Reaction of Cyclic Halonium Ions and Alkylene Dihalides with Polystyryllithium. Preparation of Haloalkylated Polystyrene

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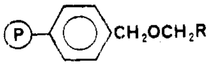
The use of polymeric reagents, catalysts, and substrates in synthesis[1-13] has prompted a search for functionalized polymers to serve the varied needs.[4-18] Our search for a recyclable polymer for use in synthesis of chiral substances[19] identified the need for a functionalizable polymer capable of withstanding strongly basic and moderately acidic conditions. Commercially available chloromethylated polystyrene is readily converted to the functionalized benzylic ethers **1**. However, these suffer sufficient benzylic ether cleavage in 6 M ethanolic HCl to warrant our search for a substitute. Thus, synthesis of precursors to nonbenzylic ether **2** was undertaken.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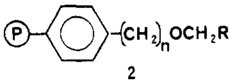
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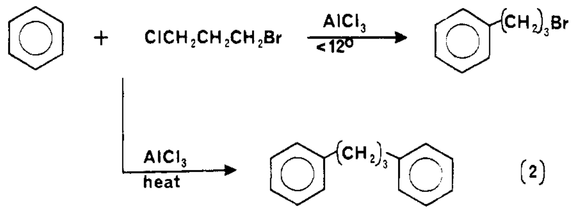
One approach to **2** is through reaction of dihalides with simple aromatic compounds under alkylation conditions. Although monosubstitution sometimes occurs, earlier studies[20,21] have shown that the major reaction pathway involves displacement of both halogens. Presence of a second halogen in an alkyl halide slows alkylation rates,[22] and hence the (haloalkyl)arene is more reactive than the dihaloalkane. Thus through a combination of intra- and intermolecular alkylations, complex mixtures may result.

Tsukervanik and Yatsimirskii[23] reported that the commercially available mixed dihalide 1-chloro-3-bromopropane reacts with benzene at 6–12 °C in the presence of $AlCl_3$ to give a 60% yield of (3-bromopropyl)benzene, but at a higher temperature diphenylpropane is the product (eq 1 and 2). Schmerling et al.[24] have found that


(1)

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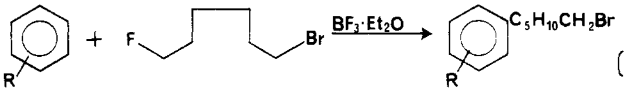
certain dihaloalkanes will selectively undergo monosubstitution when the halogens are at primary–secondary or primary–tertiary positions. However, the reactions are not always free of rearrangement products or byproducts. A better procedure for monosubstitution appears to that of Olah and Kuhn.[20] When chloro-, bromo-, or iodoalkyl fluorides are reacted with benzene at temperatures ranging from −20 to +20 °C in the presence of boron trihalide catalysts, the fluoride is selectively displaced, giving (haloalkyl)benzene derivatives in yields of 57–94% (eq 3).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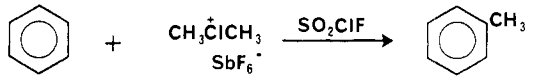
Another suggested procedure comes from the report of Olah et al.,[25] who found that dialkylhalonium ions are reactive alkylating agents toward benzene, toluene, and ethylbenzene. These reactions in SO_2ClF solution generally occur rapidly even at −50 °C, giving the alkylated aromatic and free alkyl halide (eq 4). The use of cyclic halonium ions, which would give the haloalkyl aromatic, has not been reported.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Because our attempts to adapt the reactions of eq 1 and 3 to the synthesis of precursors of **2** were not fully satisfactory,[26-28] we investigated the reaction of cyclic halonium ions[29] or their precursor alkyl dihalides[5] with polystyryllithium.

By use of the method of Farrall and Fréchet,[5] throughly washed macroreticular polystyrene was lithiated with *n*-butyllithium–tetramethylethylenediamine (*n*-BuLi–TMEDA) in cyclohexane to give polystyryllithium containing 1.5–2.0 mequiv of Li/g. The beads were washed twice with cyclohexane. A sulfur dioxide solution of the respective halonium ion **3–5** was slowly added under ni-

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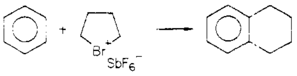
(1) Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327.
(2) Leznoff, C. C. *Chem. Soc. Rev.* **1974**, *3*, 65.
(3) Neckers, D. C. *J. Chem. Educ.* **1975**, *52*, 695.
(4) Mitchell, A. R.; Kent, S. B. H.; Engelhard, M.; Merrifield, R. B. *J. Org. Chem.* **1978**, *43*, 2845 and references therein.
(5) Farrall, M. J.; Fréchet J. M. J. *J. Org. Chem.* **1976**, *41*, 3877.
(6) Crosby, G. A.; Kato, M. *J. Am. Chem. Soc.* **1977**, *99*, 278.
(7) Gait, M. J.; Sheppard, R. C. *J. Am. Chem. Soc.* **1976**, *98*, 8514.
(8) Orlowski, R. C.; Walter, R.; Winkler, D. *J. Org. Chem.* **1976**, *41*, 3701.
(9) Pittman, C. U., Jr.; Smith, L. R. *J. Am. Chem. Soc.* **1975**, *97*, 1749.
(10) Atherton, E.; Clive, D. L. J.; Sheppard, R. C. *J. Am. Chem. Soc.* **1975**, *97*, 6584.
(11) Fréchet, J. M. J.; Haque, K. E. *Tetrahedron Lett.* **1975**, 3055.
(12) Chapman, P. H.; Walker, D. *J. Chem. Soc., Chem. Commun.* **1975**, 690.
(13) Buis, J. T. W. A. R. M.; Tesser, G. I.; Nivard, R. J. F. *Tetrahedron* **1976**, *32*, 2321.
(14) Collman, J. P.; Hegedes, L. S.; Cooke, M. P.; Norton, J. R.; Dolcetti, G.; Marquardt, D. N. *J. Am. Chem. Soc.* **1972**, *94*, 1789.
(15) Mitchell, A. R.; Erikson, B. W.; Ryabtser, M. N.; Hodges, R. S.; Merrifield, R. B. *J. Am. Chem. Soc.* **1976**, *98*, 7357.
(16) Takaishi, N.; Imai, H.; Bertelo, C. A.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 264.
(17) Warshawsky, A.; Kalir, R.; Patchornik, A. *J. Org. Chem.* **1978**, *43*, 3151.
(18) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149.
(19) McManus, S. P.; Colwell, A. R.; Brooks, R., submitted for publication. Colwell, A. R. M.S. Thesis, The University of Alabama in Huntsville, May 1978.
(20) Olah, G. A.; Kuhn, S. J. *J. Org. Chem.* **1964**, *29*, 2317.
(21) Olah, G. A. "Friedel-Crafts Chemistry"; Wiley-Interscience: New York, 1973; pp 172-4, 442-5.
(22) Ransley, R. L. *J. Org. Chem.* **1968**, *33*, 1517.
(23) Tsukervanik, I.; Yatsimirskii, K. *J. Gen. Chem. USSR (Engl. Transl.)* **1940**, *10*, 1075.
(24) Schmerling, L.; Welch, R. W.; West, J. P. *J. Am. Chem. Soc.* **1956**, *78*, 5406. Schmerling, L.; Welch, R. W.; Lewis, J. P. *Ibid.* **1957**, *79*, 2636.
(25) Olah, G. A.; DeMember, J. R.; Mo, Y. K.; Svoboda, J. J.; Schilling, P.; Olah, J. A. *J. Am. Chem. Soc.* **1974**, *96*, 884.
(26) In our laboratory the reaction of benzene with commercially available 1-bromo-3-chloropropane and $AlCl_3$[23] proceeded to only 5% completion after several hours. Because the reaction would be even slower with cross-linked polystyrene, we opted to adapt Olah and Kuhn's method[20] and obtained goods yields of an ortho and para mixture of bromoalkylated toluene. However, conversion of 1,6-dibromohexane to the required 1-bromo-6-fluorohexane was incomplete, and the two dihalides codistilled. This procedure was not attempted on polystyrene because of the our fear of double alkylation (cyclization) under the conditions necessary for reaction with the polymer (cf. ref 27).
(27) In preliminary experiments we found that benzene or toluene reacted with tetramethylenebromonium hexafluoroantimonate in SO_2 between −20 to −78 °C to give mainly cyclization product, presumably by reaction of the initially formed 4-bromobutylbenzene with the liberated $HSbF_6$; e.g., see ref 20 and 28.



(28) Bruson, H. A.; Kroeger, G. W. *J. Am. Chem. Soc.* **1940**, *62*, 36.
(29) Olah, G. A.; Peterson, P. E. *J. Am. Chem. Soc.* **1968**, *90*, 4675.

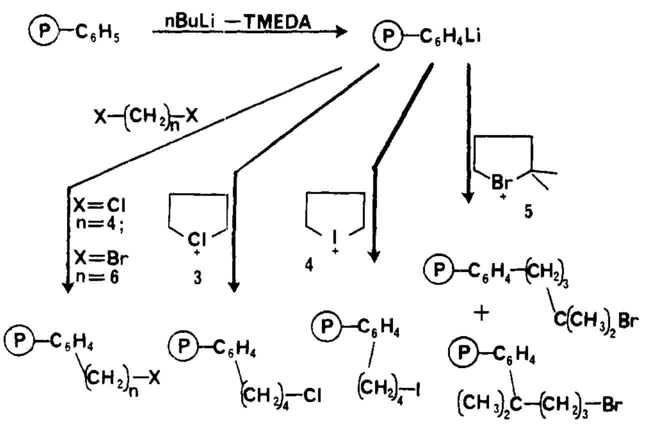
0022-3263/80/1945-2717$01.00/0

Table I. Product Analysis of the Reaction of Polystyryllithium with Halonium Ions and Dihalides

haloalkylating agent	% X found	mequiv of X/g[a]	infrared analysis, cm^{-1} [b] CH$_2$X	RArR′	CX
tetramethylenechloronium ion (3)	5.44	1.5	1250 (m)	1115 (m)	730 (m)[c]
1,4-dichlorobutane	0.31	0.09	1250 (m)	1115 (m)	*d*
1,1-dimethyltetramethylenebromonium ion (5)	3.08	0.39	1250 (m)	1115 (m)	*d*
1,6-dibromohexane	3.56	0.45	1250 (m)	1105 (vw)	*d*
tetramethyleneiodonium ion (4)	7.12	0.56	1250 (w)	1115 (vw)	*e*

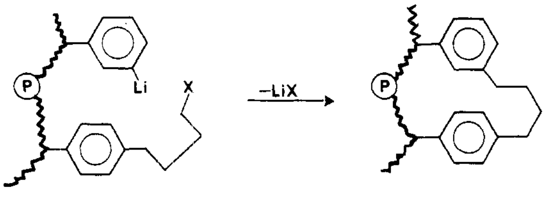
[a] The polystyryllithium had 1.5-2.0 mequiv of Li/g. [b] The starting polystyrene resin has no absorption at 1250 cm^{-1} and a very weak (vw) absorption at 1105 cm^{-1}. [c] Shoulder on the strong aryl peak at 750 cm^{-1}. [d] Not observed but possibly obscured by the aryl absorption at 750 (Cl) or 690 cm^{-1} (Br). [e] Not expected in the infrared range recorded.

Scheme I



trogen to the supercooled suspension (~-10 to -20 °C) of the beads in cyclohexane. For comparison the dihalide precursors to **3** and **5** were also reacted with polystyryllithium in cyclohexane. The haloalkylated polystyrenes (Scheme I) were characterized by infrared spectroscopic analysis (appearance of CH$_2$X at 1250 cm^{-1} and a band at ~1115 cm^{-1} characteristic of the dialkylarene) and elemental analysis for the halogen. The relative efficiency of all of these reactions[30] is shown by the data in Table I.

The reaction with the tetramethylenechloronium ion (**3**) is shown to be the most efficient at functionalization. Its precursor, 1,4-dichlorobutane, gives the poorest result. Interestingly, the iodonium ion **4** and bromonium ion **5** are indicated to be suprisingly inefficient. However, we believe this finding is a consequence of intrapolymeric interactions. All three of the halonium ions are expected to react rapidly with any polymer-bound aryllithium site contacted. If there is a neighboring aryllithium site appropriately disposed, displacement of the second halogen may occur (eq 5). This reaction would be competitive with reaction by the neighboring aryllithium with halonium ions. While the reaction with halonium ions would occur with a more favorable $\Delta H^{\ddagger}$, the intramolecular character of the cyclization (cross-linking) would give it a more favorable $\Delta S^{\ddagger}$ term and perhaps a more favorable $\Delta G^{\ddagger}$.[31]



(5)

The above explanation is given support by the observation that the more easily displaceable halogens, bromide and iodide,[32] are found in low concentrations in the products from both the halonium ion and the dihalide reactions.[33] Conversely, chloride from the chloronium ion reaction is present in near quantitative amounts while it is nearly absent from the dichloride reaction. Assuming primary chloride is very slowly displaced by polymer-bound aryllithium under the conditions employed, the result is very little cyclization after chloronium ion ring opening and very little reaction of 1,4-dichlorobutane with polystyryllithium.

The infrared spectral analysis supports the above argument in part. The first and third entries of Table I show strong evidence (bands at 1250 and 1115 cm^{-1}) for reaction and for halogen in the product. The latter two show weak evidence for halogen (CH$_2$X) and less evidence for disubstituted aryl. Therefore, it is possible (but surprising) that the more stable halonium ions and the dihalides showed poor reactivity toward the polystyryllithium.

In conclusion, the reaction of the tetramethylenechloronium ion with an insoluble, cross-linked, polystyryllithium resin gives a high yield of chlorobutylated polystyrene. Because of low reactivity of the haloalkylating agent or of intrapolymeric displacement reactions, the other haloalkylating agents proved unsatisfactory. Nevertheless, the chloroalkylated product should prove to be an excellent alternative to chloromethylated polystyrene for general use.[34]

Experimental Section

Materials and Analysis. The macroreticular, cross-linked, polystyrene resin (Rohm and Haas XE-305) was thoroughly washed[5] before use. 1,4-Dichlorobutane, 1,4-diiodobutane, and 1,6-dibromohexane were purchased as reagent grade and were used without additional purification. All reaction solvents except sulfur dioxide (Matheson) were dried, distilled, and stored with protection from moisture. Filtration and washing of the polymer beads were efficiently carried out by using a pressure filter system.[35] Infrared spectra were recorded as KBr disks with a Beckman Acculab I. Elemental analyses were performed by Gailbraith Laboratories, Inc.

The halonium ions were prepared as previously described[36,37] from the appropriate tetramethylene or hexamethylene dihalide.

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[30] The specific degree of functionality of the polystyryllithium is not known in individual examples (cf. ref 5).

[31] For a discussion of the effect of intramolecularity, see: Capon, B.; McManus, S. P. "Neighboring Group Participation"; Plenum: New York, 1976; Vol. 1, pp 43-58. Such reactions in these polymers are common. Cf.: Fréchet, J. M. J.; deSmet, M. D.; Farrall, M. J. *J. Org. Chem.* **1979**, *44*, 1774.

[32] Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; Cornell University Press: Ithaca, NY, 1969; pp 453-7.

[33] Farrall and Fréchet[5] also reported a relatively poor yield for bromoethylation with ethylene dibromide.

[34] We have found that chlorine displacement should be carried out in the presence of crown ethers or phase-transfer agents. Cf.: N'Guyan, T. D.; Boileau, S. *Tetrahedron Lett.* **1979**, 2651; Worster, P. M.; McArther, C. R.; Leznoff, C. C. *Agnew Chem., Int. Ed. Engl.* **1979**, *18*, 221. See also Fréchet et al.[31]

[35] Designed by L. R. Duckwall and R. Smith. Cf.: Colwell, A. R.[19]

[36] Bonazza, B. R.; Peterson, P. E. *J. Org. Chem.* **1973**, *38*, 1010. Henrichs, P. M.; Peterson, P. E. *J. Am. Chem. Soc.* **1973**, *95*, 7449. See also: Olah, G. A.; Westerman, P. W.; Melby, E. G.; Mo. Y. K. *Ibid.* **1974**, *96*, 3565.

[37] Peterson, P. E.; Bonazza, B. R.; Henrichs, P. M. *J. Am. Chem. Soc.* **1973**, *95*, 2222.

The iodonium ion was recrystallized[37] from CH_2Cl_2 and SO_2. The halonium ions were stored as their SbF_6^- salts in SO_2 at -80 °C until use.

Polystyryllithium (1.5-20 mequiv of Li/g) was prepared by direct lithiation of polystyrene in cyclohexane by using n-BuLi–TMEDA.[5] The product was washed twice with dry cyclohexane before use.

Reaction of Halonium Ions with Polystyryllithium. Tetramethylenechloronium Ion. To a magnetically stirred supercooled (-10 to -20 °C) suspension of polystyryllithium (2.8 g, 1.5-2.0 mequiv of Li/g) in 50 mL of dry cyclohexane under dry N_2 was rapidly added 50 mL of a solution of tetramethylenechloronium hexafluoroantimonate (34 mmol) in SO_2 at -40 °C [prepared from 1,4-dichlorobutane (4.32 g, 34 mmol) and antimony pentafluoride (7.34 g, 34 mmol)]. Stirring was continued as the temperature was allowed to slowly approach room temperature. The resin became dark brown from the initial deep reddish orange color of the aryllithium. After 1 h the resin was pressure filtered by using dry N_2 and was washed sequentially with nine 200-mL portions of H_2O, THF, and MeOH in the respective proportions 9:1:0, 7:3:0, 1:1:0, 3:7:0, 1:8:1, 0:7:3, 0:1:1, 0:3:7, 0:0:1. The chlorobutylated polystyrene was dried on the pressure filter (2 psi of N_2) for 0.5 h and in a drying pistol at 78 °C (0.5 mmHg) for 15 h. The product analysis is summarized in Table I.

1,1-Dimethyltetramethylenebromonium hexafluoroantimonate in 50 mL of SO_2 was prepared from 1,6-dibromohexane (9.3 g, 34 mmol) and SbF_5 (7.34 g, 34 mmol) and allowed to stand at -80 °C until complete rearrangement of the initially formed mixture of bromonium ions reached equilibrium.[35] Reaction with polystyryllithium and product workup was carried out as described above for the chloronium ion. The product analysis is summarized in Table I.

Tetramethyleneiodonium hexafluoroantimonate was recrystallized, redissolved in 100 mL of SO_2, and reacted with polystyryllithium, and the product was worked up as described for the chloronium ion above. The product analysis is summarized in Table I.

Acknowledgment. The Rohm and Haas Co. is gratefully acknowledged for a generous sample of the XE-305 resin. Dr. Paul Peterson kindly provided details of the preparation and handling of the halonium ions and served as a gracious host for S.P.M during a sabbatical at the University of South Carolina during 1974–1975 when this work was conceived. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. 3, 73558-10-8; **4**, 41143-82-2; **5**, 73558-49-3; 1,4-dichlorobutane, 110-56-5; 1,4-diiodobutane, 628-21-7; 1,6-dibromohexane, 629-03-8; polystyrene, 9003-53-6.

Nuclear Magnetic Resonance Study of the Molecular Complexes of Annelated Benzenes

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Many methods have been used to obtain the formation constants for (K) and properties of the weak molecular complexes (DA) between electron donors (D) and electron acceptors (A).[1,2] One procedure that has been widely used involves the evaluation of K from the measurement of the changes in the chemical shift of one component as the concentration of the second component is altered.[1-7] Since the rate of formation and dissociation of the complex is rapid on the NMR time scale, the observed spectra is a weighted average of the spectra of the free and complexed component. If one component is present in a large excess over the other (i.e., if $[D]_0 \gg [A]_0$ where $[D]_0$ and $[A]_0$ are the total concentration of D and A, respectively), K may be calculated by using eq 1. The difference between the chemical shift observed for a nucleus in A in pure solvent and A in the solvent plus D is Δ, while the difference between the chemical shifts in A in pure solvent and undissociated DA is given as Δ_0.

$$\Delta/[D]_0 = -K\Delta + K\Delta_0 \tag{1}$$

Values of Δ_0 for protons have been reported for a large number of complexes containing π acceptors such as nitro-substituted benzenes[1,2] as well as polar acceptors such as dimethylformamide,[3] cyclic imides,[4] pyrimidines,[5] and purines.[6] Electron donors used in these studies have been alkyl- and methoxybenzenes, biphenyls, and stilbenes.[1-7] The results of these studies indicate that for complexes with a series of donors having similar structures but widely varying donor abilities a given acceptor has an almost constant value of Δ_0. These observations can be interpreted by using eq 2[7] which is based upon an analogy with the changes in chemical shifts caused by solvent effects.

$$\Delta_0 = \Delta_w + \Delta_a + \Delta_e \tag{2}$$

Differing contributions of dispersion forces to the chemical shift of A in the complex and A in solution are responsible for Δ_w, while Δ_e represents the effect of differences in the electric fields in free A and complexed A and contains contributions to Δ_0 from both charge transfer and polarization. The effect of the magnetic anisotropy of D on the chemical shift of A is represented by Δ_a. In a set of similar complexes in the same solvent the contributions of Δ_w and Δ_e remain constant. Since in a series of substituted benzenes the magnetic anisotropy is almost constant, the value of Δ_a also remains constant. Biphenyl compounds do not follow this pattern because in some of these complexes the diamagnetic anisotropy of one of the benzene rings may reinforce the anisotropy of the donor ring, causing Δ_a and Δ_0 to be larger than those observed for complexes of simple benzene derivatives, while steric factors in other biphenyl complexes may preclude this reinforcement.

From the above arguments it appeared to us that proton NMR studies of molecular complexes could provide a procedure by which the variation of the ring currents for a series of donor molecules could be established. Such a procedure would obviate the necessity for interpreting the chemical shifts of the free molecules in terms of the several factors besides ring current effects that can be involved. We have chosen to test this idea by examining the complexes of the small-ring benzocycloalkenes. It is well established that as the cycloalkyl ring(s) fused to the benzene ring decreases in size, the steric strain on the aromatic ring increases, and several effects on the reactivity and properties of the benzene rings may be observed.[8-10] The NMR

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(1) R. Foster, "Organic Charge-Transfer Complexes", Academic Press, New York, 1969.

(2) R. Foster, "Molecular Complexes", Vol. 2, R. Foster, Ed., Crane, Russak, and Co., New York, 1974, Chapter 3.

(3) A. A. Sandoval and M. W. Hanna, *J. Phys. Chem.*, **70**, 1203 (1966).

(4) N. Kulevsky and R. Foster, *J. Phys. Chem.*, **79**, 846 (1975).

(5) F. Rosenthal, *Tetrahedron Lett.*, 3333 (1969).

(6) A. Doresi, L. Paslillo, and P. A. Temussi, *J. Phys. Chem.*, **80**, 274 (1976).

(7) H. J. M. Andriessen, W. H. Laarhoven, and R. J. F. Nivard, *J. Chem. Soc., Perkin Trans. 2*, 861 (1972).