RELATIONSHIP OF STRUCTURE TO SENSITIVITY IN ELECTRON CAPTURE ANALYSIS

III. CHLORONITROBENZENES, ANILINES AND RELATED DERIVATIVES

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An attempt at a delineation of molecular electron capture sensitivity values into relative sensitivity contributions of structural moieties of chlorinated pesticides[1] and isomeric chlorophenyl *m*-fluorosulfonylbenzoates[2] was described earlier. This type of investigation has been further extended to non-pesticidal classically substituted benzenes, and comprises the subject of the present report. The compounds employed in this study were primarily isomeric chloro-nitrobenzenes and -anilines, chosen because of their facile detection by electron capture.

Benzene derivatives containing halogen substituents were chromatographed during several Friedel-Crafts isomerization studies by OLAH and his co-workers[3-5]. STOCK AND BAKER employed gas chromatography for the measurement of partial rate factors for non-catalytic chlorination of halobenzenes[6]. Chromatography of halonitrobenzenes and dihaloanilines was reported by DODSWORTH[7]; while BOMBAUGH studied the analysis of mono- and dichloroaniline isomers[8].

Several fundamental papers have discussed the general response of the electron capture detector[9-11]. Detector response to halogenated C_1 to C_6 organics, including halogenated inorganics and Freons was described by CLEMONS AND ALTSHULLER[12]. The response to primary and secondary alkylamines as their N-substituted nitro-anilines following reaction with 2,4-dinitrofluorobenzene was denoted by DAY *et al.*[13].

The principal objective of this study was to evaluate, if possible, the relative contribution of chloro-, nitro- and amino-aryl substituents and the influence of location on the ring on the overall sensitivity of the molecule during electron capture gas chromatographic analysis.

EXPERIMENTAL

The compounds utilized in this investigation were obtained from various commercial sources. Melting points of the derivatives were determined on a Fisher-Johns Melting Point Apparatus and were compared to literature values for purity evaluations.

Gas chromatography was carried out on a 3 ft. by 0.25 in. O.D. pyrex glass column packed with 4 % QF-1 (trifluoropropylmethyl silicone fluid) on 80–100 mesh acid-washed DMCS-pretreated Chromosorb G. The column was housed in an Aerograph Model 600-B gas chromatograph containing a 250 mC titanium tritide foil

TABLE I

GAS CHROMATOGRAPHY OF SUBSTITUTED BENZENES

Compound	Mol. wt.	Melting point (°C)		Relative elution[a]
		Lit.	Observed	
$2\text{-}NO_2\text{-}4\text{-}Cl\text{-}NH_2\phi$	162.0	115–116	114–116	12.56
$o\text{-}DiNO_2\phi$	168.1	116–118	117–118	8.88
$m\text{-}NO_2NH_2\phi$	138.1	112–113	111–112	8.34
$m\text{-}DiNO_2\phi$	168.1	89.57	87–88	7.07
$p\text{-}Cl_2\phi$	147.0	53–54	52.5–53.5	5.13
$2,4,5\text{-}Cl_3NO_2\phi$	226.5	[b]	54–56	3.77
$o\text{-}NO_2NH_2\phi$	138.1	71–72	70.5–71	3.54
$2,3\text{-}Cl_2NO_2\phi$	192.0	61–62	60–61	2.50
$3,4\text{-}Cl_2NO_2\phi$	192.0	40–42	39–41	2.12
$2,4\text{-}Cl_2NO_2\phi$	192.0	30–32	31–32	2.08
$2,5\text{-}Cl_2NO_2\phi$	192.0	52–54	51–53	1.94
$o\text{-}BrNO_2\phi$	202.0	36–39	38.5–40.5	1.79
$2,3,6\text{-}Cl_3NH_2\phi$	196.5	74.5–76	74–75.5	1.77
$2,3\text{-}Cl_2NH_2\phi$	162.0	24	[c]	1.67
$o\text{-}ClNO_2\phi$	157.5	32–33	32.5–33	1.56
$2,4\text{-}Cl_2NH_2\phi$	162.0	61–63	61–62	1.46
$2,5\text{-}Cl_2NH_2\phi$	162.0	49–50	48–49	1.44
$p\text{-}ClNO_2\phi$	157.5	83.84	82.5–83.5	1.00
$m\text{-}ClNO_2\phi$	157.5	44–45	44–45	0.94
$F\phi$	96.1	−41.9	[c]	0.83
$o\text{-}BrNH_2\phi$	172.0	32	30.5–31	0.71
$m\text{-}ClNH_2\phi$	127.5	−10.4	[c]	0.71
$o\text{-}FNO_2\phi$	141.1	−6	[c]	0.63
$p\text{-}FNO_2\phi$	141.1	27	[c]	0.46
$o\text{-}ClNH_2\phi$	127.5	−2 to −1	[c]	0.42
$m\text{-}FNO_2\phi$	141.1	3.6	[c]	0.38
$o\text{-}FNH_2\phi$	111.1	−28.95	[c]	0.12

[a] Column: 3 ft. by 0.25 in. pyrex glass coiled column packed with 4 % QF-1 on 80–100 mesh AW DMCS-Chromosorb G. Conditions: column temperature, 105°; nitrogen carrier, 15 p.s.i.g.; signal attenuation, 1 × 4; 250 mC titanium tritide.
[b] 45°, minimum.
[c] Liquid at room temperature.

concentric detector and a Model 600-D electrometer. Column oven bath temperature was maintained by a Barber-Colman Model 293C Capacitrol heat controller. Experimental operating conditions are given in the footnotes to Table I.

RESULTS AND DISCUSSION

The theory of electron capture by eluting solute molecules has been discussed by LOVELOCK[10], JOHNSON[14], and others, as the *in situ* formation of negative molecular solute ions. When nitrogen carrier gas is employed, the electron current apparently originates via beta bombardment of the nitrogen molecules, from the tritium source[15]. Migration of the negative molecular ions to the positive cell electrode along with the uncaptured electrons is minimized both by the momentum of the much heavier molecular ion in the transient carrier stream, and by recombination of the negative molecular ion with a positive nitrogen molecule ion. The latter reaction probably

TABLE II
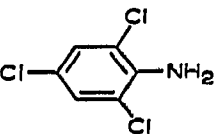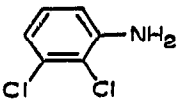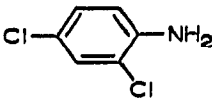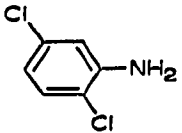
RELATIVE SENSITIVITIES OF CHLORONITROBENZENES
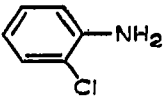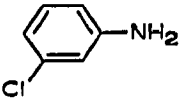
Compound	Structure	Relative sensitivity
2,3-Cl$_2$NO$_2\phi$		2.34
m-ClNO$_2\phi$		2.21
2,5-Cl$_2$NO$_2\phi$		2.12
2,4,5-Cl$_3$NO$_2\phi$		2.10
o-ClNO$_2\phi$		1.66
3,4-Cl$_2$NO$_2\phi$		1.13
2,4-Cl$_2$NO$_2\phi$		1.11
p-ClNO$_2\phi$		1.00

culminates in dissociation into uncharged nitrogen and solute molecules at the detector exit, with the net result of an observed decrease in electron current during detector residence of an eluted solute containing an electron capturing group in its structure.

The wide response range of electron capture to various structures is well known. In this study (utilizing the benzene nucleus as a model) the objectives included: (1) the experimental determination of relative sensitivity values for the various derivatives employed, (2) the elucidation (if possible) of the relative contribution of the aryl substituents present, and (3) the evaluation (if possible) of the relative importance of group interactions in di- and higher substituted compounds via consideration of the spatial arrangements of substituents (o,m,p) on the ring.

The sensitivities of all compounds were initially determined in units of chromatogram peak area (mm^2) per nanogram of compound injected. The sensitivity values thus obtained were ratioed to that of 2,4-dichloronitrobenzene (employed as the

TABLE III

RELATIVE SENSITIVITIES OF CHLOROANILINES

Compound	Structure	Relative sensitivity
2,4,6-Cl$_3$NH$_2\phi$		0.0164
2,3-Cl$_2$NH$_2\phi$		0.00484
2,4-Cl$_2$NH$_2\phi$		0.00394
2,5-Cl$_2$NH$_2\phi$		0.00133
o-ClNH$_2\phi$		0.000100
m-ClNH$_2\phi$		0.0000312

standard). The mean of reproducible replicate sensitivity measurements for each compound was used in the relative sensitivity calculation. All analyses were run back-to-back with the standard. The relative sensitivity data were placed on a molecular scale by simple multiplication by the molecular weight ratio of the standard to the compound. For interpretive purposes, the related standard for all compound results was then changed to p-chloronitrobenzene.
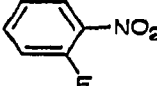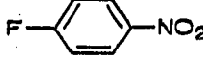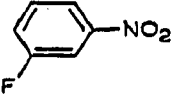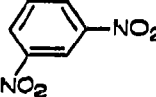
Chromatographic behavior
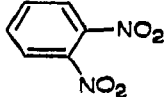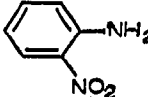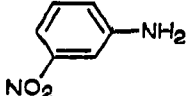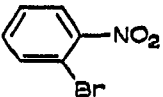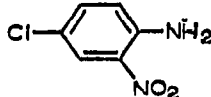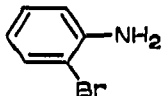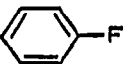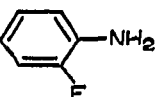
The gas chromatographic elution results are given in Table I. The contribution towards increased retention appeared to be roughly in the order of Cl > NO$_2$ > NH$_2$ > F, although position of attachment to the ring obviously plays a contributing role as may be discerned for the various isomeric categories analyzed (viz. dinitro, dichloronitro, dichloroamino, etc.).

Sensitivity consideration

The role of "electron-capturing" groups present within a solute molecule was approximated by a linear relation to the net sensitivity of the molecule. This approach was initially discussed in a study involving the electron capture analysis of pesticides[1].

The relative mole sensitivity ratios for chloronitrobenzene derivatives are given

TABLE IV

RELATIVE SENSITIVITIES OF MISCELLANEOUS DERIVATIVES

Class	Compound	Structure	Relative sensitivity
Fluoronitrobenzenes	o-FNO$_2\phi$		0.740
	p-FNO$_2\phi$		0.685
	m-FNO$_2\phi$		0.206
Dinitrobenzenes	m-diNO$_2\phi$		1.63
	o-diNO$_2\phi$		1.29
Nitroanilines	o-NO$_2$NH$_2\phi$		0.302
	m-NO$_2$NH$_2\phi$		0.260
Miscellaneous	p-Cl$_2\phi$		1.88
	o-BrNO$_2\phi$		1.22
	2-NO$_2$-4-Cl-NH$_2\phi$		0.214
	o-BrNH$_2\phi$		0.00166
	Fϕ		0.000107
	o-FNH$_2\phi$		0.000000686

in Table II. The following cursory observations were noted: (1) the sensitivity increased in general with an increase in the number of chlorine atoms; (2) *p*-chloro (to NO_2) attachment significantly diminished the sensitivity of the molecule (consideration of molecular dipoles would be in agreement with this, yet it would be difficult to rationalize the experimental sensitivity of *p*-dichlorobenzene which has a moment of zero unless electron attraction at the microscopic level in the vicinity of the chlorine atom is likewise considered); (3) *m*-chloro attachment contributed more than *o*-chloro attachment; and (4) chlorine atoms substituted vicinally contributed more than non-vicinal dichloride attachment.

Sensitivity data for chloroanilines are given in Table III. Somewhat similar remarks to those cited above for the chloronitrobenzenes may be made, with the exception that *o*-chloro attachment appeared to contribute more greatly than *m*-chloro substitution. A profound decline in sensitivity was observed for the aniline derivatives. The results noted for the chloronitrobenzenes and anilines are consistent with the electron withdrawing and releasing character of aryl Cl, NO_2 and NH_2 moieties. Relative sensitivity determinations for derivatives of related miscellaneous types are listed in Table IV.

While general trends regarding the sensitivity contributions of the NO_2, Cl, NH_2 and F substituents might be approximated by examination of Tables II through IV, it was felt that a more quantitative measure of such contributions could be afforded by linear regression analysis of coded moieties located at specific ring locations. The calculations were performed on a Control Data Corporation Model 3600 computer in two approaches to the data: (a) by physical presence of substituents, alone; and (b) by physical presence and point of attachment. The computations obtained by physical presence considerations alone involved the simultaneous solution of equations such as

$$2A + B = 2.34$$
$$A + B = 2.21, \text{ etc.}$$

where A and B represent a chloro and nitro substituent, respectively, and 2.34 and 2.21 are the respective relative sensitivity values of 2,3-dichloronitrobenzene and *m*-chloronitrobenzene, given in Table II. This was done for the 18 chloro-containing derivatives. The solutions to the Cl, NO_2 and NH_2 substituents treated in this way represent the regression coefficients (slopes) of a multi-dimensional plot of relative sensitivity as a function of frequency of appearance of the substituents, and were:

chloro   0.110
nitro   —0.00061
amino   —1.67

This implies that Cl > NO_2 ≫ NH_2. These values substituted back into the equation predicted the relative sensitivities given in Table V.

It was felt that a more accurate picture could be obtained if points of attachment to the ring were considered as well. The coding for this approach was obtained from the model
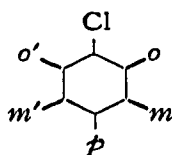
TABLE V

EXPERIMENTAL *vs.* PREDICTED SENSITIVITIES (PHYSICAL PRESENCE ONLY)

Compound	Relative sensitivity	
	Experimental	Predicted
$2,3\text{-}Cl_2NO_2\phi$	2.34	1.74
$m\text{-}ClNO_2\phi$	2.21	1.63
$2,5\text{-}Cl_2NO_2\phi$	2.12	1.74
$2,4,5\text{-}Cl_3NO_2\phi$	2.10	1.85
$p\text{-}Cl_2\phi$	1.88	1.74
$o\text{-}ClNO_2\phi$	1.66	1.63
$m\text{-}DiNO_2\phi$	1.63	1.52
$o\text{-}DiNO_2\phi$	1.29	1.52
$3,4\text{-}Cl_2NO_2\phi$	1.13	1.74
$2,4\text{-}Cl_2NO_2\phi$	1.11	1.74
$p\text{-}ClNO_2\phi$	1.00	1.63
$2\text{-}NO_2\text{-}4\text{-}Cl\text{-}NH_2\phi$	0.214	—0.0445
$2,4,6\text{-}Cl_3NH_2\phi$	0.0164	0.175
$2,3\text{-}Cl_2NH_2\phi$	0.00484	0.0658
$2,4\text{-}Cl_2NH_2\phi$	0.00394	0.0658
$2,5\text{-}Cl_2NH_2\phi$	0.00133	0.0658
$o\text{-}ClNH_2\phi$	0.000100	—0.0439
$m\text{-}ClNH_2\phi$	0.0000312	—0.0439

in which individual variables for the Cl, NO_2 and NH_2 substituents were considered by each of the five ring available positions in the 18 chloro-containing derivatives analyzed. Equations were written such that all possible codings were used for each compound, equated to its relative sensitivity. Regression analysis showed that o and o', and m and m' assignments for the substituents were equivalent, and produced the following slopes for the respective aryl moieties:

	Cl	NO_2	NH_2
ortho	0.314	0.219	—1.57
meta	0.0684	0.146	—1.63
para	0.362	—0.267	—1.45

The size of the values indicates their relative importance to molecular sensitivity. The large negative values obtained for NH_2 attachment reflect the great decrease in sensitivity noted for the aniline derivatives. Substitution of these values back into the coded equations gave predicted sensitivities for the derivatives for this manner of coding, and these are shown in Table VI.

It may easily be noted from Tables V and VI that the predicted values become very poor at very low experimental sensitivities. It is felt that the predicted multi-dimensional plot of relative sensitivity *vs.* frequency of occurrence of specific groups in these compounds is somewhat linear for a small range of the plot (*e.g.* relative sensitivity of 1.00 to 2.00), but that the total sensitivity range is probably a curvilinear plot, and either polynomial regression or separate analysis of small ranges of relative sensitivity data might afford improved predictions. The delineation of compound molecular sensitivity values obtained by electron capture gas chromatographic

TABLE VI

EXPERIMENTAL *vs.* PREDICTED SENSITIVITIES (PHYSICAL PRESENCE AND POINT OF ATTACHMENT)

Compound	Relative sensitivity	
	Experimental	Predicted
$2,3$-$Cl_2NO_2\phi$	2.34	1.91
m-$ClNO_2\phi$	2.21	1.55
$2,5$-$Cl_2NO_2\phi$	2.12	1.96
$2,4,5$-$Cl_3NO_2\phi$	2.10	1.94
p-$Cl_2\phi$	1.88	1.77
o-$ClNO_2\phi$	1.66	1.63
$3,4$-$Cl_2NO_2\phi$	1.13	1.67
$2,4$-$Cl_2NO_2\phi$	1.11	1.46
p-$ClNO_2\phi$	1.00	1.14
2-NO_2-4-Cl-$NH_2\phi$	0.214	0.108
$2,4,6$-$Cl_3NH_2\phi$	0.0164	0.0153
$2,3$-$Cl_2NH_2\phi$	0.00484	0.121
$2,4$-$Cl_2NH_2\phi$	0.00394	—0.0325
$2,5$-$Cl_2NH_2\phi$	0.00133	0.170
o-$ClNH_2\phi$	0.000100	—0.163
m-$ClNH_2\phi$	0.0000312	—0.224

analysis remains of sufficient interest (for predictabilities of detection, structure studies, etc.) to warrant more detailed investigation by approaches analogous to those described in this paper.

ACKNOWLEDGEMENTS

SUMMARY

In an extension of an earlier study describing the delineation of molecular sensitivity values for pesticides obtained via electron capture gas chromatographic analysis using a multiple linear regression program, relative sensitivity data were obtained for classical substituted benzenes for the purpose of estimating the quantitative contribution of individual aryl substituents (*viz.* Cl, NO_2 and NH_2 groups) to the overall molecular electron capture sensitivity values, and in order to evaluate the efficacy of a multiple linear regression model for this purpose. Values were obtained for individual substituents located at different positions of attachment to the ring. Indications are that the NH_2 substituent in aniline derivatives substantially diminishes sensitivity. The possibility that the moiety contributions for wide ranges of compound sensitivities may be curvilinear is suggested.

REFERENCES

1 W. L. ZIELINSKI, Jr., L. FISHBEIN AND L. MARTIN, Jr., *J. Gas Chromatog.*, in press.
2 W. L. ZIELINSKI, Jr. AND L. FISHBEIN, *J. Chromatog.*, 28 (1967) 293.
3 G. A. OLAH, W. S. TOLGYESI AND R. E. A. DEAR, *J. Org. Chem.*, 27 (1962) 3441.
4 G. A. OLAH, W. S. TOLGYESI AND R. E. A. DEAR, *J. Org. Chem.*, 27 (1962) 3449.
5 G. A. OLAH, W. S. TOLGYESI AND R. E. A. DEAR, *J. Org. Chem.*, 27 (1962) 3455.
6 L. M. STOCK AND F. W. BAKER, *J. Am. Chem. Soc.*, 84 (1962) 1661.
7 P. G. DODSWORTH, in M. VAN SWAAY (Editor), *Gas Chromatography 1962*, Butterworths, London, 1963, pp. 273–291.
8 K. J. BOMBAUGH, *Anal. Chem.*, 37 (1965) 72.
9 J. E. LOVELOCK AND S. R. LIPSKY, *J. Am. Chem. Soc.*, 82 (1960) 431.
10 J. E. LOVELOCK AND N. L. GREGORY, in *Gas Chromatography*, Academic Press, New York, 1962, pp. 219–229.
11 R. A. LANDOWNE AND S. R. LIPSKY, *Anal. Chem.*, 34 (1962) 726.
12 C. A. CLEMONS AND A. P. ALTSHULLER, *Anal. Chem.*, 38 (1966) 133.
13 E. W. DAY, Jr., T. GOLAB AND J. R. KOONS, *Anal. Chem.*, 38 (1966) 1053.
14 R. E. JOHNSON, *Canisus College Institute on Gas Chromatography*, Buffalo, New York, April, 1961.
15 K. P. DIMICK AND H. HARTMANN, *145th Am. Chem. Soc. Meeting, Cincinnati, Ohio, January, 1963*.