Mechanism of the Facile Formation and Hydrolysis of Esters of o-Nitrobenzeneselenenic Acid: New Insight into the Mechanism of Nucleophilic Substitution Reactions of o-Nitrobenzeneselenenyl Derivatives[1a]

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o-Nitrobenzeneselenenic acid (1) undergoes rapid acid-catalyzed esterification by alcohols to afford alkyl *o*-nitrobenzeneselenenates, *o*-$O_2NC_6H_4SeOR$ (2), in high yield. The mechanism of esterification of 1 and of its reverse, the hydrolysis of 2, has been investigated. Of particular interest is the observation that the kinetic behavior of the hydrolysis of methyl *o*-nitrobenzeneselenenate (2, R = Me) in 60% dioxane parallels closely that found previously[2] for the hydrolysis of *o*-nitrobenzeneselenenic anhydride, *o*-$O_2NC_6H_4SeOSeC_6H_4NO_2$-*o* (3). Both reactions exhibit general-acid, rather than specific-H^+, catalysis with a nonlinear Brønsted plot, and both take place at surprisingly similar rates. These results and others indicate the need for modifications in the mechanisms previously proposed[2,4] for acid-catalyzed substitution reactions of 1 and its derivatives. A revised general mechanism that is believed to be able to accommodate satisfactorily the observed behavior of the various reactions is presented in Scheme I.

While most areneselenenic acids (ArSeOH) are labile and have only a transitory existence, solutions of *o*-nitrobenzeneselenenic acid, 1 (Ar = *o*-$O_2NC_6H_4$), are relatively stable.[2] Solutions of 1 can be generated by either acid-catalyzed hydrolysis of the corresponding selenenic anhydride (ArSeOSeAr + H_2O → 2ArSeOH)[2] or fragmentation of ethyl *o*-nitrophenyl selenoxide (ArSe(O)Et → ArSeOH + CH_2=CH_2).[3]

Because of the stability of solutions of 1 the mechanisms of its reactions are easily studied. Previous papers have dealt with the reaction of 1 with thiols (ArSeOH + RSH → ArSeSR + H_2O)[4] and its oxidation by peracids, hydroperoxides, and hydrogen peroxide (ArSeOH + ROOH → $ArSeO_2H$ + ROH).[5] These studies were carried out in aqueous dioxane.

In examining the behavior of 1 in alcohol solvents, such as methanol or ethanol, we discovered that it underwent remarkably facile, acid-catalyzed conversion to the corresponding *o*-nitrobenzeneselenenate esters, 2 (eq 1). This

$$\underset{1}{o\text{-}O_2NC_6H_4SeOH} + ROH \xrightarrow{H^+} \underset{2}{o\text{-}O_2NC_6H_4SeOR} + H_2O \quad (1)$$

led us to investigate the mechanism of eq 1, and of the hydrolysis of 2 (reverse of eq 1), under various reaction conditions. The results, which are reported in this paper, suggest the need for certain revisions in the picture of the mechanism for acid-catalyzed nucleophilic substitution reactions of 1 and its derivatives that had been advanced earlier[2,4] based on studies of the reaction of 1 with thiols[4] and of the hydrolysis of *o*-nitrobenzeneselenenic anhydride (3)[2] in 60% dioxane. The modified mechanism provides further refinement in our understanding of the details of the acid-catalyzed reactions of 1 and its derivatives with nucleophiles.

Results

Rapid Formation of Selenenate Esters from 1. In the absence of added strong acid the UV-visible spectrum of 1 (λ_{max} = 427 nm) in ethanol is virtually identical with its spectrum in 60% dioxane[6] and does not change with time. Upon addition of 0.01 M $HClO_4$ there is a rapid ($t_{1/2}$ < 1 min) change in the spectrum (shift of λ_{max} to 415 nm, decrease in absorbance in the range 425–490 nm, increase in the range 385–415 nm). That this is due to the conversion of 1 to ethyl *o*-nitrobenzeneselenenate (2, R = Et) was shown by the isolation of *o*-$O_2NC_6H_4SeOEt$ (2a) in >90% yield from an experiment in which a 0.01 M solution of 1 in ethanol was acidified with 0.005 M perchloric acid. Similar treatment of a 0.01 M solution of 1 in methanol led to *o*-$O_2NC_6H_4SeOMe$ (2b) in 90% yield. Formation of *o*-nitrobenzeneselenenate esters from 1 and alcohols (eq 1) is therefore acid-catalyzed and surprisingly facile.

Kinetics of the Reaction of 1 with Alcohols. The kinetics of the reaction of seven different alcohols with 1 were studied at 25 °C in acetonitrile containing 1–3 M alcohol. Trifluoromethanesulfonic acid was used as the acid catalyst, and the ionic strength was kept constant at 0.2 with CF_3SO_3Na. The kinetics of the reaction of 1 with ethanol were also examined in anhydrous ethanol. In all cases conversion of 1 to 2 followed good first-order kinetics; the rate constants k_1 are collected in Table I.

For each reaction k_1 is proportional to $[H^+]$. At the same time the data in Table I show that there is surprisingly little dependence of $(k_1/[H^+])$ on either alcohol concentration or alcohol structure.

Kinetics of the Hydrolysis of Methyl *o*-Nitrobenzeneselenenate (2b). Addition of an acid catalyst to a solution of methyl *o*-nitrobenzeneselenenate (2b) in 60% dioxane is followed by the change in the UV-visible spectrum of the solution expected for the hydrolysis of the methyl ester to 1 (eq 2).

$$o\text{-}O_2NC_6H_4SeOCH_3 + H_2O \xrightarrow{H^+} o\text{-}O_2NC_6H_4SeOH + CH_3OH \quad (2)$$

Rates of hydrolysis of 2b in 60% dioxane were measured at 25 °C at constant ionic strength (0.02) in a series of carboxylic acid buffers and in dilute perchloric acid solutions. The experimental first-order rate constants k_{hyd} are given in the first section of Table II.

These data show that the hydrolysis of 2b is *general acid* catalyzed, catalysis by both H_3O^+ and buffer acids being

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Table I. Kinetics of the Reaction of Alcohols with *o*-Nitrobenzeneselenenic Acid[a]

solvent	alcohol	acid cat.	[ROH], M	10^2[H^+], M	10^2k_1, s^{-1}	$(k_1/[H^+])$, M^{-1} s^{-1}
ethanol	CH_3CH_2OH	$HClO_4$	~17	0.050	0.064 ± 0.005	1.3
				0.10	0.14 ± 0.01	1.4
				0.39	0.72	1.8
				0.50	0.83 ± 0.01	1.7
				0.78	1.4	1.8
				1.07	1.9 ± 0.3	1.8
				3.1	6.0	1.9
				5.2	9.8 ± 1.2	1.9
				10.2	14.5 ± 1.0	1.4
		CF_3SO_3H	~17	0.20	0.26	1.3
				0.39	0.57	1.5
				0.78	1.1	1.4
				1.55	2.3	1.5
				3.1	4.6	1.5
MeCN	CH_3CH_2OH	CF_3SO_3H	1.0	0.50	0.82	1.6
				1.0	1.5	1.5
			1.5	0.50	0.89	1.8
				1.0	1.6	1.6
			2.0	0.50	0.93	1.9
				1.0	1.8	1.8
			2.5	0.50	0.91	1.8
				1.0	1.8	1.8
			3.0	0.50	0.96	1.9
				1.0	1.9	1.9
	CH_3OH	CF_3SO_3H	2.0	0.50	1.03	2.1
				1.0	2.1	2.1
			2.5	0.50	1.15	2.3
				1.0	2.5	2.5
			3.0	0.50	1.3	2.6
				1.0	2.7	2.7
	FCH_2CH_2OH	CF_3SO_3H	2.0	0.50	0.74	1.5
				1.0	1.3	1.3
			3.0	0.50	1.1	2.2
				1.0	2.0	2.0
	$HOCH_2CH_2OH$	CF_3SO_3H	2.0	0.50	0.68	1.4
				1.0	1.3	1.3
			2.5	0.50	0.77	1.5
				1.0	1.5	1.5
			3.0	0.50	0.83	1.7
				1.0	1.7	1.7
MeCN	$PhCH_2OH$	CF_3SO_3H	2.0	0.50	0.53	1.1
				1.0	0.99	0.99
			2.5	0.50	0.56	1.1
				1.0	1.12	1.1
			3.0	0.50	0.58	1.2
				1.0	1.2	1.2
	$NCCH_2CH_2OH$	CF_3SO_3H	2.0	0.50	0.38	0.76
				1.0	0.79	0.79
	$(CH_3)_2CHOH$	CF_3SO_3H	2.0	0.50	0.42	0.84
				1.0	0.87	0.87
			2.5	0.50	0.46	0.92
				1.0	0.87	0.87
			3.0	0.50	0.50	1.0
				1.0	0.96	0.96

[a] All runs at 25 °C with $[I]_0$, 1.0×10^{-4} M; ionic strength maintained at 0.2 by addition of lithium perchlorate (runs in ethanol) or sodium trifluoromethanesulfonate (runs in acetonitrile).

observed. The catalytic constants k_{HA} (and the pK_a of HA in 60% dioxane) for the different acids are as follows:[7] H_3O^+, 1.1 (−1.30); CF_3CO_2H, 0.73 (2.8); CCl_3CO_2H, 0.71 (3.3); Cl_2CHCO_2H, 0.062 (4.03); $NCCH_2CO_2H$, 0.011 (5.1); $ClCH_2CO_2H$, 0.010 (5.48); HCO_2H, 0.0016 (6.10).

The kinetics of the hydrolysis of **2b** were also measured in acetonitrile containing 1–4 M water, using either CF_3SO_3H or Cl_2CHCO_2H as the acid catalyst. The rate constants are tabulated in the second section of Table II.

Kinetics of the Reaction of Methyl *o*-Nitrobenzeneselenenate (2b) with 1-Butanethiol. Selenenate ester **2b** reacts readily with 1-butanethiol in an acid-catalyzed reaction to give a product having the same UV spectrum as the product of the reaction of **1** with the thiol, which has been shown[4] to be *o*-$O_2NC_6H_4SeSBu$-*n*. The kinetics of this reaction (eq 3) were examined in both

$$o\text{-}O_2NC_6H_4SeOCH_3 + n\text{-}BuSH \xrightarrow[H^+]{k_{RSH}} o\text{-}O_2NC_6H_4SeSBu\text{-}n + CH_3OH \quad (3)$$

methanol and MeCN–2 M MeOH using CF_3SO_3H as the acid catalyst and with the thiol present in sufficient stoichiometric excess so that first-order kinetics would be observed for the disappearance of **2b**. Rate constants, k_1, for the various reaction conditions are tabulated in Table III[8] (supplementary material). Salient features of the

(7) For all acids except formic k_{HA} was obtained from the slope of a plot of k_{hyd} vs. [HA]; with formic acid the variation of k_{hyd} with concentration of buffer components was more complex ($k_{hyd} = k_{H_3O^+}[H_3O^+] + k_{HA}[HA] + k_2[HA][A^-]$), and k_{HA} for HCO_2H was obtained from the intercept of a plot of $(k_{hyd} - k_{H_3O^+}[H_3O^+])/[HA]$ vs. $[A^-]$. The pK_a's for the various acids in 60% dioxane are taken from ref 2.

(8) See paragraph at end of paper regarding supplementary material.

Table II. Kinetics of the Hydrolysis of Methyl o-Nitrobenzeneselenenate[a]

solv	reactn conditns	$[H_2O]$, M	pH[b]	[HA], M	$[A^-]$, M	$10^3 k_{hyd}$, s^{-1}
60% dioxane	0.02 N $HClO_4$	20	1.70	0.020		20.6
	0.01 N $HClO_4$	20	2.00	0.010		10.9
	0.005 N $HClO_4$	20	2.30	0.005		5.4
	1:1 CF_3CO_2H–$CF_3CO_2^-$ buffer	20	2.80	0.020	0.020	15.4
				0.010	0.010	7.9
				0.005	0.005	3.9
	1:1 Cl_3CCO_2H–$CCl_3CO_2^-$ buffer	20	3.30	0.020	0.020	14.6
				0.010	0.010	6.9
				0.005	0.005	3.7
	1:1 Cl_2CHCO_2H–$Cl_2CHCO_2^-$ buffer	20	4.03	0.020	0.020	1.3
				0.010	0.010	0.73
				0.005	0.005	0.47
	1:1 $NCCH_2CO_2H$–$NCCH_2CO_2^-$ buffer	20	5.10	0.020	0.020	0.23
				0.015	0.015	0.16
				0.010	0.010	0.116
	1:1 $ClCH_2CO_2H$–$ClCH_2CO_2^-$ buffer	20	5.48	0.020	0.020	0.21
				0.015	0.015	0.15
				0.010	0.010	0.108
	1:1 HCO_2H–HCO_2^- buffer	20	6.10	0.020	0.020	0.108
				0.015	0.015	0.067
				0.010	0.010	0.036
MeCN	0.02 M CF_3SO_3H	2.0	c	0.020		25
	0.01 M CF_3SO_3H	1.0	c	0.010		12.7
		2.0		0.010		12.7
		3.0		0.010		12.1
		4.0		0.010		12.1
	0.005 M CF_3SO_3H	2.0	c	0.005		6.3
	5:1 Cl_2CHCO_2H–$Cl_2CHCO_2^-$ buffer	2.0	c	0.020	0.004	0.31
				0.015	0.003	0.22
				0.010	0.002	0.15
		4.0	c	0.020	0.004	0.49
				0.015	0.003	0.37
				0.010	0.002	0.28

[a] All runs at 25 °C with initial concentration of **2b**, 1×10^{-4} M; ionic strength maintained constant at either 0.02 (runs in 60% dioxane) or 0.2 (runs in acetonitrile). [b] pH's of buffer from ref 2. [c] pH of solution not known.

results are as follows: (a) in methanol $k_1 = k_{RSH}[H^+][n\text{-BuSH}]$, with $k_{RSH} = 38\ M^{-2}\ s^{-1}$; (b) in acetonitrile–2 M MeOH k_1, while still strictly proportional to $[H^+]$, appears to show somewhat less than a strict first-order dependence on [n-BuSH]; (c) at a given acid and thiol concentration the rate in acetonitrile–2 M MeOH is 3 times faster than in methanol.

Discussion

The kinetic data in Table I and the isolation of alkyl o-nitrobenzeneselenenates (**2**) in high yield from the reaction of o-nitrobenzeneselenenic acid (**1**) with alcohols in acid solution show that esterification of **1** (eq 1) is acid-catalyzed and rapid. The fact that the four alcohols MeOH, EtOH, $PhCH_2OH$, and i-PrOH all react with **1** at approximately the same rate argues that esterification takes place by nucleophilic substitution by the oxygen of the alcohol at the selenium atom of **1**. Were the reaction occurring by nucleophilic attack of **1** on the R group of ROH_2^+ in an S_N2 reaction, the pattern of reactivity of the alcohols would be $PhCH_2OH > MeOH \gg EtOH \gg i\text{-PrOH}$.[9a] Were the reaction proceeding by an S_N1 process in which dissociation of the protonated alcohol to R^+ and H_2O is followed by capture of the carbocation by **1**, benzyl alcohol should react much faster than any of the other alcohols.[9b]

Two other significant features of the kinetics of eq 1 are evident from Table I. First, in acetonitrile–ROH solvent mixtures the rate shows little dependence on [ROH]. Second, although the six primary alcohols ($R'CH_2OH$) in Table I differ significantly in the inductive effect of R' (σ^* for R' varying from 0.0 to +1.3), there is only a 2.7-fold overall variation in $k_1/[H^+]$ with R'. A large decrease in electron density on the alcohol oxygen associated with going from $R'CH_2OH$ to rate-determining transition state would be anticipated to lead to a more significant decrease in $k_1/[H^+]$ with increasing positive σ^*.

The kinetics of the acid-catalyzed hydrolysis of methyl o-nitrobenzeneselenenate (**2b**) in 60% dioxane (first section of Table II) are also noteworthy, particularly in their similarity to the kinetics[2] of the hydrolysis of o-nitrobenzeneselenenic anhydride (**3**) in the same medium. Like the hydrolysis of **3**, the hydrolysis of **2b** is *general-acid*, rather than specific-H^+, catalyzed. As in the hydrolysis of **3**, a Brønsted plot of log k_{HA} vs. pK_a of HA is *nonlinear*, with $\alpha \simeq 0.8$ for acids with $pK_a \geq pK_a$ of trichloroacetic acid and $\alpha \simeq 0$ for the strongest acids (H_3O^+, CF_3CO_2H, and Cl_3CCO_2H). Also interesting is the fact that for most acids as catalysts the rate of hydrolysis of **2b** is either approximately the same, or somewhat faster, than the rate of hydrolysis of **3** under the same conditions. For a methyl ester to hydrolyze at the same, or a slightly faster, rate than the corresponding anhydride is certainly unusual.

In acetonitrile containing 1–4 M H_2O the rate of the H_3O^+-catalyzed hydrolysis of **2b** shows no dependence on $[H_2O]$ (second section of Table II). On the other hand, in the same media the rate of the Cl_2CHCO_2H-catalyzed hydrolysis of **2b** does show an increase in rate with water concentration that is roughly proportional to $[H_2O]$.[10]

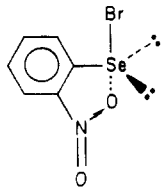
Several aspects of the behavior of the H^+-catalyzed reaction of **2b** with 1-butanethiol (eq 3) should also be noted. In methanol the rate is strictly first order in [n-BuSH], while in acetonitrile–2 M MeOH the dependence on [n-

(9) (a) Streitwieser, A., Jr. "Solvolytic Displacement Mechanisms"; McGraw-Hill: New York, 1962; p 13. (b) *Ibid.*, p 75.

(10) The same type of behavior is observed for the hydrolysis of anhydride **3** in acetonitrile–water solvents (Kang, S.-I., unpublished results).

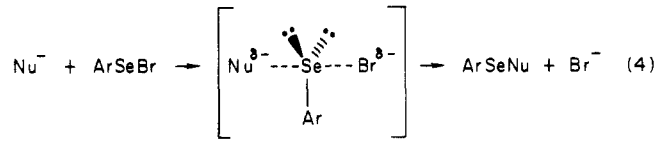
BuSH] appears to be slightly less than first order. At a given [H^+] the rate constant for the reaction is about 3 times faster in MeCN–2 M MeOH than in pure methanol. This and a related result[11] suggest that the reactions of **2b** (or 1) with neutral nucleophiles in MeCN–MeOH, or MeCN–H_2O, are likely to be subject to a modest solvent effect such that the rate constant decreases somewhat with increasing concentration of the protic solvent. A solvent effect of this nature could be responsible in significant measure for the fact that the rate of esterification of 1 in MeCN–ROH mixtures does not exhibit the increase in rate with increasing [ROH] expected from mass law considerations. It could also be an important factor in the lack of dependence on [H_2O] of the rate of H_3O^+-catalyzed hydrolysis of **2b** in acetonitrile–water.

As prelude to detailed consideration of possible mechanisms for the various reactions, it is important to recall that coordination of the *o*-nitro group to selenium in the manner shown in 4 has been shown by Austad[12a] to cause

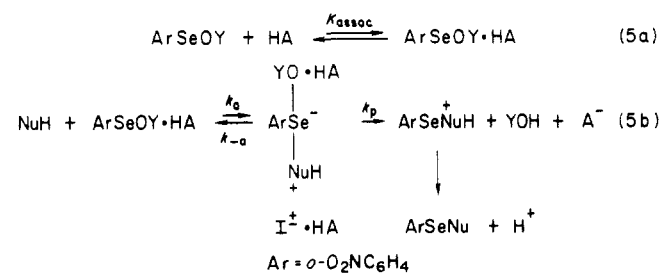


4

o-$O_2NC_6H_4SeBr$ to undergo nucleophilic substitution at a rate that is $>10^6$ *slower* than the rate of reaction of the same nucleophile with PhSeBr. In 4 the oxygen of the nitro group, by occupying one apical position, prevents easy, one-step displacement (eq 4) of the halogen from the other apical position by the attacking nucleophile. *Nucleophilic substitutions of o-$O_2NC_6H_4SeBr$ and other similarly stabilized o-nitrobenzeneselenenyl derivatives, such as* 1, 2, *or* 3, *therefore have to take place by more complex mechanisms than eq 4.*



To account for the nonlinear Brønsted plot associated with general-acid catalysis in the hydrolysis of 3, Kice, McAfee, and Slebocka-Tilk[2] have advanced the mechanism shown in eq 5 (NuH = H_2O, YO = ArSeO). They pro-

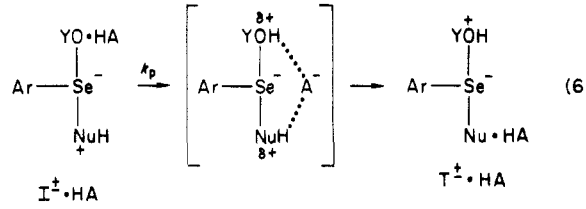


posed that the lifetime of $I^{\pm}$ was so short that general-acid catalysis of the departure of YO had to take place by a "preassociation" mechanism where the catalyzing acid HA was already present in the encounter complex when $I^{\pm}$ was formed. The nonlinear Brønsted plot was thought to arise because $k_p > k_{-a}$ for the strongest (lowest pK_a) acids, while $k_p < k_{-a}$ for the weaker acid catalysts. An analogous mechanism (NuH = *n*-BuSH; YO = OH) was proposed[4] for the acid-catalyzed reaction of 1 with 1-butanethiol.

While the hydrolysis of **2b** (eq 2) exhibits general-acid catalysis with a nonlinear Brønsted plot that is closely analogous to the behavior found[2] for the hydrolysis of 3, considerations arising from the easy reversibility of eq 2 demonstrate that its mechanism *cannot* be as shown in eq 5. Since eq 2 is easily reversible and methanol and water should act similarly as nucleophiles, whatever mechanism is written for the hydrolysis of **2b** must be one where identical roles are assigned for the catalyzing acid and the nucleophile (MeOH) in the reverse reaction, the esterification of 1 by methanol (eq 1, ROH = MeOH). As depicted in eq 5 step k_p would not do this, because it would postulate that while the mechanism for the hydrolysis of **2b** was reaction of H_2O with encounter complex **2b**·HA, the mechanism for the reverse reaction was equilibrium protonation of 1 followed by general-base-(A^-) catalyzed reaction of 1-H^+ with MeOH. Such a formulation is obviously unrealistic and untenable. In view of the striking similarity in the detailed kinetic behavior for the hydrolyses of **2b** and 3, it now seems likely that, contrary to earlier belief,[2] the mechanism for the hydrolysis of 3 is also not as depicted in eq 5.

In considering the proper assignment of mechanisms to the hydrolysis reactions we will first adopt the premise that all the acid-catalyzed nucleophilic substitution reactions of 1 and its derivatives should be accommodated in a single, unifying, and conceptually straightforward mechanistic scheme. We will see that with suitable and reasonable modifications in eq 5 this appears to be possible. A mechanism for the hydrolysis of 2 and 3 based on the alternate premise that these hydrolyses take place by an entirely different mechanism than reaction of a thiol with 1 or **2b** will be presented and discussed subsequently.

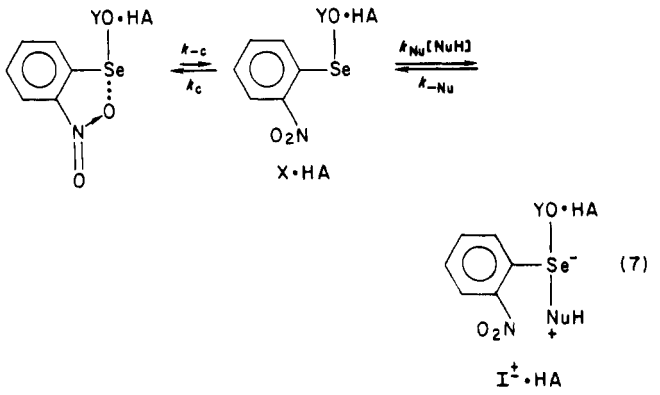
If step k_p in eq 5 is modified (eq 6) so that transfer of the proton from HA to YO is accompanied by transfer of the proton from the NuH^+ group to the incipient A^- ion, the necessary symmetry in mechanism for the hydrolysis of **2b** and esterification of 1 is achieved while general-acid catalysis is still retained.



While Austad[12] has suggested that attack of a nucleophile on the selenium atom of an *o*-nitrobenzeneselenenyl derivative, such as in step k_a of eq 5, should involve NuH "pushing the nitro group out of the way to coordinate with Se", we feel it may be more appropriate to picture the process as a sequence of two steps: (a) loss of coordination between the NO_2 group and selenium (step k_{-c} of eq 7); (b) reaction of the intermediate (X·HA) so formed with the nucleophile (step k_{Nu} of eq 7). Since X·HA, lacking coordination of the nitro group to selenium, should be a particularly reactive intermediate, the transition state for step k_{Nu} could well occur early and be closer to (X·HA + NuH) than to $I^{\pm}$·HA in structure, and it would be understandable if k_{Nu} for a series of $R'CH_2OH$ showed little dependence on R'. Furthermore, particularly under conditions where the reacting nucleophile is present in high concentration, it is also possible that $k_{Nu}[NuH] \geq k_c$.

(11) Measurements of the rate of reaction of 1 with *n*-BuSH in MeCN–2 M H_2O (Table III, supplementary material) show that the reaction is ~7.5 times faster in this medium than it is in 60% dioxane.

(12) (a) Austad, T. *Acta Chem. Scand., Ser. A* **1975**, *29A*, 895; (b) *Ibid.* **1977**, *31A*, 93.



When breakdown of $I^{\pm}$·HA to products is faster than k_{-Nu}, this would result in a less than first-power dependence of reaction rate on [NuH].

With separation of the formation of $I^{\pm}$·HA into two consecutive steps and the modification in step k_p the mechanism in eq 5 becomes as depicted in Scheme I. A complete kinetic analysis of Scheme I, assuming that the steady-state approximation is applicable to the concentrations of X·HA, $I^{\pm}$·HA, and $T^{\pm}$·HA, gives

$$k_{exptl} = k_{-c}K_{assoc}[HA] \times \left\{\frac{k_{-YO}k_pk_{Nu}[NuH]}{k_ck_{-Nu}(k_{-p} + k_{-YO}) + k_pk_{-YO}(k_c + k_{Nu}[NuH])}\right\} \quad (8)$$

In the hydrolysis of **2b** (NuH = H_2O; YO = OMe) the structural similarity of $I^{\pm}$·HA and $T^{\pm}$·HA suggests $k_{-YO} \simeq k_{-Nu}$ and $k_p \simeq k_{-p}$. If that is so, eq 8 becomes

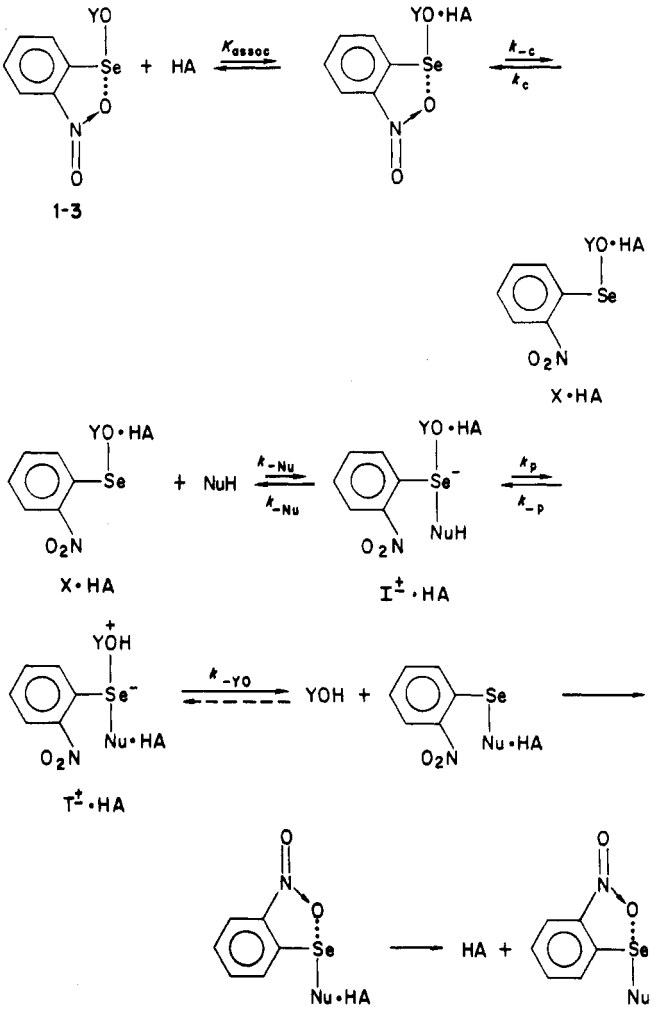
$$k_{exptl} = k_{-c}K_{assoc}[HA]\left\{\frac{k_pk_{Nu}[H_2O]}{k_ck_{-Nu} + 2k_ck_p + k_pk_{Nu}[H_2O]}\right\} \quad (9)$$

If with the most acidic catalysts, such as H_3O^+, $k_p > k_{-Nu}$, then $2k_ck_p \gg k_ck_{-Nu}$ and eq 9 simplifies to $k_{exptl} = k_{-c}K_{assoc}[HA]\{k_{Nu}[H_2O]/(2k_c + k_{Nu}[H_2O])\}$. The rate, being independent of k_p, will be independent of the pK_a of the catalyzing acid. In addition, if $k_{Nu}[H_2O]$ is comparable to k_c in magnitude, a less than first-order dependence of k_{exptl} on $[H_2O]$ is possible. For weaker (higher pK_a) acids it is assumed that $k_p < k_{-Nu}$ and that $k_ck_{-Nu} > (2k_pk_c + k_pk_{Nu}[H_2O])$. Equation 9 accordingly reduces to $k_{exptl} = k_{-c}K_{assoc}[HA](k_pk_{Nu}[H_2O]/k_ck_{-Nu})$. The rate, being dependent on k_p, will decrease with increasing pK_a of HA. It should also show a first-order dependence on $[H_2O]$. The mechanism in Scheme I can therefore account for both the nonlinear nature of the Brønsted plot for the hydrolysis of **2b** in 60% dioxane and the fact that k_{exptl} for the Cl_2CHCO_2H-catalyzed hydrolysis exhibits a much more pronounced dependence on $[H_2O]$ in acetonitrile–water than does the rate for the H_3O^+-catalyzed hydrolysis.

If $k_p > k_{-Nu}$ for catalysis by strong acids of the esterification of 1 (NuH = ROH; YO = OH), eq 8 will reduce to an expression similar to that for H_3O^+ catalysis of the hydrolysis of **2b**, i.e., $k_{exptl} = k_{-c}K_{assoc}[H^+]\{k_{Nu}[ROH]/(2k_c + k_{Nu}[ROH])\}$. If $k_c \simeq k_{Nu}[ROH]$ a less than first-order dependence on [ROH] can obtain. That k_{Nu} could show little dependence on the structure of the alcohol has already been pointed out.

Given the considerably greater proton basicity of an alkoxy vs. an alkylthio group,[13] it would be expected that $k_p \gg k_{-p}$ and $k_{-YO} > k_{-p}$ for the reaction of a thiol with either 1 or **2b** (NuH = *n*-BuSH; YO = OH or OMe); eq 8 will become $k_{exptl} = k_{-c}K_{assoc}[HA]\{k_pk_{Nu}[RSH]/(k_ck_{-Nu} + k_ck_p + k_pk_{Nu}[RSH])\}$. This is almost identical in form to eq 9, and for a case where $k_p > k_{-Nu}$ (as might be anticipated for catalysis by H^+) it will reduce to $k_{exptl} = k_{-c}K_{assoc}[HA]\{k_{Nu}[RSH]/(k_c + k_{Nu}[RSH])\}$. At the concentrations (≤0.04 M) of thiol used it is expected that under most circumstances k_c is enough larger than k_{Nu}[RSH] so that k_{exptl} will be strictly proportional to [RSH], although for the reaction of **2b** with *n*-BuSH in MeCN–2 M MeOH a somewhat less than first-order dependence on [RSH], such as would be expected when $k_{Nu}[NuH] \simeq k_c$, appears to be observed.

Scheme I. Proposed Mechanism for Acid-Catalyzed Nucleophilic Substitution Reactions of *o*-Nitrobenzeneselenenic Acid and Its Derivatives



1, YO = OH; 2, YO = OR; 3, YO = o-$O_2NC_6H_4SeO$; NuH = H_2O, ROH, or RSH

For the hydrolysis of **3** (NuH = H_2O; YO = *o*-$O_2NC_6H_4SeO$) the structures for $I^{\pm}$·HA and $T^{\pm}$·HA suggest that $k_{-YO} > k_{-Nu}$ and $k_{-p} > k_p$. For weaker acids as catalysts it seems reasonable that both $k_{-Nu} > k_p$ and $k_{-YO} > k_{-p}$. If $k_{Nu}[H_2O]$ is comparable to k_c, eq 8 will simplify to $k_{exptl} = k_{-c}K_{assoc}[HA](k_pk_{Nu}[H_2O]/k_ck_{-Nu})$. If $k_p > k_{-Nu}$ for catalysis by H_3O^+ and therefore $(1 + (k_{-Nu}/k_p)) \simeq 1$, eq 8 becomes

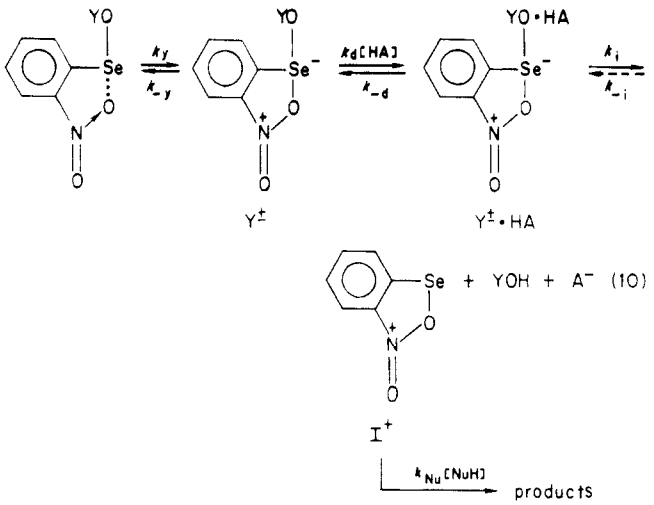
$$k_{exptl} = k_{-c}K_{assoc}[H_3O^+] \times \left\{\frac{k_{Nu}[H_2O]}{k_c(1 + (k_{-Nu}/k_p)(k_{-p}/k_{-YO})) + k_{Nu}[H_2O]}\right\}$$

If $(k_{-Nu}/k_p) \simeq (k_{-YO}/k_{-p})$, certainly not an unreasonable assumption, then k_{exptl} for the H_3O^+-catalyzed hydrolysis

(13) Arnett, E. M. *Prog. Phys. Org. Chem.* **1963**, *1*, 223. See Table X (p 319) or Tables XXA (p 351) and XXVIIA (p 398).

should be approximately equal to $k_{-c}K_{assoc}[H_3O^+]\{k_{Nu}[H_2O]/(2k_c + k_{Nu}[H_2O])\}$, an expression that is the same as that for the H_3O^+-catalyzed hydrolysis of **2b** and that is consistent with the experimental observation that the two H_3O^+-catalyzed reactions have similar rates.

The experimental behavior of all the acid-catalyzed nucleophilic substitution reactions of **1** and its derivatives seems to be able to be satisfactorily accommodated by the mechanism in Scheme I in a straightforward fashion. At the same time, it should be recognized that an alternate interpretation of the various results is also possible, one that starts with the premise that the hydrolyses of **2** and **3**, and esterification of **1**, take place by an entirely different mechanism than the reactions of **1** and **2b** with a thiol. In this alternate interpretation the acid-catalyzed dissociative mechanism shown in eq 10 is presumed to apply for the



hydrolysis of **2** (YO = OR; NuH = H_2O), esterification of **1** (YO = OH; NuH = ROH), or hydrolysis of **3** (YO = o-$O_2NC_6H_4SeO$; NuH = H_2O). Since under the reaction conditions employed $k_{Nu}[NuH] > k_{-i}[YOH]$ the rate-determining step for each of these reactions will be prior to step k_{Nu}. The mechanism can therefore account for the lack of dependence of the rate of esterification of **1** on alcohol structure and for the lack of dependence on $[H_2O]$ and [ROH], respectively, of the rates of H^+-catalyzed hydrolysis of **2b** and esterification of **1**. If $k_i < k_{-d}$ for the weaker acid catalysts, but $k_i > k_{-d}$ for the most acidic catalysts, such as H_3O^+, the mechanism can account for the nonlinear Brønsted plots observed with the hydrolyses of both **2b** and **3** in 60% dioxane.

In this alternative interpretation for the results the mechanism for the reaction of a thiol with **1** or **2b** is considered to take place by an entirely different mechanism than eq 10. This could be either the mechanism in eq 5 that was suggested earlier[4] or the modification of that mechanism shown in Scheme I (NuH = RSH). The experimental observations that rule out the mechanism in eq 10 for the thiol reactions are summarized in a footnote.[14] The failure of the thiol reactions to use the mechanism in eq 10 would be attributed to the fact that the concentrations of *n*-BuSH used (≤0.04 M) are too low for capture of I^+ by thiol to be adequately competitive with the capture of I^+ by YOH (which will be either H_2O or MeOH and will be present in high concentration as a component of the solvent).

While this alternate interpretation involving a dichotomy of mechanism for the two groups of reactions is tenable, the principle of Occam's razor would suggest that the simpler single mechanism in Scheme I should probably be preferred. Beyond that we have another concern regarding eq 10. If it is assumed to be the mechanism for hydrolysis of **2b**, then for the H_3O^+-catalyzed hydrolysis (where $k_i > k_{-d}$) $k_{H_3O^+} = k_d(k_y/k_{-y})$, and since $k_d \simeq 10^{10}$ M^{-1} s^{-1}, $k_y/k_{-y} \simeq 10^{-10}$. This would require the free energy of $Y^{\pm}$ to be 13 kcal/mol greater than that of **2b**, a value that seems surprisingly large given the close structural relationship between **2b** and $Y^{\pm}$.

One final note: while the Discussion has centered on the mechanism for the interconversion of **1** and **2**, the potential utility of the acid-catalyzed esterification of **1** as an extremely simple and mild synthetic procedure for the preparation of alkyl esters of *o*-nitrobenzeneselenenic acid should also be kept in mind.

Experimental Section

Preparation and Purification of Reagents. *o*-Nitrobenzeneselenenic anhydride[2] and ethyl *o*-nitrophenyl selenide[3] were prepared and purified as previously described. The various alcohols and 1-butanethiol were of the highest purity commercially available and were further purified by fractional distillation. Acetonitrile (Aldrich, spectrophotometric grade) was distilled before use. Dioxane was purified[15] to remove peroxides and water, and after fractional distillation, the anhydrous solvent was frozen and stored at −20 °C to prevent the formation of peroxides prior to use. All water used in the kinetic studies was doubly distilled from glass. The acids used as catalysts were of the highest purity commercially available.

Preparation of Solutions of *o*-Nitrobenzeneselenenic Acid (1). Ethyl *o*-nitrophenyl selenide (0.23 g, 1 mmol) was dissolved in 2 mL of methylene chloride and the solution cooled to −20 °C. A solution of 1.1 mmol of *m*-chloroperoxybenzoic acid in 2 mL of ether was then added gradually with stirring. The reaction mixture was kept at −20 °C until TLC showed that no selenide remained unoxidized. The reaction mixture was then promptly transferred to a separatory funnel, 10 mL more methylene chloride was added, and the solution was extracted with 5 mL of ice-cold, 0.71 N aqueous potassium hydroxide. The organic layer was washed once, separated, dried ($MgSO_4$), and filtered. The dried filtrate containing ethyl *o*-nitrophenyl selenoxide was allowed to stand at room temperature for 5–12 h until decomposition of the selenoxide to **1** and ethylene was complete. The solvent was then removed at reduced pressure at below room temperature, and the residue of **1** was immediately dissolved in an organic solvent (MeCN, EtOH, or MeOH) to give a solution having the desired concentration. The concentration of **1** (ϵ 3.8×10^3) was ascertained from the absorbance of the solution at the long wavelength λ_{max} of **1** (420–427 nm depending on solvent).

Reaction of 1 with Alcohols. Products. To 10 mL of a 0.01 M solution of **1** in either methanol or ethanol was added 20 μL of a 2.5 M solution of perchloric acid in the same alcohol. The progress of the reaction was monitored by TLC and was complete in a few minutes. At that point the reaction solution was filtered through ~5 g of silica gel that had been premoistened with methylene chloride and was contained in a small sintered-glass funnel. (The purpose of this procedure is to remove the perchloric acid.) The silica gel was then washed five times with 10 mL portions of methylene chloride. The combined filtrates from two runs were evaporated under reduced pressure.

In the case of the reaction with methanol the evaporation was halted when 1–2 mL of solvent remained, and the solution was placed in the freezer. Orange needles of methyl *o*-nitrobenzeneselenenate (0.045 g, 97%), mp 52–53 °C (lit.[16] 52 °C),

(14) Given the first-order dependence of rate on [*n*-BuSH], if the reactions of **1** or **2b** with *n*-BuSH were proceeding by eq 10, the rate-determining step would have to be capture of I^+ by thiol (step k_{Nu}). This in turn would require that the experimental first-order rate for the H^+-catalyzed reaction of **1** (or **2b**) with *n*-BuSH be slower than the rate of formation of I^+, the latter being equal to the rate of esterification of **1** (or hydrolysis of **2b**) under the same conditions. The experimental results show this is not true.

(15) Fieser, L. F.; Fieser, M. F. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 333.

separated and were filtered off: ^{1}H NMR (acetone-d_6) δ 3.94 (s, 3 H), 7.35–8.60 (m, 4 H); mass spectrum, m/e 233 (M^+, ^{80}Se), 202 (M^+ – MeO); UV (60% dioxane) λ_{max} 419 nm (ϵ 3.7 × 10^3).

In the reaction with ethanol all of the solvent was removed and the residue was taken up in hexane. The hexane solution was filtered through a plug of glass wool contained in a disposable pipet, and the hexane was removed under reduced pressure. The residue was kept under high vacuum for 4 h at room temperature to remove the last traces of solvent. This gave 0.047 g (96%) of ethyl *o*-nitrobenzeneselenenate as an orange-red oil: IR (neat) 3092, 3076, 2970, 2926, 2876, 1589, 1566, 1506, 1446, 1325, 1300, 1097, 1024, 833, 731 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 1.30 (t, 3 H), 4.02 (q, 2 H), 7.3–8.6 (m, 4 H); mass spectrum, m/e 247 (M^+, ^{80}Se), 202 (M^+ – EtO); UV (60% dioxane) λ_{max} 418 nm (ϵ 3.7 × 10^3). Anal. Calcd for $C_8H_9NO_3Se$: C, 38.88; H, 3.67. Found: C, 38.75; H, 3.55.

Kinetics. The solvent (3.5 mL), either ethanol or acetonitrile–alcohol, containing the desired amounts of acid catalyst and salt being used to maintain ionic strength, was placed in a 1-cm cell in the thermostated cell compartment of a UV–visible spectrophotometer. There was then added by microsyringe 35 μL of a 10^{-2} M solution of **1** in either ethanol or acetonitrile, and the decrease in the absorbance (A) of the solution with time at 460 nm was recorded. A plot of log ($A - A_\infty$) vs. time for each run was linear.

Hydrolysis of 2b. Kinetics. The same general procedure used to study the kinetics of the esterification of **1** was employed. The selenenate ester (35 μL of a 10^{-2} M solution in either dioxane or acetonitrile) was added to 3.5 mL of either 60% dioxane or acetonitrile–H_2O containing the proper concentrations of buffer (or strong acid) and salt used to maintain constant ionic strength. The progress of the hydrolysis was determined by measuring the increase in the absorbance of the solution at 460 nm.

Reaction of 2b with 1-Butanethiol. Kinetics. A solution of **2b** (10^{-4} M) in either methanol or acetonitrile–MeOH and containing the desired concentrations of trifluoromethanesulfonic acid and sodium trifluoromethanesulfonate was placed in a cell in the spectrophotometer. Once thermal equilibrium was reached, the reaction was initiated by the addition via microsyringe with good mixing of the appropriate amount of a 2 M solution of *n*-BuSH in either methanol or acetonitrile–MeOH. The reaction of the thiol with **2b** was followed by measuring the decrease in optical density at 440 nm.

Reaction of 1 with 1-Butanethiol. Kinetics. The same procedure as just outlined for the reaction of the thiol with **2b** was employed, except that the solvent was acetonitrile–water.

Registry No. **1**, 56790-60-4; **2a**, 99642-70-3; **2b**, 56790-61-5; CH_3CH_2OH, 64-17-5; CH_3OH, 67-56-1; FCH_2CH_2OH, 371-62-0; $HOCH_2CH_2OH$, 107-21-1; $PhCH_2OH$, 100-51-6; $NCCH_2CH_2OH$, 109-78-4; $(CH_3)_2CHOH$, 67-63-0; *n*-BuSH, 109-79-5; *o*-$O_2NC_6H_4SeSBu$-*n*, 81398-78-9; $CH_3CH_2SeC_6H_4$-*p*-NO_2, 65275-58-3; $CH_3CH_2Se(O)C_6H_4$-*p*-NO_2, 65275-45-8.

Supplementary Material Available: Tabulation of results of individual kinetic runs for reaction of *n*-BuSH with **2b** (in MeOH and MeCN–MeOH) and with **1** (MeCN–H_2O) (1 page). Ordering information is given on any current masthead page.

(16) Holzle, G.; Jenny, W. *Helv. Chim. Acta* **1958**, *41*, 331.

Identification of the Rotamers of Hexakis(2-methoxyphenyl)benzene and Hexakis(2-methylphenyl)benzene

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Seven isomers are observed for both hexakis(2-methoxyphenyl)benzene (compound **1**) and hexakis(2-methylphenyl)benzene (compound **2**). Theoretically seven achiral rotamers and one pair of enantiomeric rotamers were predicted, so that eight isomers are expected to be observed by NMR in achiral solvents. From the methoxy (methyl) region of the ^{1}H NMR spectra of **1** (**2**), only pairwise interchangeable assignments can be achieved, since the rotamers have pairwise identical NMR patterns. Thus $2^4 = 16$ global assignments are possible. The molar fractions of the isomers of **1** (**2**) at equilibrium in *o*-dichlorobenzene (kerosene) at 393 K (487 K) were evaluated in terms of the interactions between adjacent pairs of peripheral aryl rings. This resulted in two global assignments, one corresponding to mainly repulsive, the other to mainly attractive steric interactions between these adjacent pairs of peripheral rings. The capacity factors of the isomers upon HPLC on silica allowed a definite choice between the global assignments for **1**, using a Hammett-like equation. In the case of **2**, it was not possible to make a definite choice between the global assignments upon chromatographical grounds.

The stereochemistry of hexaarylbenzenes has been studied less extensively than that of many other polyaryl systems.[1,10] Only in 1977 Gust[2] pointed out the possibility of isomerism arising from hindered rotation around the bonds between the peripheral aryl rings (P-rings) and the central benzene ring (C-ring), provided at least two P-rings lack local C_2 symmetry. Gust[2,3] was the first to prepare such hexaarylbenzenes and to observe this isomerism. He found two isomers for all the compounds studied, whenever these contain two dissymmetrical, ortho-substituted P-rings. These isomers could be separated at room temperature but were converted into an equilibrium mixture at higher temperatures. He considered these isomers[4] as the rotamers[4] expected if the internal rotation of the ortho-substituted P-rings is slow on the laboratory time scale

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(1) (a) Willem, R.; Pepermans, H.; Hallenga, K.; Gielen, M.; Dams, R.; Geise, H. J. *J. Org. Chem.* **1983**, *48*, 1890. (b) Willem, R.; Pepermans, H.; Hoogzand, C.; Hallenga, K.; Gielen, M. *J. Am. Chem. Soc.* **1981**, *103*, 2297. (c) Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 1535. (d) Mislow, K.; Gust, D.; Finocchiaro, P.; Boettcher, R. J. *Fortschr. Chem. Forsch.* **1974**, *47*, 1. (e) Brocas, J.; Gielen, M.; Willem, R. "The Permutational Approach to Dynamic Stereochemistry"; McGraw-Hill: New York, 1983; pp 262–269, 286–292, 471–533.

(2) Gust, D. *J. Am. Chem. Soc.* **1977**, *99*, 6980.

(3) Gust, D.; Patton, A. *J. Am. Chem. Soc.* **1978**, *100*, 8175.

(4) In general, "rotamer" is just a particular term for an isomer in the case of rotational isomerism. In this paper "rotamer" is used exclusively for the theoretically predicted isomers. In contradistinction, the experimentally observed isomers are named systematically "isomer".

0022-3263/86/1951-0301$01.50/0