation reactions promoted by sodium the easiness with which the dealkylation occurs follows the order ArSeR > ArSR > ArOR. These results indicate that the σ^* MO of the C–Se bond has a lower energy than that of the C–S bond and that the σ^* MO of the C–O bond has a considerably higher energy.[17,18] It has also been suggested that in the case of the aryl alkyl ethers the fragmentation does not occur through radical anion intermediates but rather through the dianions.[15]

This latter procedure is very useful in synthetic applications. In fact, when the symmetrically substituted bis(alkylselenyl)benzenes **9c**, **33**, and **21** or (alkylthio)-phenyl alkyl selenides **14**, **24**, and **18** are added to the solution of sodium in HMPA, the monoanions **35**, **36**, and **20** and **13**, **25**, and **17c** are formed (Scheme VI). These can now be treated with an alkyl iodide to give all the possible bis(alkylselenyl)benzenes and (alkylthio)phenyl alkyl selenides containing two different alkyl groups. The results of these reactions are collected in Scheme VI, where all the compounds deriving from all the possible combinations of the methyl, ethyl, and isopropyl groups are indicated. We have not effected all the reactions reported in Scheme VI but only these for which reaction yields are reported in parentheses. This procedure has a particular synthetic relevance in the case of the compounds containing the methyl or the ethyl group, which could not be obtained by nucleophilic aromatic substitution. It can also be observed that in the case of the synthesis of the Ar(SR)SeR_1 compounds it is not necessary to start from the symmetrically substituted compounds **14**, **24**, and **18**. Since the dealkylation occurs selectively at the alkyl sel-

(16) Also in this case the use of HMPA can be avoided. In the case of ethers and thioethers good yields of the dealkylation products were obtained using sodium in DMA.[1]

(17) C. Galli and J. F. Bunnett, *J. Am. Chem. Soc.*, **103**, 7140 (1981).
(18) R. A. Rossi, *Acc. Chem. Res.*, **15**, 164 (1982).

enium bond, it is possible to start from any compound of the type $Ar(SR)SeR_2$ and to effect the exchange of the alkyl group linked to the selenium atom to give compounds of the type $Ar(SR)SeR_1$.

In conclusion, the results presented in this paper demonstrate that alkylselenium groups can be easily introduced into an aromatic ring by nucleophilic displacement of unactivated chlorine atoms. The synthetic utility of these reactions is greatly enhanced by the fact that the products thus obtained can be selectively dealkylated either by nucleophilic aliphatic substitutions or by electron transfer. The versatility of these processes is exemplified by the results collected in Schemes IV–VI. In the present paper the monoanions $C_6H_4(SR)Se^-$ and $C_6H_4(SeR)Se^-$ and the dianions $C_6H_4(S^-)Se^-$ and $C_6H_4(Se^-)_2$ have been used only to obtain all the possible compounds of the type $Ar(SeR)SeR_1$ or $Ar(SeR)SR_1$ with R and R_1 equal to methyl, ethyl, or isopropyl. It is clear, however, that these anions can be used for many other purposes and that, therefore, these reactions can certainly have much wider synthetic applications than those presented in this paper.

Experimental Section[19]

All the aryl halides employed in this work were commercial products. The *p*-chlorophenyl methyl sulfide,[6] the *o*-, *m*- and *p*-chlorophenyl isopropyl sulfides,[3] and the *p*-methoxyphenyl methyl selenide[20] were prepared as described in the literature. Aryl alkyl selenide dibromides were obtained by treatment of the aryl alkyl selenides with excess bromine in CCl_4; the products were purified by crystallization from CCl_4.

Lithium methyl selenide was prepared[13] by adding dropwise methyllithium (commercial solution 1.6 M in ether, 1.1 mol) to a stirred suspension of powdered gray selenium (1 atom) in THF (10 mL for 0.5 g of selenium) at room temperature and under nitrogen. After 15 min all the selenium was consumed, and a white suspension was obtained.

Reactions of Aryl Halides with MeSeLi. General Procedure. A solution of the aryl halide (0.01 mol) in dry DMF was added to the suspension of MeSeLi in THF prepared as described above (for the amount of MeSeLi, see Table I). The flask was immersed into a silicone oil bath kept at 120 °C, and the ether and THF were left to distill off under nitrogen. The resulting brown solution was stirred at 120 °C for the times indicated in Table I. The progress of the reaction was monitored by TLC and/or GLC after treatment of small aliquots of the reaction mixture with the appropriate alkyl iodide. The cooled reaction mixture was treated with the alkylating agent and then poured on water. Extraction with ether followed by the usual workup gave a residue which was chromatographed through a silica gel column by using mixtures of ethyl ether and petroleum ether as the eluant. Reaction conditions and reaction yields are collected in Table I. Physical and spectral data of the products obtained are reported below. The vicinal coupling constant in the ethyl and isopropyl groups was 7 Hz in every case.

Phenyl methyl selenide (4): oil; NMR δ 7.4–7.2 (m, 2 H), 7.2–7.0 (m, 3 H), 2.25 (s, 3 H). Dibromide: mp 122–124 °C (lit.[21] mp 115–116 °C); NMR δ 8.0–7.7 (m, 2 H), 7.5–7.3 (m, 3 H), 3.85 (s, 3 H).

***o*-Chlorophenyl methyl selenide (7a)**: bp 54–55 °C (0.1 mm) [lit.[20] bp 49–50 °C (0.07 mm)]; NMR δ 7.25–6.9 (m, 4 H), 2.25 (s, 3 H).

***m*-Chlorophenyl methyl selenide (7b)**: bp 54–56 °C (0.1 mm) [lit.[20] bp 54–55 °C (0.2 mm)]; NMR δ 7.3 (m, 1 H), 7.2–7.0 (m, 3 H), 2.3 (s, 3 H).

***p*-Chlorophenyl methyl selenide (7c)**: mp 26–28 °C (lit.[22] mp 28–28.5 °C); NMR δ 7.25, 7.10 (AA′BB′, 4 H), 2.3 (s, 3 H).

***p*-Chlorophenyl ethyl selenide (10)**: bp 84–86 °C (3 mm) [lit.[23] bp 85 °C (1 mm)]; NMR δ 7.3, 7.1 (AA′BB′, 4 H), 2.85 (q, 2 H), 1.4 (t, 3 H).

***p*-Chlorophenyl isopropyl selenide (11)**: bp 55 °C (1.5 mm); NMR δ 7.35, 7.1 (AA′BB′, 4 H), 3.35 (septet (spt), 1 H), 1.35 (d, 6 H). Anal. Calcd for $C_9H_{11}ClSe$: C, 46.26; H, 4.75. Found: C, 46.52; H, 4.70.

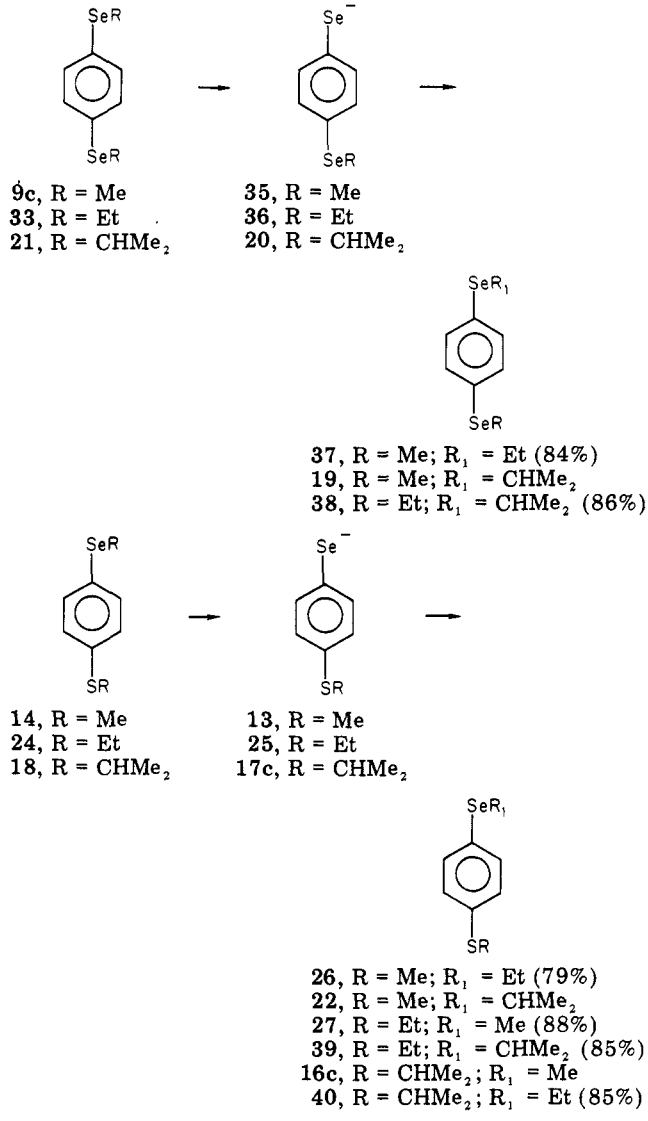
***p*-(Methylthio)phenyl methyl selenide (14)**: mp 74–75 °C; NMR δ 7.2, 7.0 (AA′BB′, 4 H), 2.4 (s, 3 H), 2.25 (s, 3 H). Anal. Calcd for $C_8H_{10}SSe$: C, 44.24; H, 4.65. Found: C, 44.02; H, 4.90.

***o*-(Isopropylthio)phenyl methyl selenide (16a)**: oil; NMR δ 7.35–6.95 (m, 4 H), 3.35 (spt, 1 H), 2.25 (s, 3 H), 1.3 (d, 6 H). Anal. Calcd for $C_{10}H_{14}SSe$: C, 48.97; H, 5.76. Found: C, 48.69; H, 5.74.

***m*-(Isopropylthio)phenyl methyl selenide (16b)**: oil; NMR δ 7.35 (m, 1 H), 7.15–7.0 (m, 3 H), 3.35 (spt, 1 H), 2.3 (s, 3 H), 1.25 (d, 6 H). Anal. Found: C, 48.68; H, 5.75. Dibromide: oil; NMR δ 7.85–7.2 (m, 4 H), 3.85 (s, 3 H), 3.45 (spt, 1 H), 1.35 (d, 6 H). Anal. Calcd for $C_{10}H_{14}Br_2SSe$: C, 29.65; H, 3.49. Found: C, 30.02; H, 3.38.

***p*-(Isopropylthio)phenyl methyl selenide (16c)**: oil; NMR δ 7.15 (s, 4 H), 3.2 (spt, 1 H), 2.25 (s, 3 H), 1.2 (d, 6 H). Anal.

Scheme VI



9c, R = Me
33, R = Et
21, R = $CHMe_2$

35, R = Me
36, R = Et
20, R = $CHMe_2$

37, R = Me; R_1 = Et (84%)
19, R = Me; R_1 = $CHMe_2$
38, R = Et; R_1 = $CHMe_2$ (86%)

14, R = Me
24, R = Et
18, R = $CHMe_2$

13, R = Me
25, R = Et
17c, R = $CHMe_2$

26, R = Me; R_1 = Et (79%)
22, R = Me; R_1 = $CHMe_2$
27, R = Et; R_1 = Me (88%)
39, R = Et; R_1 = $CHMe_2$ (85%)
16c, R = $CHMe_2$; R_1 = Me
40, R = $CHMe_2$; R_1 = Et (85%)

(19) NMR spectra were recorded ($CDCl_3$ solutions) at 90 MHz on a Varian EM-390 instrument. IR spectra were recorded in CH_2Cl_2 solutions on a Perkin-Elmer 1320 instrument. Elemental analyses were carried out on a C. Erba Elemental Analyzer, Model 1106. GLC analyses were performed on a Hewlett-Packard 5830 chromatograph with a 20-in. 10% UCW 982 column; quantitative analyses were effected with internal standards, and calibrations for area response differences were carried out for each reaction by using pure samples.

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Found: C, 48.70; H, 5.54. Dibromide: mp 76–77 °C; NMR δ 7.8, 7.35 (AA'BB', 4 H), 3.85 (s, 3 H), 3.5 (spt, 1 H), 1.25 (d, 6 H). Anal. Found: C, 29.15; H, 3.69.

p-(Isopropylthio)phenyl isopropyl selenide (18): oil; NMR δ 7.25, 7.15 (AA'BB', 4 H), 3.3 (2 spt, 2 H), 1.4 (d, 6 H), 1.25 (d, 6 H). Anal. Calcd for $C_{12}H_{18}SSe$: C, 52.73; H, 6.65. Found: C, 52.95; H, 6.33.

p-(Methylselenyl)phenyl isopropyl selenide (19): oil; NMR δ 7.35, 7.2 (AA'BB', 4 H), 3.35 (spt, 1 H), 2.3 (s, 3 H), 1.35 (d, 6 H). Anal. Calcd for $C_{10}H_{14}Se_2$: C, 41.11; H, 4.84. Found: C, 41.32; H, 4.75.

p-Bis(isopropylselenyl)benzene (21): oil; NMR δ 7.3 (s, 4 H), 3.4 (spt, 2 H), 1.4 (d, 12 H). Anal. Calcd for $C_{12}H_{18}Se_2$: C, 45.01; H, 5.68. Found: C, 45.36; H, 5.62.

p-(Methylthio)phenyl Isopropyl Selenide (22). This compound was obtained from the reaction of **11** with MeSNa under the same experimental conditions described above for the reactions with MeSeLi: oil; NMR δ 7.35, 7.05 (AA'BB', 4 H), 3.35 (spt, 1 H), 2.4 (s, 3 H), 1.35 (d, 6 H). Anal. Calcd for $C_{10}H_{14}SSe$: C, 48.97; H, 5.76. Found: C, 50.05; H, 5.68.

2-(Methylselenyl)biphenyl: oil; NMR δ 7.3–7.0 (m, 9 H), 2.1 (s, 3 H). Anal. Calcd for $C_{13}H_{12}Se$: C, 63.16; H, 4.90. Found: C, 63.53; H, 4.69.

3-(Methylselenyl)biphenyl: oil; NMR δ 7.5–7.1 (m, 9 H), 2.25 (s, 3 H). Anal. Found: C, 62.98; H, 5.02.

4-(Methylselenyl)biphenyl: mp 108–110 °C (lit.[24] mp 92 °C); NMR δ 7.6–7.1 (m, 9 H), 2.35 (s, 3 H). Anal. Found: C, 63.16; H, 5.02.

2-(Methylselenyl)naphthalene: mp 52–53 °C (lit.[25] mp 54 °C); NMR δ 7.7–7.15 (m, 7 H), 2.3 (s, 3 H).

4-(Methylselenyl)quinoline: mp 48–50 °C; NMR δ 8.5 (d, J = 4.5 Hz, 1 H), 8.0–7.65 (m, 2 H), 7.6–7.25 (m, 2 H), 7.05 (d, J = 4.5 Hz, 1 H), 2.35 (s, 1 H). Anal. Calcd for $C_{10}H_9NSe$: C, 54.06; H, 4.09. Found: C, 53.90; H, 4.27.

4-Biphenyl selenocyanate: mp 94 °C (lit.[26] mp 94 °C); NMR δ 7.6–7.2 (m); IR (CH_2Cl_2) 2155 cm^{-1}.

2-Naphthyl selenocyanate: mp 60–61 °C (lit.[25] mp 68 °C); NMR δ 7.9 (m, 1 H), 7.7–7.3 (m, 6 H); IR (CH_2Cl_2) 2155 cm^{-1}. Anal. Calcd for $C_{11}H_7NSe$: C, 56.91; H, 3.04; N, 6.03. Found: C, 56.65; H, 3.13; N, 6.02.

Dealkylation Reactions with MeSNa. General Procedure. A solution of the aryl alkyl selenide (0.01 mol) and MeSNa (0.06 mol) in DMF (20 mL) was stirred under nitrogen at 100 °C. The progress of the reaction was monitored by TLC and/or GLC after treatment of small aliquots of the reaction mixture with the appropriate alkyl iodide. The cooled reaction mixture was treated with the alkylating agents, poured on water, and worked up in the usual way. The residue was purified by column chromatography on silica gel by using mixtures of petroleum ether and ethyl ether as the eluant. Scheme IV summarizes the results obtained. Reaction yields are reported in the Results and Discussion. Physical and NMR data of the products obtained are reported below; reaction times are indicated first. Bis(isopropylselenyl)-benzene (**21**), obtained from **19** after 4.5 h, has been described above.

p-(Methylthio)phenyl ethyl selenide (26): 8 h; oil; NMR δ 7.3, 7.0 (AA'BB', 4 H), 2.85 (q, 2 H), 2.3 (s, 3 H), 1.4 (t, 3 H). Dibromide: mp 102–104 °C; NMR δ 7.7, 7.2 (AA'BB', 4 H), 4.15 (q, 2 H), 2.5 (s, 3 H), 1.85 (t, 3 H). Anal. Calcd for $C_9H_{12}Br_2SSe$: C, 27.64; H, 3.10. Found: C, 27.82; H, 3.11.

p-(Ethylthio)phenyl methyl selenide (27): 5 h; oil; NMR δ 7.25, 7.1 (AA'BB', 4 H), 3.85 (q, 2 H), 2.3 (s, 3 H), 1.25 (t, 3 H). Dibromide: mp 87–89 °C; NMR δ 7.7, 7.25 (AA'BB', 4 H), 3.85 (s, 3 H), 3.0 (q, 2 H), 1.35 (t, 3 H). Anal. Calcd for $C_9H_{12}Br_2SSe$: C, 27.64; H, 3.10. Found: C, 27.52; H, 3.21.

p-Methoxyphenyl ethyl selenide (30): 5 h; oil [lit.[27] bp 94–95 °C (1 mm)]; NMR δ 7.35, 6.7 (AA'BB', 4 H), 3.7 (s, 3 H), 2.8 (q, 2 H), 1.35 (t, 3 H). Dibromide: mp 104–106 °C; NMR δ 7.7, 6.9 (AA'BB', 4 H), 4.1 (q, 2 H), 3.8 (s, 3 H), 1.85 (t, 3 H). Anal. Calcd for $C_9H_{12}Br_2OSe$: C, 28.83; H, 3.23. Found: C, 29.02; H, 3.31.

Dealkylation Reactions with Sodium. General Procedure. To a solution of **19** or **16c** (0.01 mol) in HMPA (20 mL) stirred under nitrogen at 100 °C were added small pieces of sodium (4 equiv). The progress of the reaction was monitored by TLC and/or GLC after treatment of small aliquots of the reaction mixture with ethyl iodide. The cooled reaction mixture was treated with methyl, ethyl, or isopropyl iodide, poured on water, and worked up in the usual way. Purification of the residue was effected by column chromatography under the conditions described above. The results obtained are summarized in Scheme V. Physical and NMR data of compounds **21**, **14**, and **18** are reported above; those of the other compounds obtained are given below.

p-Bis(methylselenyl)benzene (9c): mp 80–81 °C (lit.[28] mp 81 °C); NMR δ 7.2 (s, 4 H), 2.3 (s, 6 H).

p-Bis(ethylselenyl)benzene (33): mp 18–20 °C; NMR δ 7.25 (s, 4 H), 2.85 (q, 4 H), 1.35 (t, 6 H). Anal. Calcd for $C_{10}H_{14}Se_2$: C, 41.11; H, 4.84. Found: C, 40.95; H, 4.90.

p-(Ethylthio)phenyl ethyl selenide (24): mp 28–29 °C; NMR δ 7.3, 7.1 (AA'BB', 4 H), 2.9 (q, 2 H), 2.85 (q, 2 H), 1.35 (t, 3 H), 1.25 (t, 3 H). Anal. Calcd for $C_{10}H_{14}SSe$: C, 48.97; H, 5.77. Found: C, 48.78; H, 5.66.

Dealkylation Reactions with a Solution of Sodium in HMPA. General Procedure. Small pieces of sodium (4–5 equiv) were added with stirring to HMPA (15 mL) kept under nitrogen at 100 °C. To the resulting solution was added dropwise the aryl alkyl selenide (0.01 mol) dissolved in the minimum amount of HMPA. The progress of the reaction was monitored as described above. The cooled reaction mixture was treated with the appropriate alkyl iodide, and the reaction products were isolated after the usual workup as reported above. The reactions effected and the products obtained are indicated under the Results and Discussion and summarized in Scheme VI. Compounds **26** and **27**, obtained from **14** and **24**, respectively, have been described above. Physical and NMR data for the remaining compounds are given below. (Reaction times were of the order of 1–3 h).

p-(Methylselenyl)phenyl ethyl selenide (37): oil; NMR δ 7.3, 7.15 (AA'BB', 4 H), 2.85 (q, 2 H), 2.3 (s, 3 H), 1.4 (t, 3 H). Anal. Calcd for $C_9H_{12}Se_2$: C, 38.86; H, 4.36. Found: C, 39.00; H, 4.13. This compound was also obtained from **33**.

p-(Ethylselenyl)phenyl isopropyl selenide (38): oil; NMR δ 7.3, 7.15 (AA'BB', 4 H), 3.35 (spt, 1 H), 2.85 (q, 2 H), 1.4 (t, 3 H), 1.35 (d, 6 H). Anal. Calcd for $C_{11}H_{16}Se_2$: C, 43.15; H, 5.28. Found: C, 43.00; H, 5.26.

p-(Ethylthio)phenyl isopropyl selenide (39): oil; NMR δ 7.35, 7.05 (AA'BB', 4 H), 3.35 (spt, 1 H), 2.9 (q, 2 H), 1.35 (d, 6 H), 1.25 (t, 3 H). Anal. Calcd for $C_{11}H_{16}SSe$: C, 50.95; H, 6.23. Found: C, 51.12; H, 6.44.

p-(Isopropylthio)phenyl ethyl selenide (40): oil; NMR δ 7.3, 7.15 (AA'BB', 4 H), 3.3 (spt, 1 H), 2.85 (q, 2 H), 1.4 (t, 3 H), 1.25 (d, 6 H). This compound was also obtained from **16c**. Dibromide: mp 78–80 °C; NMR δ 7.7, 7.3 (AA'BB', 4 H), 4.15 (q, 2 H), 3.5 (spt, 1 H), 1.85 (t, 3 H), 1.35 (d, 6 H). Anal. Calcd for $C_{11}H_{16}Br_2SSe$: C, 31.52; H, 3.86. Found: C, 31.80; H, 3.75.

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Registry No. **3a**, 108-90-7; **3b**, 108-86-1; **4**, 4346-64-9; **5**, 52251-58-8; **6a**, 95-50-1; **6b**, 541-73-1; **6c**, 106-46-7; **7a**, 1658-01-1; **7b**, 1694-00-4; **7c**, 37773-29-8; **8a**, 87136-85-4; **8b**, 87136-86-5; **8c**, 54019-84-0; **9a**, 84451-35-4; **9b**, 87136-87-6; **9c**, 40400-26-8; **10**, 52754-56-0; **11**, 87136-88-7; **12**, 123-09-1; **13**, 87136-89-8; **14**, 70086-65-6; **15a**, 34560-82-2; **15b**, 55698-06-1; **15c**, 7205-62-1; **16a**, 87136-90-1; **16b**, 87136-91-2; **16c**, 87136-92-3; **17a**, 87136-93-4; **17b**, 87136-94-5; **17c**, 87136-95-6; **18**, 87136-96-7; **19**, 87136-97-8; **20**, 87145-04-8; **21**, 87136-98-9; **22**, 87136-99-0; **23**, 87137-00-6; **24**, 87137-01-7; **25**, 87137-02-8; **26**, 87137-03-9; **27**, 87137-04-0; **28**, 1694-07-1; **29**, 87137-05-1; **30**, 37773-41-4; **32**, 87155-45-1; **33**, 87137-06-2; **34**, 87137-07-3; **35**, 87137-08-4; **36**, 87137-09-5; **37**, 87137-10-8; **38**, 87137-11-9; **39**, 87155-46-2; **40**, 87137-12-0; MeLi,

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Neighboring Group Participation in the Pyrrole Series[1]

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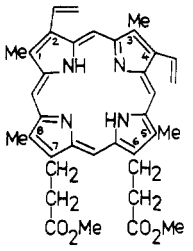
With use of proton and carbon-13 NMR spectroscopy of deuterium- and carbon-13-labeled substrates, the transformation of certain (2-hydroxyethyl)pyrroles (**4**, **18**, **21**) into the corresponding (2-haloethyl)pyrroles (using thionyl chloride/pyridine or triphenylphosphine/carbon tetrabromide) is shown to proceed with scrambling of the two carbons in the side chain. The mechanism is proposed to involve neighboring group participation by the pyrrole nucleus to give an ethylenepyrrolonium ion, **17**. When a nuclear ester is conjugated with the carbon bearing the hydroxyethyl side chain and the adjacent peripheral β position is unsubstituted (e.g., pyrrole **25**), the transformation into (2-chloroethyl)pyrrole **26** proceeds without scrambling. In contrast, the β-methylpyrrole **21** was transformed into a mixture of (2-chloroethyl)pyrroles (**33** and **34**) when treated with thionyl chloride/pyridine. Using carbon-13-enriched porphyrins, conversion of (2-hydroxyethyl)porphyrins into the corresponding 2-chloroethyl derivatives is shown to take place without scrambling of the side-chain carbons and therefore without anchimeric assistance by the porphyrin nucleus.

Several different types of strategy have been employed in synthetic approaches[2-8] to regioselectively labeled derivatives of protoporphyrin IX dimethyl ester (**1**). As the



corresponding iron(III) porphyrindicarboxylic acids (hemins), these compounds have been used successfully in a series of high-resolution NMR[9-22] and resonance Raman[23-25] studies of hemes, hemoproteins, and of various structure–activity relationships. It was anticipated[1] that a simple sequence of reactions (**2** → **7**) could be used to accomplish regioselective deuterium labeling of the α methylene groups in pyrrole **7** and that this could be built into the corresponding labeled protoporphyrin IX dimethyl ester (**1**).[26,27] In this paper we report on our attempts to

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(26) These methylene groups are the only protons in protoporphyrin IX dimethyl ester (1), which we have, so far, failed to deuterate regioselectively. They are of critical importance since their labeling will solve the problem of "non-heme" resonances in the proton NMR spectra of several hemoproteins. In certain of these spectra the number of resonances experiencing hyperfine shifts is greater than the number of protons in the hemes that need to be identified, and the extra resonances are no doubt associated with protein resonances in the heme pocket that are in close proximity to the iron atom; labeling of the methylenes in the propionic side chains that are adjacent to the porphyrin ring will finally enable the "non-heme" resonances to be recognized by difference spectroscopy.
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