Crown Ethers as Molecular Bromine Carriers for Bromination Reactions

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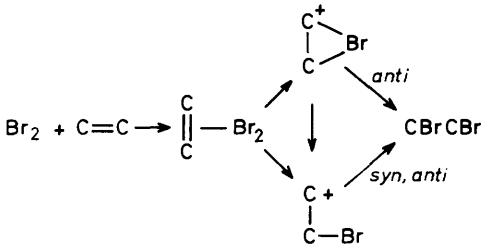
Macrocyclic polyethers (crown ethers) form molecular complexes with bromine that may be used as reagents for the bromination of olefins and acetylenes. We have used 12-crown-4, 15-crown-5, 18-crown-6, polydibenzo-18-crown-6, dibenzo-18-crown-6, and 6-crown-2(dioxan) as carriers for bromine, and have investigated the thermodynamics of complex formation and the kinetics and stereochemistry of bromine addition to *cis*- and *trans*-β-methylstyrene. Formation constants for the ethers are similar implying that all interactions are similar to the known 6-crown-2·Br_2 polymeric structure, and do not involve encapsulation by the macrocycle. Kinetic results also indicate very little difference between the rates of bromination as the ethers are varied. The stereoselectivity of addition, however, is significantly changed as a function of the ether. The solid dibenzo- and polydibenzo-18-crown-6 ether complexes exhibit very high stereoselectivity for *anti*-bromination, whilst the other ethers and carriers such as silica gel, alumina, and montmorillonite show enhanced formation of *syn*-addition, compared with other modes of bromine delivery (*e.g.* free Br_2, pyr·Br_2). The use of poly-dibenzo-18-crown-6 as a stationary phase column-packing, enabling stereospecific or stereoselective bromination, is the preferred technique for such brominations.

DESPITE many papers concerning the bromination of olefins that have appeared in the literature during the last 30 years, a clear understanding of the mechanism of this reaction continues to be a matter of considerable interest.[1] A mechanism that has received a general consensus involves the interaction of the olefin with the bromine molecule to form a π-complex in a rapid pre-equilibrium, followed by the rate-determining formation of a bromonium ion.[2-5] This ion may then either react stereospecifically with a bromide ion to form an *anti*-addition product, or open up to give a carbonium ion that will react in a non-stereospecific fashion to yield both the *syn*- and *anti*-addition products (Scheme).



SCHEME

It has been suggested that the solvent plays an important role in these reactions by determining whether the intermediate is the bromonium or the carbonium ion.[6] This suggestion stems from the very different stereoselectivities of bromine addition that are found as the solvent polarity varies. In non-polar solvents, high yields of *anti*-addition products occur and have been cited as evidence for bromonium ion participation, whilst in polar solvents good yields of *syn*-addition products were taken to signify solvent-stabilized open carbonium ions.

Recently this hypothesis has been challenged.[7] Ruasse and Dubois, arguing from kinetic data obtained by studying the bromination of olefins in a series of solvents of varying Y values,[8] concluded that solvent changes could not lead to significant variations in the bromine bridging as nucleophilic solvation was absent in the transition state. They concluded that the variations in stereoselectivity noted in various solvents must be in some way related to the ability of the solvent to stabilize different conformations of the open carbonium ion.

Macrocyclic polyethers are able to stabilize cationic species other than simple metal systems,[9] and to form reasonably stable molecular-bromine complexes.[10] We have tried to determine to what degree olefin bromination is affected by the interaction of polyethers with the various positively charged intermediates which may be involved in the process. A preliminary communication of some of the results reported in this paper has appeared.[11]

RESULTS AND DISCUSSION

Bromine–Crown Complexes.—As first reported by Schori and Jagu-Grodzinski,[10] the reaction between bromine and dibenzo-18-crown-6 (DBC) leads to good yields of the crystalline complex 2 DBC·Br_2; this complex is essentially insoluble in all solvents. The other crowns we have studied, 12-crown-4, 15-crown-5, 18-crown-6, and poly-DBC, each form weak complexes with bromine and in some cases these may also be isolated, but, in general, oils precipitate out of a chloroform solution and it was not possible to obtained reproducible systems with constant bromine content. The polydibenzo-18-crown-6 * contains the structural unit of a 9,10-dihydroanthracene which is known to be oxidised to 9,10-dibromoanthracene upon treatment with bromine. Upon such treatment of the polycrown we observed the formation of hydrogen bromide, and the

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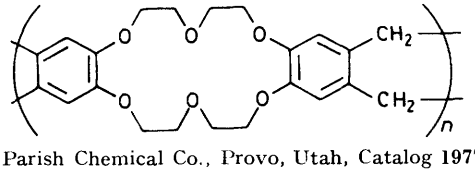


Parish Chemical Co., Provo, Utah, Catalog 1977

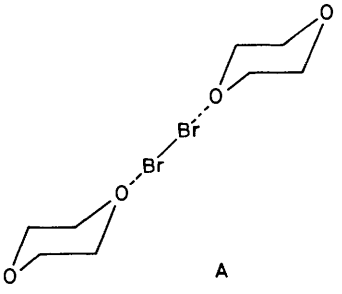
analysis of the resulting complex showed it to be a molecular bromine complex of a poly-9,10-dibromoanthracene bridged 18-crown-6. As this complex was formed a clearly distinguishable volume contraction occurred; this might be expected to result from the removal of the flexibility associated with the transformation of the bridging methylene groups into a rigid aromatic framework. The formation constants for the 12-crown-4, 15-crown-5, 18-crown-6, and 6-crown-2 bromine complexes have been determined in a carbon tetrachloride–ethyl bromide solvent system, as described in the literature.[10] Because of the insolubility of the resulting bromine complexes, it was not possible to determine the values for the DBC and polycrown complexes. The results of the formation-constant study are reported in Table 1. It is abundantly clear that no

TABLE 1

Formation constants for crown·Br_2 complexes, determined as in ref. 9 at 26 °C in CCl_4–EtBr(1 : 1)

Ether	k_F (l mol^{-1})
Dioxan	1.2
12-Crown-4	2.2
15-Crown-5	0.8
18-Crown-6	1.0

macrocyclic effect is operating since all the k_F values are essentially identical. This result demonstrates that the complexes formed are equivalently bonded and thus resemble the dioxan·Br_2 structure reported by Hassel,[12] *i.e.* polymeric in nature with the ether bridged by the bromine molecule, as shown in structure A.



A

Bromination of cis- *and* trans-β-*Methylstyrene.*—Ralston and Yates performed a series of brominations of this system in which they varied the solvent conditions.[6] Their results illustrated that as the polarity of the solvent increased the amount of *syn*-addition(*erythro*-dibromide for the *cis*-methylstyrene, *threo*- for the *trans*-methylstyrene) also increased. We have repeated this study as an internal standard to observe the effect of using the various crown-bromine complexes [and the related pyridine·Br^2(py·Br_2) complex] upon the stereochemistry of the bromination reaction. We obtained excellent agreement with the Yates study and the results for the *cis*- and *trans*-olefin brominations are recorded in Tables 2 and 3 respectively, along with those obtained using DBC, dioxan, and py·Br_2 complexes. The variation of solvent polarity and *syn*-addition is not without some minor perturbation. This may be best observed when comparing the results of bromination in carbon tetrachloride and dioxan, which have similar dielectric constants. The results with dioxan illustrate its excellent solvating properties in cases where direct interaction with an electron-deficient centre is very significant (shown in structure B). This has been observed in other related reactions involving the hydrolysis of epoxides.[13]

TABLE 2

% *anti*-Addition to *cis*-β-methylstyrene

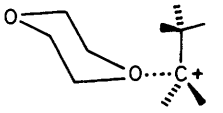
	Brominating reagent		
Solvent	Br_2	Py·Br_2	DBC·Br_2
C_6H_{12}	85	97	100
CCl_4	78	83	95
CH_2Cl_2	72	84	100
$MeNO_2$	46	62	96
MeCN	69	59	98
$C_4H_8O_2$	25	46	25

TABLE 3

%*anti*-Addition to *trans*-β-methylstyrene

	Brominating reagent		
Solvent	Br_2	Py·Br_2	DBC·Br_2
C_6H_{12}	92	99	100
CCl_4	90	99	100
CH_2Cl_2	90	97	100
$MeNO_2$	81	86	100
MeCN	89	90	100
$C_4H_8O_2$	79	89	100

The results in Tables 2 and 3 illustrate the distinct utility of the DBC·Br_2 complex with respect to the bromination reaction. In all of the various solvent systems we note enhanced stereoselectivity with this reagent (*cf.* Br_2, dioxan·Br_2, or py·Br_2 reagents). This result is particularly marked for the *trans*-methylstyrene where essential stereospecificity of *anti*-bromination is obtained. Only in dioxan does the stereoselectivity of the crown



B

system dramatically decrease, probably because of the ability of this solvent to compete effectively with the crown for the bromine molecule as well as the specific solvation noted above. It is important to realize that the DBC·Br_2 and polycrown·Br_2 reagents are insoluble in the solvents used in this study and the exact nature of the interaction between the olefin substrate and the bromine reagent may be a type of surface interaction. In a separate experiment we placed the DBC·Br_2 complex in a Soxhlet apparatus. Using dichloromethane as solvent, a bromination of *cis*-β-methylstyrene resulted in the same product ratios as with free bromine. This clearly implicates *solid* DBC·Br_2 as the stereoselective reagent. Although this reagent is insoluble, release of the co-ordinated bromine gives the monomeric DBC which is soluble and thus the problem of separating it from the dibro-

mide product arises; the reagent of choice is therefore the polycrown·Br_2 system. We have found that packing a chromatography column with the material suspended in carbon tetrachloride and then passing bromine through this column until it is loaded presents an excellent system for subsequent, highly stereoselective brominations. The totally insoluble nature of the polymer eliminates the separation problem, and the column may be recharged upon depletion of the complexed bromine.

To investigate the possibility that the stereoselectivity observed is a surface phenomenon we have examined briefly the behaviour of other insoluble carriers, *e.g.* silica gel, alumina, and montmorillonite, each of which readily absorbs bromine. We found that each of these systems produces a very pronounced effect upon the stereochemistry of the bromination (Table 4). In each

TABLE 4

% *anti*-Addition to *cis*- and *trans*-β-methylstyrene using Br_2·adsorbent systems

Solvent	Adsorbent	*cis*-Olefin	*trans*-Olefin
CCl_4	None	78	90
CCl_4	SiO_2	35	85
CCl_4	Montmorillonite	69	86
CCl_4	Al_2O_3	66	88
CCl_4	Poly-DBC	96	100

case high yields of the *syn*-addition product were obtained, although the reproducibility was not as good as for the other reagents. This result probably stems from the ability of anionic centres in these macromolecular structures to stabilize open carbonium ion centres directly, thus reducing the stability of the brominium ions under these conditions. The result does suggest that surface stabilization of the various intermediates is important in the bromination process, but that the degree of this stabilization depends upon the structure and charge characteristics of the surface. In the case of the neutral polyethers the bromonium ion is stabilized, whereas on the highly charged surfaces of silica gel, alumina, and montmorillonite the open ions are stabilized. It is of interest that the brominations performed on these latter surfaces produced some of the highest relative yields of *syn*-addition products recorded, whilst for the former the highest relative yields of *anti*-addition products resulted.

Attempts to use the other crown ethers as carriers for bromination were considerably less successful. Since it proved very difficult to isolate the various crown·Br_2 complexes, we resorted to using the crown as solvent for the bromination reaction. Thus, a typical reaction involved dissolving bromine in the crown solvent and then adding the olefin substrate, analysing the mixture of products directly. The results, presented in Table 5, illustrate the fact that little enhancement of stereoselectivity occurs in this reaction mode. Relative to dioxan there is enhanced stereoselectivity toward *anti*-addition, but in general the data are poor compared with the results obtained using the solid reagents DBC·Br_2 and polycrown·Br_2. It seems that the crowns are acting in much the same way as dioxan and are capable of stabilizing the open carbonium-ion, albeit to a lesser extent; this is probably due to steric considerations.

In summary, the most significant aspect of this work is the use of the polycrown as a stationary phase for the

TABLE 5

% *anti*-Addition to *cis*- and *trans*-β-methylstyrene using macrocyclic polyethers as solvent

Solvent	*cis*-Olefin	*trans*-Olefin
12-Crown-4	33	81
15-Crown-5	38	82
18-Crown-6	54	84
6-Crown-2	25	79

chromatographic stereoselective bromination of olefins. The results are often stereospecific, and there are no problems of product separation from contaminants. The problem of dealing with the potentially hazardous, physiological characteristics of the macrocycles are avoided, since the polycrown system is nonvolatile and insoluble in most common solvents. Finally the column packing may be repeatedly recharged with little or no loss of activity.

Kinetic Studies.—A kinetic study of the bromination of stilbenes with dicyclohexyl-18-crown-6·Br_2 has been reported.[14] It was found that there are no significant rate variations in the presence of this macrocycle when only bromine and the stilbene were in the reaction mixture. We have briefly investigated the rates of bromination of methylstyrene with Br_2, Br_2·6-crown-2, Br_2·12-crown-4, and Br_2·18-crown-6 in methanol. The rates of the various reactions are: Br_2, 1 070 l mol^{-1} s^{-1} ; Br_2·6-crown-2, 1 260 l mol^{-1} s^{-1}; Br·12-crown-4 1 540 l mol^{-1} s^{-1}; and Br_2·18-crown-6, 1 330 l mol^{-1} s^{-1}. The variations in rate are small but reproducible. In the presence of the carriers the rate is enhanced by between 30 and 50%. It is generally claimed that the rate-determining step in the bromination reaction is the transformation of the π-complex (olefin·Br_2) to the bromonium ion. The crowns used in this kinetic study were those that showed no big enhancement of stereoselectivity. This signifies little interaction between the bromonium ion and the crown, a result in keeping with the small rate variations.

EXPERIMENTAL

The various crown ethers used in this study were purchased from the Parish Chemical Company, Provo, Utah. The *cis*- and *trans*-β-methylstyrene were purchased from I.C.N. Pharmaceuticals and Aldrich Chemical Company respectively. Typical reactions of the β-methylstyrene with the various Br_2 systems are described below.

Reaction with Br_2.—In a 100-ml round-bottomed flask, wrapped in aluminium foil and maintained at a temperature of 25 °C, the *cis*- or *trans*-olefin (100 mg) was stirred in the desired solvent (50 ml). To this solution was added dropwise a small excess of a 10% bromine solution in the same solvent. The reaction mixture was stirred for 30 min and then analysed directly using ^1H n.m.r. spectroscopy.

In the case of the *cis*-styrene the two possible products are the *erythro*-dibromide (*syn*-addition) and the *threo*-dibromide (*anti*-addition). For the former isomer the methyl reson-

ance appears at δ 8.0 (*J* 6.2 Hz), and for the latter it appears at δ 8.4 (*J* 6.6 Hz). Thus, by using ^{1}H n.m.r. spectroscopy it is simple to determine the relative yields of the *syn*- and *anti*-addition products. For the *trans*-methylstyrene the *erythro*- and *threo*-products represent the *anti*- and *syn*-addition products respectively. The results of the addition of bromine in the various solvents utilized are presented in Tables 2 and 3.

Reaction with DBC·Br_2.—In a round-bottomed flask wrapped in aluminium foil the *cis*- or *trans*-methylstyrene (100 mg) was dissolved in the appropriate solvent (50 ml). To this solution was added DBC·Br_2 (1 g, 2.28 mmol). The mixture was stirred for 12 h, the solution filtered, and the solvent removed under reduced pressure. The residue was dissolved in CCl_4 and the ratio of the products of *syn*- and *anti*-addition determined. The results are presented in Tables 2 and 3.

Reactions with Pyridine·Br_2(*Py*·Br_2) *and Dioxan*·Br_2.—The reactions with these two brominating reagents were performed as above.

Reaction of Br_2 *with* β-*Methylstyrene in Crown Solvent*.—Bromine (80 mg, 0.5 mmol) was added to the appropriate crown ether (500 mg) and the mixture stirred for 0.5 h in a round-bottomed flask wrapped in aluminium foil. The methylstyrene (50 mg, 0.43 mmol) was then added and the mixture stirred for an additional 10 min. The reaction products were examined directly by n.m.r. to determine the stereochemical outcome of the reaction. The results are presented in Table 5.

Using Poly-dibenzo-18-*Crown*-6.—Polycrown was suspended in CCl_4 (50 ml) and treated with a 10% bromine solution in CCl_4. This procedure caused the evolution of HBr and the colour of the suspended material became dark brown. After stirring for 30 min the reaction mixture was filtered and washed with CCl_4 until no Br_2 was evident in the washings. Analysis indicated that the product was a 1 : 1-adduct of 9,10-dibromo-poly-anthracene-18-crown and Br_2 (Found: Br, 45.88. Calc. for the adduct: Br, 45.66%. This analysis was performed by Canadian Microanalytical Lab., Vancouver, B.C.

A small chromatography column (20 × 1.0 cm) was then packed with the polycrown-bromine complex in a CCl_4 slurry. A solution of methylstyrene (100 mg, 0.85 mmol) was placed upon the column and eluted through with CCl_4. The eluant was collected and, upon concentration, was analysed by ^{1}H n.m.r. spectroscopy. The column may be readily regenerated by passing a 10% bromine solution in CCl_4 through the column and then washing with CCl_4 until no Br_2 is released.

Brominations using SiO_2, Al_2O_3, or *Montmorillonite*–Br_2 *Systems*.—Bromine (1.0 g) was added to 5.0 g of the desired adsorbant, SiO_2, Al_2O_3, or montmorillonite, and the mixture stirred for 10 min. The methylstyrene (100 mg) was added and stirring continued for 5 min. The reaction mixture was extracted with CCl_4, concentrated, and the products analysed by ^{1}H n.m.r. spectroscopy. The results are presented in Table 4.

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