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EVIDENCE FOR CAGED INTERMEDIATE SPECIES
IN A FORMAL NUCLEOPHILIC AROMATION SUBSTITUTION

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Among the methods which have been used for the synthesis of arylstannanes is the reaction of a stannylanionoid with a halobenzene, eq. 1.[1]

$$R_3Sn^-,Na^+ + Ar\text{-}X \rightarrow R_3Sn\text{-}Ar + NaX \qquad (1)$$

Yields of arylstannanes obtained range from about 20% to 80%, and iodobenzenes and bromobenzenes are more reactive than chlorobenzenes. The reactions occur with remarkable ease as exemplified by our observation that, in tetraglyme at o°, trimethylstannylsodium reacts with bromobenzene to form trimethylphenylstannane as fast as it does with n-butylbromide to form _n_-butyltrimethylstannane. This suggests that the mechanism in the case of the aryl halide is different from that for activated nucleophilic aromatic substitution. It was of interest, therefore, to ascertain which, if any, of the other known mechanisms for nucleophilic aromatic substitution is involved.[2]

In initial experiments it was observed that small to moderate amounts of arene, formed by reduction of the aryl halide were present among the reaction products. In order to establish whether an aryl anion was an intermediate which could be trapped by a good proton donor a series of experiments was carried out in which _t_-butyl alcohol was present in the original reaction mixture in tetraglyme along with bromobenzene and trimethylstannylsodium. The products were analyzed for trimethylphenylstannane and benzene. These accounted quantitatively for the amounts of bromobenzene (used in excess) consumed. Fig. 1 shows that the proportion of benzene increases sharply when the alcohol/stannylsodium ratio is small (<3), levels off, and remains constant (actually up to a ratio of at least 20). Conversely, the

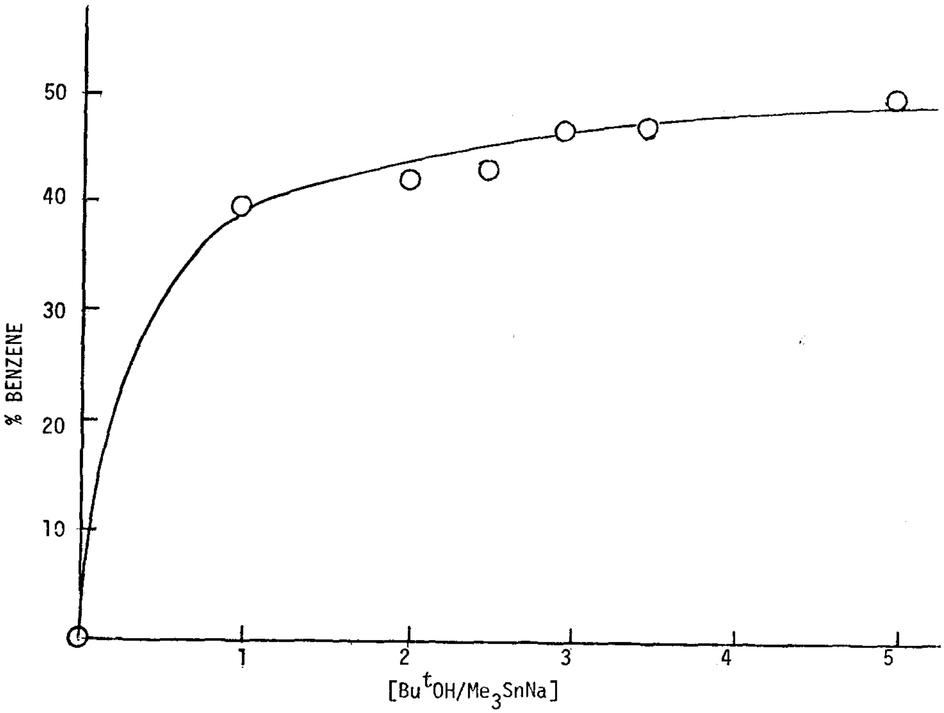

Fig. 1. Effect of t-butyl alcohol concentration on benzene yield.

proportion of trimethylphenylstannane (not shown) falls off from 100% as the mirror image of the benzene plot. One interpretation for these observations is that two reactions are occurring in competition; one involves direct substitution to form trimethylphenylstannane; the other involves nucleophilic displacement on bromine leading to formation of phenylsodium which can react with the trimethylbromostannane to form additional substitution product and with solvent or with the more acidic t-butyl alcohol, when it is present, to form benzene. Another interpretation has all of the reaction proceeding via the second pathway to form the products shown in brackets in eq. 2.[3] In this scheme the

$$\begin{tikzcd}
\emptyset Br + Me_3Sn^-,Na^+ \rightarrow & {[\emptyset^-,Na^+ \quad BrSnMe_3]} \arrow[r, "k_s"] \arrow[d, "k_{diff.}"] & \emptyset SnMe_3 + NaBr \\
\emptyset H & \emptyset^-,Na^+ + BrSnMe_3 \arrow[l, "Bu^tOH"', "k_r"] \arrow[ur, "k_s'"'] &
\end{tikzcd} \qquad (2)$$

product distribution depends, first on the magnitudes of k_s for substitution product formation in the cage and the rate of diffusion k_{diff} of the species from the cage; and secondly on the relative magnitudes of k_r and k_s' and the concentrations of alcohol and trimethylbromostannane.

The two mechanisms can be distinguished by an examination of the effect of solvent viscosity on the product distribution, for a decrease in viscosity would increase k_{diff}, and the result would be an increase in the proportion of benzene in the product mixture. This has been done using 1,2-dimethoxyethane (DME) and tetraglyme (TG) solvent mixtures[4] with the results displayed in Table 1 with p-bromotoluene used as the substrate for experimental convenience.

Table 1

Effect of Solvent Viscosity on Reduction and Substitution Product Distribution[a]

DME/TG (v/v)	$\%\emptyset CH_3$	$\emptyset CH_3/Ar\underline{Sn}$[b]	$\eta(cP)$[c]	$(1/\eta)^{1/2}$
0	49	.96	2.93	0.58
20	55	1.22	1.80	0.74
40	60	1.50	1.21	0.91
60	64.0	1.78	0.87	1.07
80	69	2.23	0.60	1.29

[a] Reactant concentrations: ArBr, 0.20 M; Me_3SnNa, 0.10 M; Bu^tOH/Me_3SnNa, 5.0; T, 25°.

[b] $p\text{-}MeC_6H_4SnMe_3$.

[c] Solutions were 0.5 M in Bu^tOH; 0.2 M in ArBr; and 0.06 M in decane (internal standard) in order to approximate reaction medium at start of reaction.

Koenig and Deinzer have shown that the ratio of the yield of product formed from a radical escaped from a cage to that formed within the cage should vary inversely as the square root of the viscosity.[5] Least squares treatment of the data in Table 1 results in the expression: $\emptyset CH_3/Ar\underline{Sn} = -0.09 + 1.78\ (\eta)^{-1/2}$ with correlation coefficient 0.999 and standard deviation 0.026. The linear correlation is fully consistent with the mechanism of eq. 2, and the zero intercept indicates that only substitution product is formed in the cage. This new type of cage effect may well occur in other bimolecular polar reactions, and the dependence of product distribution on viscosity has obvious synthetic implications.

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References

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   b) H. Gilman and S. D. Rosenberg, ibid., 74, 531 (1952);
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(2) See J. F. Bunnett, Accts. Chem. Res., 5, 139 (1972) and references cited therein.

(3) Such a possibility has been considered for nucleophilic displacements on haloalkynes (R. Tanaka, M. Rodgers, R. Simonaitis and S. I. Miller, Tetrahedron, 27, 2651 (1971).

(4) Independent experiments have shown that tetraglyme is so much more effective in solvating sodium ions than simpler ethers that one may reasonably assume that it is by far the dominant solvating species even when it constitutes only 20% of the DME/TG solvent.

(5) T. Koenig and M. Deinzer, J. Amer. Chem. Soc., 90, 7014 (1968).