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Synthesis and Multinuclear Magnetic Resonance Study of Para-Substituted Phenyl Selenobenzoates

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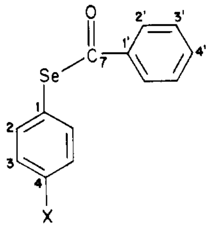
Eleven para-substituted *Se*-phenyl selenobenzoates, nine of which have not been previously reported, have been synthesized and characterized. The substituents include NO_2, CN, $C(O)CH_3$, $C(O)OCH_2CH_3$, F, Cl, Br, CH_3, OCH_3, and $N(CH_3)_2$. Selenium-77 and carbon-13 NMR chemical shifts and $^{77}Se-^{13}C$ spin-spin coupling constants have been obtained and assigned. Infrared carbonyl absorption frequencies were also determined. Selenium-77 chemical shifts ranged from 622.9 ppm for the dimethylamino-substituted compound to 650.4 ppm for the cyano-substituted compound. Single- and dual-substituent parameter analyses of the substituent chemical shifts for ^{77}Se, C-1 of the phenyl ring, and the carbonyl carbon were performed. Single- and dual-substituent parameter analyses of the infrared carbonyl absorptions were done in conjunction with the above correlations. Although the ^{77}Se chemical shift data did not give a good "fit", all other treatments gave an excellent fit. These results indicate that mesomeric substituents interact strongly with the aromatic ring and that the SeC(O)Ph moiety is electron deficient with respect to the substituted benzene.

The recent application[2] of selenium-77 nuclear magnetic resonance spectroscopy to proteins to which selenium was covalently bound by modification with 6,6′-diselenobis(3-nitrobenzoic acid) (DSNB)[3] demonstrated the feasibility of this technique to study selenium in biomolecules. This study represented our initial step in the use of NMR to investigate both naturally occurring macromolecules containing selenium and selenium analogues of selected oxygen and sulfur biomolecules. In view of the less than 1% natural abundance of ^{33}S and ^{17}O, and the quadrupolar nature of these nuclei, the 7.5% natural abundance of ^{77}Se and its nuclear spin ($I = {}^1/_2$) make it particularly useful and appealing as an NMR probe. The wide chemical shift range of selenium-77 (~2800 ppm) and its sensitivity to its electronic environment are features that are particularly useful for macromolecular NMR studies.[4] Further use of this technique not only requires a compilation of chemical shift data for various classes of selenium-containing compounds but also necessitates at least an empirical understanding of physical phenomena affecting chemical shift changes.

Our group has adopted several strategies for the incorporation of selenium into biological systems. In addition to the modification of proteins by the reagent DSNB, we are currently investigating methods for the conversion of seryl or cysteinyl peptides to their corresponding selenocysteinyl analogues with the intention of extending this approach to the modification of proteins, such as chymotrypsin and papain. In a second strategy we are preparing selenium-containing substrates and inhibitors of seryl proteases and plan to characterize their interactions with enzymes such as chymotrypsin by ^{77}Se NMR spectroscopy and biochemical means. Both of these research objectives involve the synthesis and characterization of a variety of biological selenol esters.

In conjunction with the above goals, it was necessary to systematically evaluate the spectroscopic properties (i.e., ^{77}Se and ^{13}C chemical shifts, coupling constants, carbonyl infrared absorption frequencies) of a carefully selected series of model selenol esters. This study was conducted to allow a meaningful interpretation of data obtained from the biological systems. At present, two reports have appeared in the literature dealing with ^{77}Se NMR studies of selenol esters. Jakobsen and co-workers[5] presented the first directly determined ^{77}Se chemical shifts for three selenol esters and Baiwir and co-workers[6] investigated variations in $\delta(^{77}Se)$ with the nature of R and R′ in a wide variety of selenol esters RSeC(O)R′. The latter report served the purpose of establishing the chemical shift range of this class of compounds.

In this investigation, we have determined ^{77}Se and ^{13}C chemical shifts, $^{77}Se-^{13}C$ spin-spin coupling constants, and infrared carbonyl absorption frequencies for a representative series of para-substituted *Se*-phenyl selenobenzoates (1) where X is NMe_2, OMe, CH_3, H, F, Cl, Br, $C(O)CH_3$, C(O)OEt, CN, and NO_2. The substituents were chosen because they generally display a wide range of electronic effects. The resulting data have been subjected to single- and dual-substituent parameter analyses, thus providing an electronic description of these molecules.



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Results and Discussion

The aryl selenobenzoates **1a–c** were prepared by the

$$p\text{-}X\text{-}C_6H_4\text{-}Se\text{-}C(O)\text{-}C_6H_5$$

1

a, X = H; **b**, X = CH_3; **c**, X = OCH_3; **d**, X = Cl;
e, X = Br; **f**, X = NO_2; **g**, X = CN; **h**, X = $C(O)CH_3$;
i, X = $C(O)OC_2H_5$; **j**, X = F; **k**, X = $N(CH_3)_2$

reaction sequence shown in eq 1. The aryl selenobenzoates **1d,e** were prepared by the reaction sequence shown in eq

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[1] Taken in part from the thesis of G. P. Mullen, to be submitted to the Department of Chemistry in partial fulfillment of the requirements for the Ph.D. degree.

[2] Luthra, N. P.; Costello, R. C.; Odom, J. D.; Dunlap, R. B. *J. Biol. Chem.* **1982**, *257*, 1142.

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[6] Baiwir, M.; Llabres, G.; Piette, J. L.; Christiaens, L. *Spectrochim. Acta, Part A* **1982**, *38A*, 575.

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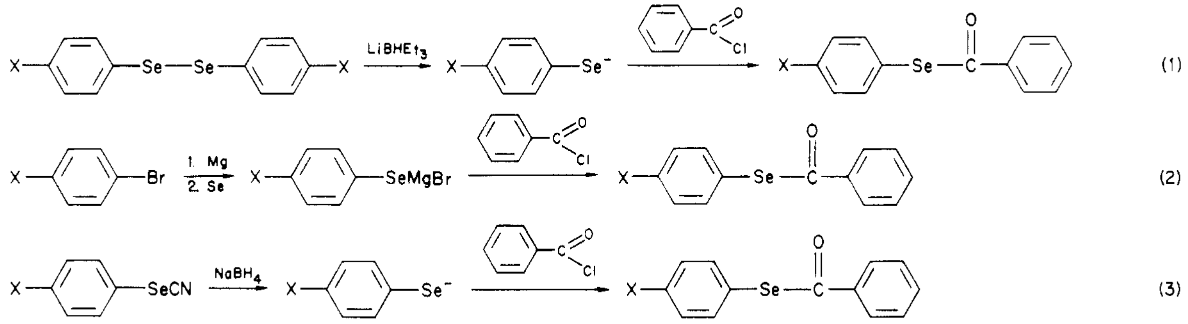

Table I. Selenium-77 and Carbon-13 NMR Parameters and Infrared Carbonyl Absorption Frequencies of Para-Substituted *Se*-Phenyl Selenobenzoates (1a–k)

substituent	$\delta(^{77}\mathrm{Se})^a$	$\delta(\mathrm{C}\text{-}1)^b$	$\delta(\mathrm{C}\text{-}2)^b$	$\delta(\mathrm{C}\text{-}3)^b$	$\delta(\mathrm{C}\text{-}4)^b$	$\delta(\mathrm{C}\text{-}1')^b$	$\delta(\mathrm{C}\text{-}2')^b$	$\delta(\mathrm{C}\text{-}3')^b$	$\delta(\mathrm{C}\text{-}4')^b$	$\delta(\mathrm{C}\text{-}7)^b$	$J_{\mathrm{Se-C\text{-}2}}{}^c$	$J_{\mathrm{Se-C\text{-}2'}}{}^c$	$\nu_{\mathrm{C=O}}{}^d$
NO_2	645.7	134.6	136.5	123.8	148.0	137.7	127.3	129.0	134.3	190.9	10.24	11.27	1690
CN	650.4	132.3	136.3	132.2	112.5	137.7	127.2	128.9	134.2	191.0	9.89	11.21	1690
$COCH_3$	642.7	132.0	135.9	128.6	135.6	138.0	127.2	128.8	133.9	191.8	9.80	10.98	*e*
CO_2Et	642.3	131.6	135.8	130.0	130.8	138.2	127.2	128.9	134.0	191.9	*f*	*f*	1689
Br	637.4	124.5	137.7	132.4	123.7	138.1	127.2	128.9	133.9	192.4	9.90	10.88	1686
Cl	637.0	123.9	137.4	129.4	135.4	138.1	127.2	128.8	133.9	192.4	10.00	10.92	1685
H	641.5	125.8	136.1	129.2	128.8	138.4	127.2	128.8	133.7	193.0	9.51	10.80	1686
F[g]	634.4	120.5	138.2	116.2	163.3	138.2	127.2	128.8	133.8	192.9	*h*	10.94	1683
CH_3	634.4	122.1	136.1	130.0	139.0	138.5	127.1	128.7	133.6	193.4	9.58	10.78	1684
OCH_3	628.9	116.0	137.6	115.0	160.3	138.4	127.1	128.7	133.6	193.9	10.34	10.70	1680
NMe_2	622.9	110.7	137.2	113.1	150.7	138.7	127.1	128.7	133.4	195.0	9.83	*i*	1676

[a] In ppm from $(CH_3)_2Se$ (60% in $CDCl_3$). [b] In ppm from Me_4Si. [c] In Hz. [d] In cm^{-1}. [e] not observed. [f] Not obtained. [g] $^{19}F-^{13}C$ spin–spin coupling was as follows: C4, 249.26 Hz; C3, 21.74 Hz; C2, 8.24 Hz; C1, 3.52 Hz. [h] Not observed due to ^{19}F coupling. [i] Not observed due to decomposition.

2. The remaining compounds **1f–k** were prepared by the reaction sequence shown in eq 3. Selenium-77 and carbon-13 chemical shift data for these para-substituted *Se*-phenyl selenobenzoates are given in Table I. Also, provided in Table I are the $^{77}Se-^{13}C$ spin–spin coupling constants, which were obtained from the ^{77}Se satellites in the ^{13}C spectra. The values of these coupling constants were used to some extent in the assignment of carbon-13 resonances. The benzoyl moiety substituted at selenium causes a predictable deshielding of the selenium resonance ($\delta(^{77}Se)$ 641) when compared to diphenyl selenide ($\delta(^{77}Se)$ 412) and selenoanisole ($\delta(^{77}Se)$ 202). The chemical shifts for the parent compound, $C_6H_5SeC(O)C_6H_5$,[6] and the *p*-methyl derivative[5] have been previously reported. In the report by Baiwir et al.[6] the ^{77}Se chemical shift for the *Se*-phenyl selenobenzoate is 13 ppm shielded from the value determined in this study, while in the report by Jakobsen et al.[5] the value for the *Se*-*p*-methyl selenobenzoate is identical. In a recent review,[4] we have noted discrepancies of up to 20 ppm for a variety of organoselenium compounds. These discrepancies can arise from the following factors: (1) concentration effects, (2) solvent effects, and (3) temperature effects on the ^{77}Se shielding of either the reference compound or the molecules under investigation. To provide some degree of uniformity and to enable researchers to compare data from different laboratories, care must be taken to state clearly the three factors described above.[7] This information is provided in the Experimental Section.

The carbonyl stretching frequencies for these compounds are also summarized in Table I. The carbonyl stretching frequency for the *p*-acetyl-substituted ester could not be obtained due to overlap with the carbonyl stretch of the acetyl group. The carbonyl stretch for the *p*-carboethoxy derivative was observed as a shoulder.

The ^{77}Se substituent chemical shifts (SCS) for aryl selenobenzoates cover a range of approximately 28 ppm. In contrast, the ^{77}Se chemical shifts of 4,4′-disubstituted diphenyl selenides[8] and 4-substituted selenoanisoles[9] are twice as sensitive to substituent effects and range over 50 ppm for similar substituents. Thus, it appears that the sensitivity to the substituent effect decreases if the selenium is bound to an electron-withdrawing group. The ^{77}Se NMR data given in Table I were analyzed by an intercept regression equation using σ and σ^+ substituent constants, and the best fit is obtained with the σ^+ scale of Brown and Okamoto.[10] The square of the correlation coefficient, r^2, is relatively low (0.88) indicating more of a trend than a good fit. Better correlations are obtained when the car-

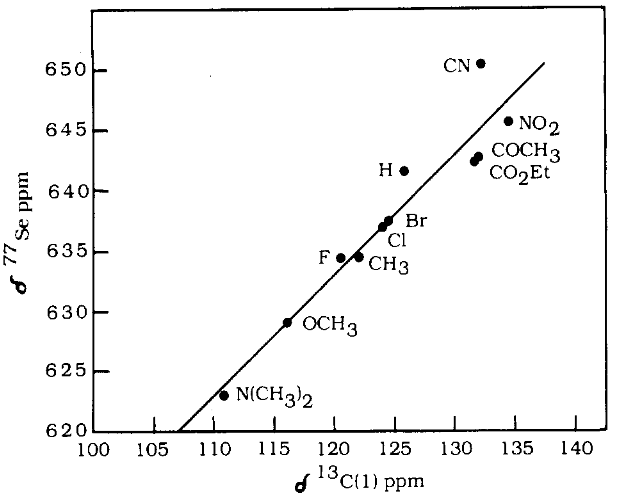

Figure 1. Plot of ^{77}Se chemical shifts vs. ^{13}C-1 chemical shifts for system 1 in $CDCl_3$.

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bon-13 chemical shifts of the ipso carbon (C-1), the carbon-13 chemical shifts of the carbonyl carbon (C-7), and the infrared stretching frequencies of the carbonyl group were fitted by an intercept equation using σ^+ substituent constants. The squares of the correlation coefficient, r^2, are 0.92, 0.94, and 0.96, respectively. Although at C-1 the r^2 for the extended Hammett[10b] σ scale gave the same value, C-7 and the infrared stretching frequencies of the carbonyl group are fitted best by the σ^+ substituent scale. In Figure 1 is a plot of ^{77}Se vs. C-1 chemical shifts. A relatively good linear relationship is obtained ($r^2 = 0.92$), indicating that substituents are effecting shielding at these two nuclei in a similar manner.

In an attempt to gain further information, the effects of substituents in the 4-position were separated into their polar and resonance contributions by means of the following dual-substituent parameter (DSP) equation.[11]

$$\mathrm{SCS} = \rho_I\sigma_I + \rho_R\bar{\sigma}_R \tag{4}$$

As stated by Craik and Brownlee, in the DSP equation, the SCS values are related to a linear combination of previously defined polar and resonance substituent parameters (σ_I and $\bar{\sigma}_R$, respectively).[12] The symbol $\bar{\sigma}_R$ denotes that any of four resonance scales ($\bar{\sigma}_R$, $\sigma_R{}^0$,[11c] $\sigma_R{}^{BA}$, $\sigma_R{}^+$) may be used for a given correlation.[12] It is usual practice to perform four separate correlations, each with a different resonance scale and then to utilize that scale which yields the best fit to the experimental data. The "goodness of fit" of a DSP correlation is judged from the "f" value[11a,12] where

$$f = \mathrm{SD}/\mathrm{RMS} \tag{5}$$

Here, SD is the standard deviation of the fit and RMS represents the root mean square value of the experimental data. In practice, $f = 0.0$–0.1 represents a moderately good correlation, and f values of 0.3 and greater represent only crude trends.[12]

A correlation analysis of the ^{77}Se chemical shift data, the ^{13}C chemical shift data (C-1 and carbonyl carbon), and the carbonyl stretching frequency data of the aryl selenobenzoates studied has been carried out using Taft's dual-parameter equation. The appropriate correlations are shown below:

$$\begin{gathered}{}^{77}\mathrm{Se\ SCS} = 2.9\sigma_I + 22.1\sigma_R{}^{BA}\\ n = 10, \quad \mathrm{SD} = 2.85, \quad f = 0.33\end{gathered} \tag{6}$$

$$\begin{gathered}{}^{77}\mathrm{Se\ SCS} = 2.5\sigma_I + 30.7\sigma_R{}^{0}\\ n = 10, \quad \mathrm{SD} = 3.22, \quad f = 0.37\end{gathered} \tag{7}$$

$$\begin{gathered}{}^{77}\mathrm{Se\ SCS} = 3.1\sigma_I + 12.2\sigma_R{}^{+}\\ n = 10, \quad \mathrm{SD} = 2.93, \quad f = 0.34\end{gathered} \tag{8}$$

$$\begin{gathered}{}^{13}\mathrm{C\ SCS(C\text{-}1)} = 7.2\sigma_I + 28.2\sigma_R{}^{0}\\ n = 10, \quad \mathrm{SD} = 0.18, \quad f = 0.024\end{gathered} \tag{9}$$

$$\begin{gathered}{}^{13}\mathrm{C\ SCS(C{=}O)} = -2.7\sigma_I - 2.7\sigma_R{}^{BA}\\ n = 10, \quad \mathrm{SD} = 0.07, \quad f = 0.055\end{gathered} \tag{10}$$

$$\begin{gathered}\nu^{X}{}_{C=O} - \nu^{H}{}_{C=O} = 4.2\sigma_I + 12.0\sigma_R{}^{BA}\\ n = 9, \quad \mathrm{SD} = 0.40, \quad f = 0.083\end{gathered} \tag{11}$$

^{77}Se Correlation Equations. The data for ^{77}Se SCS were not fitted to acceptable precision by any of the σ_R parameters. The "goodness of fit" f values were all found to be poor ($f \geq 0.33$; eq 6–8) for the $\sigma_R{}^0$, $\sigma_R{}^{BA}$, and $\sigma_R{}^+$ scales whereas the fit to the $\sigma_R{}^-$ scale was even worse. However, if the ^{77}Se chemical shift of the 4-CN selenol ester was not included in the data, eq 8 produced an improved correlation (eq 12). The f value of the fit decreased

$$\begin{gathered}{}^{77}\mathrm{Se\ SCS} = 0.42\sigma_I + 11.6\sigma_R{}^{+}\\ n = 9, \quad \mathrm{SD} = 2.03, \quad f = 0.24\end{gathered} \tag{12}$$

substantially for the correlation with $\sigma_R{}^+$. Substantial improvement was not obtained when the ^{77}Se SCS data were correlated with other scales. Also, omission of the chemical shift of any other derivative from the correlation did not improve the precision of the fit.

It has been recommended by Taft and co-workers,[11a] that to be able to apply eq 4 to a series, data with a minimal basis set of substituents are required to offer substantial assurance of a critical analysis. The substituents considered for such a minimal basis set are the following: any two of $N(CH_3)_2$, NH_2, or OCH_3, any two mesomeric withdrawing substituents of CF_3, CO_2R, CH_3CO, CN, or NO_2, both H and CH_3, and any two halogens (but not both Cl and Br). Even if the chemical shift of the cyano group is excluded, the ^{77}Se chemical shift data contain more than the minimal basis set of substituents. One of the consequences of rejecting the ^{77}Se chemical shift of the 4-cyano derivative is the increase in the value of the ratio, λ, of the resonance coefficient, ρ_R, to the polar field coefficient, ρ_I, from 3.9 to 28. This demonstrates a high degree of resonance interaction relative to the polar field effect. The fitting of eq 4 to the data could be further improved by inclusion of a third parameter as a constant intercept (eq 13). The low f value obtained in eq 13 is due to exclusion

$$\begin{gathered}{}^{77}\mathrm{Se\ SCS} = 9.7\sigma_I + 17.5\sigma_R{}^{BA} - 4.6\\ n = 9, \quad \mathrm{SD} = 0.34, \quad f = 0.04\end{gathered} \tag{13}$$

of the ^{77}Se chemical shift of the selenol ester where hydrogen is the substituent in the para position. If the chemical shift of this compound is included, then eq 14

$$\begin{gathered}{}^{77}\mathrm{Se\ SCS} = 6.5\sigma_I + 18.7\sigma_R{}^{BA} - 3.0\\ n = 10, \quad \mathrm{SD} = 1.45, \quad f = 0.18\end{gathered} \tag{14}$$

is obtained, which still gives a fit substantially better than that found in eq 12, although according to Taft[11] the use of an intercept is contrary to the application of a DSP treatment.

More recently it has been shown[13] that the DSP equation (eq 4) may be inadequate for systems where the substituents may interact strongly with other groups and a modified DSP equation (eq 15) has been formulated to

$$\mathrm{SCS} = \rho_I\sigma_I + \rho_R\sigma_R{}^0/1 - \epsilon\sigma_R{}^0 \tag{15}$$

include an "electron demand parameter", ϵ. This modified DSP nonlinear regression (DSP-NLR) equation has been most successful in the treatment of data for series that had a large λ value ($\lambda = \rho_R/\rho_I$, vide supra) in a DSP analysis.

Because we felt that (1) the SeC(O)Ph moiety was interacting strongly with the para substituent, (2) the λ value was large, and (3) the substituents that had been used met the basis set required[12] for a DSP-NLR analysis, eq 15 was used to analyze our ^{77}Se chemical shift data. Whereas the "normal" DSP treatment for nine data points (CN excluded) yielded eq 16, a DSP-NLR treatment with ϵ =

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[11] (a) Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W. *Prog. Phys. Org. Chem.* **1973**, *10*, 1. (b) Topsom, R. D. *Prog. Phys. Org. Chem.* **1976**, *12*, 1. (c) Bromilow, J.; Brownlee, R. T. C.; Lopez, V. O.; Taft, R. W. *J. Org. Chem.* **1979**, *44*, 4766. (d) Reynolds, W. F. *J. Chem. Soc., Perkin Trans. 2* **1980**, 985.

[12] Craik, D. J.; Brownlee, R. T. C. *Prog. Phys. Org. Chem.* **1983**, *14*, 1.

[13] Bromilow, J.; Brownlee, R. T. C.; Craik, D. J.; Sadek, M.; Taft, R. W. *J. Org. Chem.* **1980**, *45*, 2429.

$$
\begin{gathered}
{}^{77}\mathrm{Se\ SCS} = -0.13\sigma_{\mathrm{I}} + 29.1\sigma_{\mathrm{R}}{}^{0} \\
n = 9, \quad \mathrm{SD} = 2.65, \quad f = 0.31
\end{gathered} \qquad (16)
$$

-0.70 gave an improved fit (eq 17).

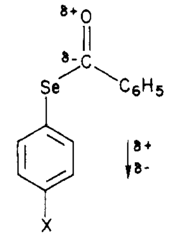
$$
\begin{gathered}
{}^{77}\mathrm{Se\ SCS} = 0.46\sigma_{\mathrm{I}} + 20.9\sigma_{\mathrm{R}}{}^{0}(1 + 0.70\sigma_{\mathrm{R}}{}^{0}) \\
n = 9, \quad \mathrm{SD} = 2.01, \quad f = 0.24
\end{gathered} \qquad (17)
$$

We next examine the validity of employing the DSP-NLR treatment to side-chain chemical-shift data. Equation 15 modifies $\sigma_R{}^0$ values to account for interactions of a substituent with some group meta or para with respect to it. One of the consequences of using eq 15 is that it modifies to a greater extent the $\sigma_R{}^0$ constants that have large values. Also, the higher the value of the electron-demand parameter, ϵ, the greater the changes in $\sigma_R{}^0$ values. For example, if $\sigma_R{}^0 = -0.5$ and the demand parameter equals -1, the $\bar{\sigma}_R$ term ($\sigma_R{}^0/1 - \epsilon\sigma_R{}^0$) also equals -1 (more than twice the original value). In effect, an appropriately chosen ϵ value can convert the $\sigma_R{}^0$ scale to one of the other three scales. We have carried out such an analysis and the results are provided in Table II. For each substituent in Table II, literature values of $\bar{\sigma}_R{}^{11a}$ along with the best calculated values of $\bar{\sigma}_R$ that we obtained using the expression $\bar{\sigma}_R = a\sigma_R{}^0/1 - \epsilon\sigma_R{}^0$, where "a" is a constant, are given. Table II also provides the values of r^2, a, and ϵ for each correlation. The correlation of $\sigma_R{}^+$ and $\sigma_R{}^{BA}$ with the calculated values is excellent ($r^2 = 0.99$ for both). The values of ϵ for $\sigma_R{}^{BA}$ and $\sigma_R{}^+$ are -0.50 and -1.25, respectively. These values of ϵ fall within the limit recommended by Bromilow and co-workers.[13] The correlation of $\sigma_R{}^-$ with the calculated value is not as high ($r^2 = 0.97$) but is certainly reasonable. The value of ϵ (+2.15) is also higher than the limiting value.

In principle, it would appear that one can go from the $\sigma_R{}^0$ scale to any of the other substituent scales or some intermediate scale using the relationship involving $\sigma_R{}^0$ and an electron demand parameter, ϵ. In the above context, the DSP-NLR analysis of the ^{77}Se SCS data (eq 17) for aryl selenobenzoates has essentially modified the $\sigma_R{}^0$ parameters so that the new values are in proximity to the $\sigma_R{}^+$ scale values. We also found that a better correlation is obtained if the DSP-NLR treatment is applied using the $\sigma_R{}^+$ scale ($f = 0.19$); however, we believe this to only be a further minimization based on eq 15. We feel the utility of using four resonance scales is twofold: (1) to provide a clear separation of polar and resonance effects and (2) to provide a discrimination between reaction types (or probe type for NMR data). On the basis of these results (Table II) we find no chemical basis for the fitting of the DSP-NLR equation to the side-chain chemical shift data.

Carbon-13 Correlation Equations. A DSP treatment of the ^{13}C SCS at the ipso carbon (C-1) yields a correlation (eq 9) whose precision of fit ($f = 0.025$) is comparable to that observed in model compounds of Bromilow et al.[13] (E.g., ^{13}C SCS data for para-substituted benzenes in $CDCl_3$ gave $f = 0.03$.) Generally such low f values are obtained for series containing noninteracting or weakly interacting substituents ($f = 0.04$ for Cl and Br substituents). As with the ^{77}Se chemical shift data, the predominant contribution to the C-1 chemical shift is a resonance or π-delocalization effect with a lesser contribution from the effect of substituent-induced polarization of the ring π elections with no delocalization. A significant observation is that, contrary to our ^{77}Se SCS treatment, inclusion of the ^{13}C SCS value of the p-cyanophenyl selenobenzoate did not produce a poorer correlation.

A DSP analysis of the ^{13}C SCS data for the carbonyl carbon (C-7, eq 10) yields an excellent fit ($f = 0.055$) using the $\sigma_R{}^{BA}$ scale. The ^{13}C resonance in these compounds exhibits a reverse substituent chemical shift dependence, i.e., electron-withdrawing substituents cause the C-7 resonance to become more shielded. This has been observed[14] previously in similar compounds and presumably results from the interaction of the substituent dipole with the side chain (in this case, SeC(O)Ph) π-system. This interaction effect results in the polarization shown in **2**. A comparison of systems where methylene,[14] oxygen,[14] or selenium is the atom or group attached to the ipso carbon shows that selenium enhances transmission of the polar field effect. With selenium, this effect, which has been shown[14] to be distance dependent, is comparable to that observed for substitution of the carbonyl group directly attached to the phenyl ring (Table III). Thus, the ρ_I value of the carbonyl group in para-substituted phenyl acetic acid[14] ($\rho_I = -1.2$) and para-substituted phenylacetate[14] ($\rho_I = -1.4$) is approximately half as much as that of para-substituted phenyl selenobenzoates ($\rho_I = -2.7$, eq 10). For comparison the ρ_I value of para-substituted ethyl benzoate[14] is -2.6.



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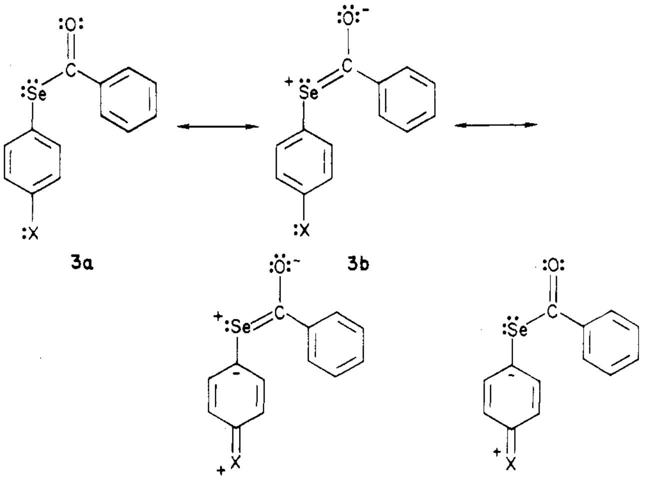
The ρ_R value in the ^{13}C SCS C-7 correlation (eq 10) is also negative and of greater magnitude than values for para-substituted phenyl acetic acids or para-substituted phenyl acetates (Table III). In all three series the value of λ is approximately 1. The negative ρ_R value most likely can be interpreted in terms of resonance structures **3a–d**.



3a **3b** **3c** **3d**

In these structures the substituent X is depicted as having an unshared pair of electrons since from our previous discussion of ^{77}Se chemical shifts it is clear that electron-donating substituents play a dominant role in determining the ^{77}Se chemical shifts. Also, the contribution to the overall electronic structure from **3c** will increase if X can provide electron density to selenium as shown. In addition, since the polarizable C=O group is formally insulated from the benzene ring, a secondary resonance structure **3d** in

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[14] Bromilow, J.; Brownlee, R. T. C.; Craik, D. J.; Fiske, P. R.; Rowe, J. E.; Sadek, M. *J. Chem. Soc., Perkin Trans. 2* **1981**, 753.

Table II. Comparison of Taft's Values of Substituent Constants ($\bar{\sigma}_R$) with Calculated Values Using the Relationship $\bar{\sigma}_R = a[\sigma_R{}^0/1 - \epsilon\sigma_R{}^0]$

substituent	$\sigma_R{}^{0\,a}$	$\sigma_R{}^{BA\,b}$	calcd $\sigma_R{}^{BA} = a[\sigma_R{}^{0\,c}/(1 - \epsilon\sigma_R{}^0)]$	$\sigma_R{}^{+\,b}$	calcd $\sigma_R{}^{+} = a[\sigma_R{}^{0\,d}/(1 - \epsilon\sigma_R{}^0)]$	$\sigma_R{}^{-\,b}$	calcd $\sigma_R{}^{-} = a(\sigma_R{}^{0\,e}/\epsilon\sigma_R{}^0)$
NO_2	0.15	0.15	0.15	0.15	0.17	0.46	0.39
$COCH_3$	0.16	0.16	0.16	0.16	0.17	0.47	0.43
$COOC_2H_5$	0.16	0.14	0.16	0.14	0.18	0.34	0.43
Br	−0.16	−0.19	−0.19	−0.30	−0.25	−0.19	−0.21
Cl	−0.18	−0.23	−0.22	−0.36	−0.30	−0.23	−0.23
F	−0.31	−0.45	−0.40	−0.57	−0.62	−0.45	−0.33
CH_3	−0.13	−0.11	−0.15	−0.25	−0.20	−0.11	−0.18
OCH_3	−0.42	−0.61	−0.59	−1.02	−1.01	−0.45	−0.39
$N(CH_3)_2$	−0.55	−0.83	−0.85	−1.75	−1.75	−0.34	−0.45

[a] Reference 11c. [b] Reference 11a. [c] $r^2 = 0.997$; $a = 1.09$; $\epsilon = -0.54$. [d] $r^2 = 0.996$; $a = 1.35$; $\epsilon = 1.05$. [e] $r^2 = 0.960$; $a = 1.77$; $\epsilon = +2.15$.

Table III. Comparison of ρ_I Values from DSP Analysis of Carbonyl Side-Chain SCS Data

molecular series	ρ_I	ρ_R
p-XPhSeCOPh	−2.7[a]	−2.7[a]
p-XPhOCOCH$_3$	−1.4[b]	−1.7[b]
p-XPhCH$_2$COOH	−1.2[b]	−1.0[b]
p-XPhCOOEt	−2.6[b]	−1.1[b]
p-XPhCOOH	−2.3[b]	−0.5[b]
p-XPhCOCH$_3$	−2.6[b]	+0.8[b]

[a] This work. [b] Reference 11d.

which resonance stabilization by the substituent induces a dipole in the benzene ring, which then polarizes the distant carbonyl group, can contribute to the ^{13}C chemical shift. This is similar to a field effect except that the magnitude of polarization of C=O is proportional to the σ_R values of the substituents.

Infrared Spectra. The DSP analysis of the infrared carbonyl stretching frequencies with a predominant contribution from $\sigma_R{}^{BA}$ is shown in eq 11. From the data in Table I, it is apparent that electron-donating substituents affect the stretching frequencies to a greater extent than electron withdrawing groups. For example, the carbonyl stretching frequency of the 4-NMe$_2$ derivative is 10 cm^{-1} less than the parent compound whereas that of 4-NO$_2$ derivative is only 4 cm^{-1} greater than the parent compound. This trend can be interpreted in terms of contributions from resonance structure **3c**.

Conclusions. The fitting of the $\sigma_R{}^{BA}$ scale for both the ^{13}C SCS C-7 and the carbonyl infrared DSP analyses indicates that mesomeric donating substituents are interacting with the aromatic ring. Certainly, mesomeric withdrawing substituents do not compete for a nonbonding selenium orbital and all DSP analyses point to an $n_{Se} \rightarrow \pi_{CO}{}^*$ interaction as illustrated by resonance structures **3b** and **3c**. The SeC(O)Ph moiety is clearly electron deficient with respect to the substituted benzene in these selenol esters.

^{77}Se chemical shifts have proven to be somewhat puzzling in this study. An induced dipole in the aromatic ring does not have a significant effect on these ^{77}Se chemical shifts. However, an intercept correlation has established that a substantial polar field effect is operable. The poor fitting of ^{77}Se SCS data to a DSP equation, regardless of the method used, in conjunction with the excellent fit of the ^{13}C SCS data in the same compounds, points out the need for further studies of correlations of various parameters of "heavy" nuclei. At first glance, it would appear that these resonance scales are incapable of treating ^{77}Se NMR data with the same precision as NMR data of "light" nuclei (e.g., ^{13}C, ^{15}N, ^{17}O, ^{19}F). However, that conclusion would be rather hasty. Chemical shifts of these heavier nuclei are not well understood and, clearly, with many more electrons and a much more polarizable electron cloud, subtle effects may be observed in their chemical shifts that have not been dealt with in nuclei of the second row of the periodic table.

Experimental Section

Spectral and Analytical Data. Selenium-77 NMR spectra were obtained in the Fourier transform mode on a Bruker WP-200 superconducting spectrometer (38.17 MHz). Measurements were made at 22 ± 1 °C in 10-mm NMR tubes using CDCl$_3$ as an internal lock solvent. Spectra were acquired by using inverse gated decoupling. Sample concentrations ranged from 0.14 to 0.19 M in CDCl$_3$. A ^{77}Se chemical shift concentration dependence study for *p*-ClC$_6$H$_4$SeC(O)C$_6$H$_5$ in CDCl$_3$ exhibited only a 0.2 ppm change in the concentration range 0.026–0.880 M. Similarly, *p*-NO$_2$C$_6$H$_4$SeC(O)C$_6$H$_5$ in CDCl$_3$ had the same chemical shift at 0.06 and 0.17 M concentration. Chemical shifts were measured with respect to (CH$_3$)$_2$Se (60% in CDCl$_3$) and are accurate to ±0.05 ppm. A positive chemical shift denotes resonances deshielded from the reference. Carbon-13 spectra were obtained in 5-mm tubes on an IBM NR-80B spectrometer (20.11 MHz). Measurements were made at ambient probe temperature using CDCl$_3$ as an internal lock solvent with sample concentrations ranging from 0.3 to 0.6 M. Chemical shifts are reported with respect to Me$_4$Si with a positive value denoting a resonance deshielded from the reference and are accurate to ±0.05 ppm. ^{77}Se–^{13}C spin–spin coupling constants are accurate to ±0.3 Hz. Infrared spectra were obtained on a Beckman IR 4210 spectrometer in 1-mm CaF$_2$ cells. Sample concentrations were 7 mM in Baker spectral grade CHCl$_3$. Measurements are accurate to ±0.5 cm^{-1}.

Melting points were obtained on a Büchi capillary melting point apparatus. Melting points and boiling points are both uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. All solvents were reagent grade and appropriately distilled by known methods. Benzoyl chloride was distilled under vacuum before use. Syntheses of all selenol esters were conducted under a nitrogen atmosphere. Compounds **1d–f** were further purified by sublimation for carbon-13 NMR measurements.

4-Substituted-phenyl selenocyanates and bis(4-substituted)phenyl diselenides were either available from previous studies[15] or prepared according to known methods.[16]

Preparation of Aryl Selenobenzoates via Diselenides. General Procedure. A solution of 0.95 M lithium triethylborohydride in tetrahydrofuran (11.5 mL, 11 mmol) was added slowly via a syringe to the bis(4-substituted-phenyl) diselenide (4.3 mmol) in tetrahydrofuran (5 mL).[17] This was followed by the dropwise addition of benzoyl chloride (1.0 mL, 8.6 mmol) in tetrahydrofuran (5 mL). The reaction proceeded at ambient temperature for approximately 12 h with stirring. After evaporation of the solvent, the residue was dissolved in ether and the resulting solution was washed twice with saturated sodium bi-

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carbonate and dried over magnesium sulfate. After evaporation of the solvent, the crude product was purified by recrystallization.

***Se*-Phenyl selenobenzoate (1a)**: recrystallized from pentane, mp 39–40 °C (lit.[18] mp 40 °C).

***Se*-*p*-Methylphenyl selenobenzoate (1b)**: recrystallized from hexanes, mp 70–71 °C (lit.[19] mp 71–72 °C).

***Se*-*p*-Methoxyphenyl selenobenzoate (1c)**: recrystallized from hexanes, mp 97–99 °C (lit.[19] mp 97 °C).

Preparation of Aryl Selenobenzoates via Grignard Reagents. General Procedure. The Grignard reagents were prepared from appropriately substituted bromobenzenes (21.2 mmol) and 0.52 g of Mg (21.2 mmol) in 100 mL of anhydrous diethyl ether under a N_2 atmosphere. Gray selenium powder (1.67 g, 21.2 mmol) was added to the warm mixture at such a rate as to maintain gentle refluxing. After the addition of selenium, the reaction mixture was stirred at room temperature for 2.5 h. To the mixture was added dropwise a solution of benzoyl chloride (2.5 mL, 21.5 mmol) in 40 mL of anhydrous diethyl ether. After the addition, the reaction mixture was stirred for 2 h and then diluted with 150 mL of CH_2Cl_2. The organic layer was washed twice with dilute HCl and once with water and then dried over $MgSO_4$. After evaporation of the solvent, the crude products were purified by recrystallization.

***Se*-*p*-Chlorophenyl selenobenzoate (1d)**: recrystallized from hexanes, mp 74–75 °C. Anal. Calcd for $C_{13}H_9ClOSe$: C, 52.82; H, 3.07; Se, 26.71. Found: C, 53.07; H, 3.29; Se, 26.91.

***Se*-*p*-Bromophenyl selenobenzoate (1e)**: recrystallized from ether/ethanol, mp 71 °C. Anal. Calcd for $C_{13}H_9BrOSe$: C, 45.91; H, 2.67; Se, 23.22. Found: C, 46.12; H, 2.73; Se, 23.06.

Preparation of Aryl Selenobenzoates via Aryl Selenocyanates. General Procedure. Solid sodium borohydride (0.13 g, 3.4 mmol; 25% excess, except in the case of *p*-acetylphenyl selenocyanate where an equivalent amount of sodium borohydride was used) was slowly added to a cooled and stirred solution (or suspension of 2.6 mmol of the appropriately substituted phenyl selenocyanate in ethanol (10 mL)).[16a] A solution of benzoyl chloride (0.30 mL, 2.6 mmol) in ethanol (5 mL) at 0 °C was then added dropwise to the mixture. The reaction mixture was brought to room temperature and then stirred overnight. The ethanol was then removed by rotary evaporation and the residue dissolved in diethyl ether (50 mL). The ether solution was washed 3 times with saturated sodium bicarbonate solution and dried over $MgSO_4$ and the solvent removed by rotary evaporation, leaving the crude product, which was purified by recrystallization.

***Se*-*p*-Nitrophenyl selenobenzoate (1f)**: recrystallized from ethanol, mp 109 °C. Anal. Calcd for $C_{13}H_9NO_3Se$: C, 51.00; H, 2.96; Se, 25.79. Found: C, 50.82; H, 2.89; Se, 25.70.

***Se*-*p*-Cyanophenyl selenobenzoate (1g)**: recrystallized from ethanol, mp 93–94 °C. IR ($CHCl_3$) (w) 2226, (m) 1690 cm^{-1}. Anal. Calcd for $C_{14}H_9NOSe$: C, 58.76; H, 3.17; Se, 27.59. Found: C, 59.21; H, 3.59; Se, 25.08.

***Se*-*p*-Acetophenyl selenobenzoate (1h)**: recrystallized from ethanol, mp 113 °C. Anal. Calcd for $C_{15}H_{12}O_2Se$: C, 59.42; H, 3.99; Se, 26.04. Found: C, 59.62; H, 4.18; Se, 25.99.

***Se*-*p*-Carbethoxyphenyl selenobenzoate (1i)**: recrystallized from ethanol, mp 81 °C. Anal. Calcd for $C_{16}H_{14}O_3Se$: C, 57.67; H, 4.23; Se, 23.69. Found: C, 57.70; H, 4.35; Se, 23.46.

***Se*-*p*-Fluorophenyl selenobenzoate (1j)**: recrystallized from hexanes, mp 56 °C. Anal. Calcd for $C_{13}H_9FOSe$: C, 55.93; H, 3.07; Se, 26.71. Found: C, 55.86; H, 3.40; Se, 28.03.

Preparation of *Se*-*p*-(Dimethylamino)phenyl Selenobenzoate (1k). To a solution of 4.8 g (26 mmol) of *p*-(dimethylamino)aniline dihydrochloride in 49 mL of 2 M HCl cooled to 0 °C was added 1.6 g (23 mmol) of $NaNO_2$ in 12 mL of water. Sodium acetate (8 g) was added followed by dropwise addition of a sodium acetate buffer (pH 4) until the pH of the reaction was 4.3. A solution of 5 g (35 mmol) of KSeCN in 30 mL of water, which had been adjusted to pH 4.3 with sodium acetate buffer, was then added at 0 °C. The reaction mixture was stirred at 0 °C for 15 min, saturated with sodium acetate to bring the pH to 5.5, and then gradually brought to room temperature followed by extraction with CH_2Cl_2 (20 mL). The CH_2Cl_2 layer was dried over $MgSO_4$ and the solvent was removed by rotary evaporation leaving the solid selenocyanate. The selenocyanate was dissolved in CH_2Cl_2 (15 mL) and absolute ethanol (20 mL) and chilled to 4 °C, and 0.88 g (23 mmol) of sodium borohydride was added in small batches under nitrogen with magnetic stirring. Benzoyl chloride (2.64 mL) in 15 mL of absolute ethanol was added and the solution stirred for 20 min. The dark green solution was evaporated to dryness under vacuum and the residue dissolved in CH_2Cl_2 (20 mL). The solution was washed twice with saturated NaCl solution and dried over $MgSO_4$ and the solvent removed by rotary evaporation leaving a green oil. The green oil was washed several times with absolute ethanol until a semisolid was obtained, which was dried over P_2O_5 under vacuum and recrystallized from ethanol. The product was found to decompose at room temperature.

Registry No. **1a**, 38447-68-6; **1b**, 62247-15-8; **1c**, 94706-43-1; **1d**, 94706-41-9; **1e**, 62593-86-6; **1f**, 94706-37-3; **1g**, 94706-38-4; **1h**, 94706-39-5; **1i**, 94706-40-8; **1j**, 94706-42-0; **1k**, 94706-44-2; $(C_6H_5Se)_2$, 1666-13-3; $(p\text{-}CH_3C_6H_4Se)_2$, 21856-94-0; $(p\text{-}CH_3OC_6H_4Se)_2$, 38762-70-8; *p*-$ClC_6H_4Br$, 106-39-8; *p*-$NCC_6H_4SeCN$, 94706-45-3; *p*-$EtO_2CC_6H_4SeCN$, 1778-11-6; *p*-$(CH_3)_2NC_6H_4SeCN$, 10272-02-3; *p*-$BrC_6H_4Br$, 106-37-6; *p*-$O_2NC_6H_4SeCN$, 19188-18-2; *p*-$AcC_6H_4SeCN$, 1442-11-1; *p*-$FC_6H_4SeCN$, 50983-89-6; KSeCN, 3425-46-5; Se, 7782-49-2; benzoyl chloride, 98-88-4; *p*-(dimethylamino)aniline dihydrochloride, 536-46-9.

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