Bromine Addition to Chloronorbornene Derivatives[1]

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The reaction of bromine with both *trans*-5,6-dichloro-2-norbornene (I) and *exo-cis*-5,6-dichloro-2-norbornene (III) in an acetic acid solution gave *trans*-adducts in a 100% yield, while the bromination of *endo-cis*-5,6-dichloronorbornene (II) afforded the *exo-cis* adduct in a *ca.* 100% yield. The latter observation was explained in terms of a sterical inhibition of the bromide ion's attack in the *endo*-direction by the two *endo*-chloro substituents. In the CCl_4 solution, however the reaction of I with bromine afforded the *exo-cis* adduct in a 64% yield, together with the *trans*-adduct (36% yield). Then, the reaction of I with bromine was carried out in several other solvents (CH_3OH, $Cl(CH_2)_2Cl$, $CH_3CO_2C_2H_5$, and CCl_4). As the polarity of the solvents (the E_T values are used here as a measure of the solvents' polarity) decreased, the formation of the *exo-cis* adduct became progressively more predominant, while the addition of bromide salt retarded the formation of the *exo-cis* adduct. Such results and the kinetic studies suggested that the *exo-cis* adduct was formed through the carbonium bromide ion-pair mechanism. The stereoisomers obtained in this study were assigned on the basis of the NMR spectra.

The authors have found, in a previous investigation,[2] that, under mild conditions, (in an acetic acid solution) favoring the polar mechanism rather than the free radical mechanism, the addition of bromine to *trans*-5,6-dicyano-2-norbornene gave the *exo-cis* adduct in a 24% yield, along with the *trans* adduct in a 76% yield. Such a formation of the *exo-cis* adduct could not be interpreted only in terms of the steric effects of cyano-substituents. In order to obtain further information on the nature of substituent effect on the *exo-cis* formation, we undertook a study of the addition of bromine to *trans*-5,6-dichloro-2-norbornene(I), *endo-cis*-5,6-dichloronorbornene(II), and *exo-cis*-5,6-dichloronorbornene(III). The chlorine atom was chosen as a substituent because of its similarity in steric environment[3] to the cyano group, but it has less inductive effect than that of the cyano group.

Experimental[4]

Starting Materials. The starting chlorides I and II. were prepared according to the procedure of Roberts[5] and were comfirmed to be the desired *trans-endo, exo*-5,6-dichloronorbornene (I) and *cis-endo*-5,6-dichloronorbornene (II) on the basis of the NMR spectral data. Their purities were above 99%, as determined by means of glc analysis. (I), mp 79—80 °C (from *n*-Hexane); yield, 11% (Found; C, 51.05; H, 5.03%). (II), bp 72.5—73 °C/15 mmHg; yield, 74% (Found; C, 51.33; H, 5.03%).

cis-exo-5,6-Dichloronorbornene was also isolated from the reaction mixture of cyclopentadiene with *cis*-dichloroethylene, along with I, in a yield of about 0.3% (bp 88 °C/20 mmHg); its identity was confirmed on the basis of NMR datum and elementary analysis (Found C, 51.56; H, 4.93%. Calcd C, 51.56; H, 4.95%), while glc analysis showed some (ca. 3%) contamination with the *endo*-isomer.

Bromination and Kinetic Study. The bromine addition reactions were carried out in the usual way in solutions of CCl_4, $CH_3CO_2C_2H_5$, CH_3CO_2H, $Cl(CH_2)_2Cl$, and CH_3OH. The addition products were isolated, according to their situation, by means of recrystallization (A), vacuum distillation (B) and preparative gas chromatography (C).[6]

The rate of addition was determined by the titration method described in the previous paper[2].

Results and Discussion

The brominations of the substrates, I, II, and III, in acetic acid were stereospecific, giving the *trans* adduct, the *exo-cis* adduct, and the *trans* adduct respectively. The stereochemistry of the addition products was confirmed on the basis of the NMR spectra. The results of microanalysis and the assignments of the NMR spectra of the adducts obtained in this investigation are listed in Tables 1 and 2 respectively.

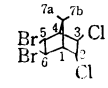
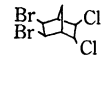
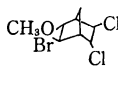
Table 1. Results of micro analysis of adducts

Adducts	Bp or Mp	C%		H%	
		Calcd	Found	Calcd	Found
(I_t)	59—60 °C (C, A)[c] (*n*-hexane)	26.04	25.90	2.50	2.44
(I_c)[a]	57.5—58.5 °C (B)	26.04	26.14	2.50	2.43
(II_c)	164.5—165.5 °C (A) (cyclohexane)	26.04	26.14	2.50	2.49
(III_t)	83—85 °C/ 10^{-3} mmHg (C)	26.04	26.11	2.50	2.30
(I_m)[b]	(B)	35.07	35.01	4.05	4.16

a) The preparative gas chromatography of the reaction mixture of I with bromine in CCl_4 afforded the *exo-cis* adduct as a crystalline compound. b) The methoxy derivative was isolated as an oily product together with I_t by the preparative gas chromatography from the reaction mixture of I with bromine in methanol. Bp of the mixture of I_t and I_m was 60—75 °C/10^{-3} mmHg. c) Alphabet in brackets shows the preparative method described in Experimental part.

As to the orientation of bromine addition, the results for the substrates, I, II, and III, show an inclination to dicyanonorbornene derivatives similar to that described in the previous paper[2] except that the bromination of *endo*-2,*exo*-3-dicyanonorbornene gave *exo-cis* adduct in a 24% yield even in acetic acid, while the bromination of I gave stereospecifically the *trans* adduct (*ca.* 100% yield). Steric terms could not interpret the difference described above because the chlorine atom may be considered to have a bulkiness similar to that of the cyano group. Such results may presumably be explained in terms of the different inductive effects.

TABLE 2. NMR SPECTRAL DATA OF ADDUCTS[a)]

Adduct[g)]	H_2	H_3	H_1 and H_4	H_5	H_6	H_{7a}	H_{7b}
 (I_t)	5.72 (6.31)	5.60 (6.14)	7.28[b)] (8.00)	5.50 (5.61)	5.50 (5.61)	7.78 (8.57)[c)]	
	$J_{2exo-1}=J_{5exo-4}=3.0$ Hz, $J_{2exo-3endo}=3.0$ Hz, $J_{7a-3endo}=2.0$ Hz						
 (II_c)[d)]	5.40 (6.66)	5.40 (6.66)	7.13 (7.77)	5.13 (5.43)	5.13 (5.43)	7.56 (9.50)	8.24 (—)
	$J_{2exo-1 \text{ and } 3exo-4}=2.8$ Hz, $J_{7b-5endo \text{ and } 6endo}=2.0$ Hz, $J_{7a-7b}=13.0$ Hz, $J_{5endo-4}=0$ Hz						
 (I_c)	5.77 (6.50)	6.28 (7.06)	7.23 (7.81)	5.77 (6.74)	5.19 (5.68)	7.59 (7.99)	7.94 (8.67)
	$J_{5endo-6endo}=7.0$ Hz, $J_{7b-5endo \text{ and } 6endo}=1.8$ Hz, $J_{7a-7b}=11.7$ Hz, $J_{2exo-1}=4.5$ Hz						
 (III_t)	5.26 (5.70)	5.86 (6.79)	7.30 (7.90)	6.15 (6.92)	5.59 (6.29)	7.91 (8.64)	7.67 (8.06)
	$J_{2endo-3endo}=6.5$ Hz, $J_{6exo-1}=5.1$ Hz, $J_{7a-7b}=11.0$ Hz, $J_{5endo-6exo}=3.5$ Hz, $J_{7a-2endo \text{ and } 3endo}=1.8$ Hz, $J_{7b-5endo}=2.0$ Hz						
 (I_m)[e),f)]	5.81 (6.12)	5.94 (6.33)	7.29 (7.79) 7.39	5.74	5.80	7.89	7.89
	$J_{2exo-3endo}=4.5$ Hz, $J_{6endo-7b}=1.8$ Hz, $J_{1-4}=0.8$ Hz, $J_{7a-3endo}=1.6$ Hz, $J_{5exo-4}=3.0$ Hz, $J_{5exo-6endo}=3.1$ Hz						

a) Chemical shifts are in ppm downfield from TMS (τ-units, in $CDCl_3$). b) Band width at half-height= 14 Hz. c) Chemical shifts in parentheses were measured in C_6H_6. This solvent was useful for separation of the overlapped signals. d) Measured in solution of $CDCl_3$ and $(CD_3)_2CO$ in the ratio of 1:1. e) Measured in solution in CCl_4. f) τ-Value for CH_3O was 6.57 ppm in CCl_4 solution. g) At first such numbering as shown in (I_t) were employed for convenience of stereochemical studies of bromine adducts. Stereochemistry of bromine atoms of adducts was elucidated by means of the magnitude of coupling constants between C_5 proton and C_6 proton and the presence of 4σ long range coupling between 7b proton and C_5 or C_6 *endo* proton (refer to assignments of lines in the previous paper[2)]). An example of the assignment of peaks in I_t is afforded here. The 100 MHz NMR spectrum of I_t shows two resonances equivalent to two protons at upfield positions. Based upon the discussion presented in the previous paper, the absorptions around τ 7.28 and 7.78 are assigned to the 1,4 protons and 7a, 7b protons, respectively. The absorptions around τ 5.72 and 5.60 exhibits a complicated AB pattern in which the upfield part is assigned to C_2 *exo* proton with great certainty compared with the chemical shift of C_2 *exo* proton in I_c. Spin decoupling experiments also revealed that the proton in I_t at τ 5.72 was coupled with the C_1 proton to the extent of 3 Hz, leading to the assignment of 3 Hz of the resulting doublet as the coupling between C_2 *exo* and C_3 *endo* protons. Irradiation of C_{7a} proton removes the 2.0 Hz coupling from the absorption at τ 5.60, confirming 2.0 Hz as a coupling of C_3 *endo* proton with C_{7a} proton. The complicated resonance at τ 5.50 is equivalent to two protons. The value of 5.0 Hz as band width at half-height may eliminate the presence of *cis* coupling between C_5 and C_6 protons. However, the presence of two stereoisomers would be possible with I_t adduct. This is the same with the *trans*-adduct I_t' of bromine to 5,6-dicyanonorbornene (I′) obtained in the previous paper whose conformational assignment remained obscure. NMR spectra of these adducts (I_t and I_t') showed the formation of only one isomer of each two stereoisomers. With I_t', one of them, 5-*exo*,6-*endo*-dibromo, 2-*endo*, 3-*exo*-dicyanonorbornane which seemed to be least probable according to their intramolecular repulsion between C_6-*endo* bromine and C_2-*endo* cyano group, does not take place intramolecular lactonization on hydrolysis. Treatment of I_t' with 15% HBr solution under reflux conditions over a 30 min period, afforded a solid material which was recrystallized from hot 15% HBr solution. mp 228—230 °C. The IR spectrum (KBr disk) exhibited a strong absorption band at 1770 cm^{-1} (γ-lactone). The NMR spectrum (DMSO-d_6) gave signals at 5.34 (1H, C_{6exo}, $J_{6-exo-1}=4.8$ Hz), 5.33 (1H, C_{5exo}, $J_{5exo-4}=3.5$ Hz, $J_{6exo-5exo}=7.1$ Hz), suggesting this compound 3-*exo*-carboxy-5-*endo*-bromo-6-*endo*-hydroxybicyclo[2,2,1]heptane-2-*endo*-carboxylic acid lactone (Found: C, 40.85; H, 3.40; Br, 30.36%; Calcd: C, 41.40; H, 3.47; Br, 30.61%). As a chlorine atom is considered to have a bulkiness similar to that of cyano group from their van der Waals radii,[7)] I_t may be also assigned to a less strained structure shown in Table 2. (The structure of I_m was also considered to be that one listed in Table 2 in connection with those of I_t' and I_t).

Kinetic studies showed that the reactions of bromine with I and II in acetic acid follow the second-order rate equation (first-order in bromine concentration and first-order in substrate concentration); the rate constants observed in these studies are summarized in Table 3. The reaction of bromine with the III substrate was too fast to be determined by such a titration method ($k(25\ °C)>273\times10^{-3}$ mol/l·s).

Table 3 shows that the reactivity increased in the substrate order of III>I>II, indicating that the *endo*-chlorine atoms retarded the bromine addition reaction. Such results appear to be analogous to the reactivities reported in the previous paper[2)] with 2,3-dicyano-5-norbornene derivatives, although the rate constants are about six times larger than those of the corresponding 2,3-dicyano-5-norbornenes.

Unlike the results of the reaction of I with bromine in acetic acid, in a relatively nonpolar solvent such as CCl_4, the *trans*-adduct (I_t) and the *exo-cis* adduct (I_c) were obtained in 37 and 63% yields respectively; their

Table 3. Rate constants of bromine addition in acetic acid

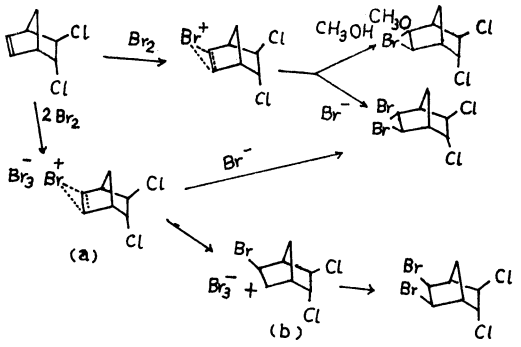
Sutbsrate	Concentration of substrate (mol/l)	Temp. (°C)	Completion (%)	$k\times10^3$ (l/mol·s)
(I)	0.0299 (0.0483)[a]	20.0	91.3	43.9
	0.0313 (0.0481)	24.9	93.2	50.0
	0.0301 (0.0484)	24.9	94.2	51.7
	0.0299 (0.0481)	29.8	91.0	62.1
	0.0309 (0.0487)	29.8	90.5	62.9
(II)	0.0301 (0.0483)	20.0	61.6	6.33
	0.0300 (0.0476)	24.7	60.1	7.58
	0.0400 (0.0475)	35.0	66.7	9.88

a) Values in brackets indicate the initial bromine concentration (mol/l).

compositions were estimated by glc.[9] As the compositions of these dibromides were estimated to depend upon the polarity of solvents, the addition of bromine to the substrate I was carried out in various solvents whose polarities had been evaluated in terms of the E_T value.[10]

Table 4 summarizes the approximate compositions of I_t and I_c obtained from the addition reaction, along with the E_T value of each solvent. Table 4 indicates that the addition became progressively less stereospecific and gave more and more *exo-cis* adduct as solvents of lower E_T values (relatively non-polar solvents) were used. Since free-radical addition has often been reported to lead to the *exo-cis* adduct[11,12] as the major product, the addition of bromine was carried out in the presence of nitrobenzene, which has been reported to be a radical inhibitor[13] (Runs No. 9 and 10), but as is shown in Table 4, no inhibiting effect by nitrobenzene was observed. The increase in the *trans*-adduct with Run No. 10 compared with that of Run No. 9 was observed. This may be considered to be the result of the increase in solvent polarity caused by the addition of nitrobenzene (polar media, E_T value=42.0). Such a finding may exclude the possibility of a radical mechanism in bromine addition in relatively non-polar solvents.

Kinetic studies showed that the addition reaction in CCl_4 followed the third-order rate equation ($dc/dt=k[Br_2]^2\times[\text{substrate}]$, $[Br_2]=0.0511$ mol/l, [substrate]=0.0309 mol/l, percentage of completion=64%, k(29.7 °C)$=5.86\times10^{-1}$ l²/mol²·s) rather than the second-order rate equation ($dc/dt=k\times[Br_2]\times[\text{substrate}]$). Such results suggest that the *exo-cis* adduct may be produced through the ion-pair mechanism shown in Scheme 1. Such an intermediate would be most stable in relatively nonpolar solvents. As the polarities of solvents increase, the ion-pair intermediate may become progressively less stable and be replaced by the bromonium-ion intermediate.



Scheme 1. Probable reaction mechanism.

The interpretation of the *cis* addition of bromine in terms of ion-pair mechanism was employed in Tamelen's report[14] with regard to the bromination of Dewar benzene in an octane solution. The formation of the *trans*-adduct from the ion-pair intermediate (b) or its precursor [(a) in Scheme 1, most probably] is possible, as is shown in Scheme 1. In order to confirm this possibility, additions were carried out with a bromide salt(tetra-*n*-butylammonium bromide) present (listed in Table 4).[15] The presence of bromide salt[16] as a source of bromide ions increases the ratio of the *trans* adduct in three different solvents ($Cl(CH_2)_2Cl$, $CH_3CO_2C_2H_5$, CCl_4), suggesting that the increase in the *trans* adduct compared with that in the absence of bromide salt may result from the bromide ion attack on this intermediate from the *endo* direction. Accordingly, the finding that the bromination of *trans*-

Table 4. Results of bromine addition to substrate I in different solvents

Run No.	Concentration of substrate (mol/l)	Solvent (ml)	Temp. (°C)	E_T-value[a]	I_t (%)	I_c[b] (%)
1	0.0188	MeOH (170)	30	55.5	100[d]	0
2	0.0124	AcOH (100)	room temp.	51.9	*ca.* 100	trace[e]
3	0.0061	$Cl(CH_2)_2Cl$ (70)	30—32	41.9	94.3	5.7
4	0.00319	$Cl(CH_2)_2Cl$ (100)	30[c]		99.0	1.0
5	0.00312	AcOEt (100)	30	38.1	80.6	19.4
6	0.00312	AcOEt (100)	30[c]		99.0	1.0
7	0.0184	CCl_4 (100)	30	32.5	37.0	63.0
8	0.00316	CCl_4 (100)	30[c]		64.5	35.5
9	0.00619	CCl_4 (70)+$C_6H_5NO_2$ (6)	66—70		32.5	67.5
10	0.00619	CCl_4 (70)+$C_6H_5NO_2$ (18)			46.9	53.1

a) These values were taken from Ref. 10. b) Analyzed by means of glc. c) Addition of 1.6 g of tetra-*n*-butyl ammonium bromide. d) 6-Bromo-5-methoxy-1-*endo*, 2-*exo*-dichloronorbornane (refer to Tables 1 and 2) was also obtained along with *trans* dibromide, (I_t). e) Small amounts of (I_c) was detected by means of glc analysis.

5,6-dicyano-2-norbornene in acetic acid afforded the *exo-cis* adduct in a 24% yield, whereas the bromination of I gave the *trans* adduct stereospecifically, may be explained in terms of the coexistence of a carbonium bromide ion pair[17] along with the bromonium ion in the former reaction. With the bromonium ion as an intermediate, a full positive charge develops through olefin carbons, which may be destabilized to some extent by a stronger electron-attracting group such as the cyano group, while, in the ion-pair intermediate, where the bromide ion may remain associated with the carbonium ion, the above substituent will not exert such an influence on the destabilization of the ion pair as is imagined in the case of the bromonium ion. Therefore, in the bromination of *trans*-5,6-dicyano-2-norbornene in acetic acid, the bromonium-ion intermediate may be destabilized to the extent of permitting the coexistence of an ion pair by the more electronegative group (C≡N).

References

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3) L. Pauling, "The Nature of the Chemical Bond," 3rd ed., Cornell University Press, Ithaca, New York (1960), p. 261.

4) All the melting points were determined on a Yanagimoto micro-melting-point apparatus and are uncorrected. The NMR spectra were obtained with a JNM-Ps-100 spectrometer, using TMS as the internal standard. Glc analysis was carried out on a Shimadzu-GC 3AH gas chromatograph equipped with a TCD apparatus using a 3 m×3 mm stainless steel column packed with Silicone DC-550 on Celite 545 (carrier gas, H_2).

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6) Preparative glc was carried out with a Shimadzu gas chromatograph GC-2C, equipped with a 4.38 m×10 mm stainless steel column packed with Silicone DC-550 on Celite 545.

7) Referring to the A-value,[8] the bulkiness of chlorine (A-value=0.4) may be expected to be rather larger than that of cyano group (A-value=0.2).

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9) In addition, the studies of the product composition as a function of the reaction time showed that the product composition did not vary with the degree of conversion.

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15) R. E. Buckles, J. M. Bader, and R. J. Thurmaier, *J. Org. Chem.*, **27**, 4523 (1962).

16) When tetra-*n*-butylammonium bromide is dissolved in a bromine solution, the equilibrium may be considered to involve bromine, monobromide salt, and tribromide salt. However, in the bromination by these salts, it is said that active species is bromine, so that the addition of monobromide in this experiment will exert little effect upon the stereochemical distribution of adducts.