The Transannular Cyclization and Hydrogen Shift in the Chlorination of 1,5-Cyclooctadiene and *cis*-Cyclooctene with Antimony(V) Chloride

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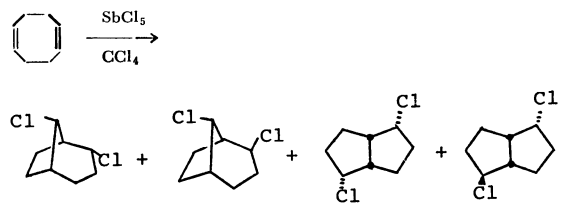
The slow addition of $SbCl_5$ to a CCl_4 solution of 1,5-cyclooctadiene or *cis*-cyclooctene gives an isomeric mixture of *endo*- and *exo*-2, *anti*-8-dichlorobicyclo[3.2.1]octanes (**1** and **2**) or an isomeric mixture of *trans*- and *cis*-1,4-dichlorocyclooctanes (**12** and **13**) respectively in a good yield. The former reaction involves the transannular cyclization, while the latter is accompanied by the transannular hydrogen shift. The addition of 1,5-cyclooctadiene to a CCl_4 solution of $SbCl_5$ (reverse addition) affords *endo*-2,6- and *endo*, *exo*-2,6-dichlorobicyclo[3.3.0]octanes (**6** and **7**) as additional products, besides **1** and **2**. In the case of *cis*-cyclooctene, however, a reverse addition produces only chlorocyclooctane. It has been revealed that a mixture of **6** and **7** is readily isomerized to a mixture of **1** and **2** by the interaction with $SbCl_5$. The 1,4-chlorination of *cis*-cyclooctene which gives **12** and **13** also occurs with VCl_4, $SeCl_4$, $PhICl_2$, and PCl_5, although the selectivity and the yield are low compared to the case of $SbCl_5$.

It has been reported that $SbCl_5$ is a good reagent for the *cis*-chlorination of simple olefins[1,2] and for the formation of *cis*-1,4-dichloro-2-butene from 1,3-butadiene.[2,3] Other features of $SbCl_5$ have recently been recognized in the favorable *cis*-chlorination of alkylphenylacetylenes[4] and in the facile isomerization of some dichloronorbornenes to other isomers.[5] As a part of the study of chlorination with $SbCl_5$, we now wish to report the unusual chlorinations of 1,5-cyclooctadiene (1,5-COD) and of *cis*-cyclooctene, both involving a transannular interaction.[6]

Results and Discussion

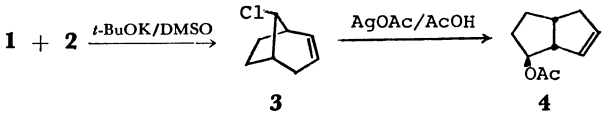
Chlorination of 1,5-COD (Table 1). When two equivalents of $SbCl_5$ in CCl_4 were slowly added to a CCl_4 solution of one equivalent of 1,5-COD at −20 °C, an isomeric mixture of *endo*- and *exo*-2, *anti*-8-dichlorobicyclo[3.2.1]octanes (**1** and **2**, respectively) was obtained in a 59% yield (**1** : **2**=67 : 33 by GLC). When equimolar amounts of $SbCl_5$ and 1,5-COD were used, the yields of **1** and **2** were increased, and the additional formation of small amounts of stereoisomeric dichlorobicyclo[3.3.0]octanes (**6** and **7**) was observed (Scheme 1). Almost identical results were obtained by the use of CH_2Cl_2 or $CHCl_3$ as the solvent. Some typical results are recorded in Table 1 (Runs 1—3).



1 **2** **6** **7**

Scheme 1.

A mixture of **1** and **2** was analyzed as $C_8H_{12}Cl_2$, did not have any absorption due to olefinic protons in its IR and NMR spectra, did not decolorize bromine in CCl_4, and was monodehydrochlorinated to *anti*-8-chlorobicyclo[3.2.1]oct-2-ene (**3**) by treatment with *t*-BuOK



3 **4**

Scheme 2.

in DMSO (Scheme 2).

Here, it was observed that **2** was more readily dehydrochlorinated than **1**, as was expected from the E2 elimination.[7] In **2**, the chlorine, two carbons (C_2 and C_3), and the hydrogen on C_3 lie in a common plane. By this procedure **1** was separated from **2**. A sharp singlet at δ 3.85 in **1** and δ 4.23 in **3** could be assigned to a *syn*-hydrogen at C_8, the absorption being very similar to that of *anti*-8-chloro-*endo*-2-(methoxymethyl)bicyclo-[3.2.1]octane[8] [δ 3.94, singlet] (See Experimental). Although the isolation of pure **2** was not achieved, a sharp singlet at δ 4.60 in the NMR spectrum of a mixture of **1** and **2** could be assigned to a *syn*-hydrogen at C_8 in **2**. This greater deshielding of the C_8-hydrogen in **2** than that in **1** may be due to the anisotropy of *exo*-chlorine at C_2. Additional proof for the structure of **3** was obtained by its reaction with silver acetate in acetic acid, which gave *exo-cis*-bicyclo[3.3.0]oct-7-en-2-yl acetate (**4**).[9] LeBel and Spurlock[10] have reported that **4** was formed by the acetolysis of the *p*-toluenesulfonate analogue of **3**.

It has been known that the transannular cyclization of 1,5-COD usually gives bicyclo[3.3.0]octane derivatives.[8] The formation of bicyclo[3.2.1]octane derivatives has been reported only in the case of the reaction with $MeOCH_2Y$ (Y=OAc, Cl, and OMe), and even in this case the main products were bicyclo[3.3.0]octane derivatives.[8] Considering that $SbCl_5$ is a very effective catalyst for isomerization between the isomeric dichloronorbornanes,[5] the most probable pathway for the formation of **1** and **2** seems to be that a mixture of *endo*-2,6- and *endo*, *exo*-2,6-dichlorobicyclo[3.3.0]octanes (**6** and **7**) is first formed through the **5** cation (*endo*-Cl) and then isomerized to a mixture of **1** and **2** by the $SbCl_5$ catalyst through the **8** cation (*exo*- and *endo*-Cl) (Scheme 3). In fact, when 1,5-COD was added all at once to a CCl_4 solution of equimolar $SbCl_5$ at −20 °C, instead of slow addition of $SbCl_5$ to a CCl_4 solution of 1,5-COD, the

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Table 1. Chlorination of 1,5-COD with $SbCl_5$

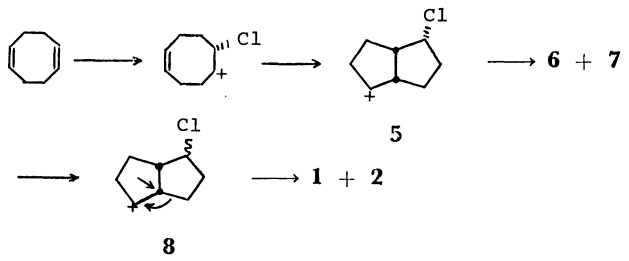
Run	1,5-COD (mmol)	$SbCl_5$ (mmol)	Solvent (ml)	Temp (°C)	Time (min)	Product Isomer distribution 1	2	6	7	Yield[a] (%)
1[b]	25	50	CCl_4 100	−20	30	67	33	<0.5	<0.5	59[c]
2[b]	25	25	CCl_4 100	−20	30	68	29	3	<0.5	72[c]
3[b]	25	25	CH_2Cl_2 100	−20	30	59	33	5	3	75
4[d]	50	25	CCl_4 100	40—50	1	35	14	35	16	83
5[d]	25	4.4	CCl_4 50	0	0.17	30	9	41	20	69
6[b]	50	25	CS_2 100	−20	30	44	17	30	9	76
7[d]	50	25	CS_2 100	40	1	29	11	40	20	71

a) Based on the amount of $SbCl_5$. Determined by GLC. b) A solution of $SbCl_5$ was slowly added. c) Based on the amount of 1,5-COD. d) A solution of 1,5-COD was added all at once.

Table 2. Chlorination of *cis*-cyclooctene

cis-Cyclooctene (mmol)	Chlorinating agent (mmol)	Solvent (ml)	Temp (°C)	Time (h)	Product Isomer distribution 10	11	12	13	Yield[a] (%)
50	$SbCl_5$ 25	CCl_4 100	−30	0.5	0	5	7	88	81[b]
20	VCl_4 2.4	CCl_4 50	25	15	20	9	56	15	63
20	VCl_4 2.5	CCl_4 50	76	2	35	22	26	17	22
10	$SeCl_4$ 3	CCl_4 50	76	5	43	0	11	46	12
50	PCl_5 25	CCl_4 50	76	3	75	19	3	3	87
50	PCl_5 25	CH_2Cl_2 50	25	10	97	<0.5	2	1	83
50	SO_2Cl_2 25	CCl_4 50	76	2	75	25	0	<0.5	81
50	$CuCl_2$ +LiCl 50 each	CH_3CN 50	82	12	55	45	0	0	24
5	$PhICl_2$ 2 (O_2)	$CHCl_3$ 10	61	0.5	55	1	9	35	80
5	$PhICl_2$ 2 (N_2)	$CHCl_3$ 10	61	0.5	74	25	0	1	89
50	$PbCl_4$ 10	CH_2Cl_2 50	−40	2	3	0	20	77	69[c]
50	$PbCl_4$ 10	CH_2Cl_2 50	−10	2	49	0	22	29	93

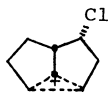
a) Based on the amount of chlorinating agent charged. Determined by GLC. b) Other product: chlorocyclooctane (2 mmol). c) Other product: chlorocyclooctane (7.7 mmol). In Ref. 13; **10**:**11**:**12**:**13**=9:0:20:70.



Scheme 3.

formation of considerable amounts of **6** and **7** besides **1** and **2** was observed (Table 1, Runs 4 and 5). Since **6** and **7** could not be isolated in a pure state, and since, also, several attempts at the preparation by different methods were unsuccessful, these structures were tentatively assigned by means of NMR spectra and the analytical data of the mixture (See Experimental). In separate experiments we observed that a mixture containing **1**, **2**, **6**, and **7** was readily converted to a mixture of **1** and **2** by treatment with $SbCl_5$. These results appear to show that the $SbCl_5$-catalyzed isomerization of a mixture of **6** and **7** to that of **1** and **2** considerably rapid and that their rates are sufficient to compete with that of the first step (producing **6** and **7**) of the chlorination. That is, in the case of the rapid addition of excess 1,5-COD, enough $SbCl_5$ did not remain to make the isomerization of **6** and **7** complete, because $SbCl_5$ turned to $SbCl_3$ as soon as chlorination took place. This finding parallels that in the chlorination of norbornene with $SbCl_5$.[5] Although we have not yet been successful in finding out the reaction conditions under which only **6** and **7** were formed, it may be worthwhile to refer to the facts that the isomerization is slower in the CS_2 solvent than in CCl_4 and that more **6** and **7** are obtained in this solvent (Table 1, Runs 6 and 7).

As has been described above, we proposed and partly confirmed that **1** and **2** could be formed through **6** and **7**. Apparently, another route for all the products may be considered when the attack of $SbCl_6^-$ on the nonclassical cation **9**, which is a stabilized form of **5**, is involved. However, the lesser stereospecificity in the bicyclo[3.2.1]octane ring formation and the complete absence of isomers of dichlorobicyclooctanes other than **1**, **2**, **6**, and **7** appear to imply that such a route is improbable.



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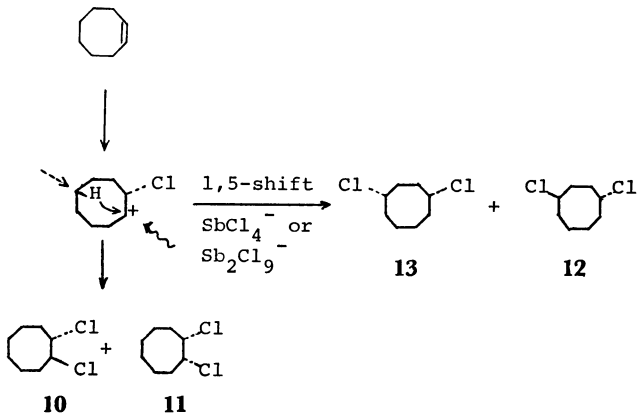
The chlorination of 1,5-COD with other chlorinatingi agents, such as Cl_2, $PhICl_2$, $CuCl_2$, $SeCl_4$, $MoCl_5$, and $PbCl_4$, gave a mixture of *cis*- and *trans*-5,6-dichlorocyclooctenes and no **1** or **2**.[11]

Chlorination of cis-*Cyclooctene (Table 2).* The application of the chlorination with $SbCl_5$ to *cis*-cyclooctene at −30 °C (the addition of $SbCl_5$ to olefin) resulted in the preferable formation of *cis*-1,4-dichlorocyclooctane (**13**, 71% yield), together with small amounts of the *trans*-1,4-isomer (**12**, 6%) and the *cis*-1,2-isomer (**11**, 4%). It was confirmed that no interconversion occurred between the 1,2- and 1,4-isomers or also between the *cis*- and *trans*-1,4-isomers under the present conditions. The reaction apparently involves a transannular 1,5-hydride shift, and the strikingly high selectivity for the formation of the *cis*-1,4-isomer **13** may be explained by assuming a hydrogen-bridged chlorocyclooctyl cation intermediate (Scheme 4), almost the same as that



Scheme 4.

proposed in the formolysis of *cis*-cyclooctene oxide.[12] Both the total yields of the products (**10**—**13**) and the selectivities affording **13** were decreased when the reaction was carried out at 0 °C or at room temperature. A reverse addition, namely, the addition of *cis*-cyclooctene to $SbCl_5$, afforded only chlorocyclooctane at −20, 20, or 76 °C, irrespective of the speed of the addition. This may be explained by the rapid hydride abstraction by $SbCl_5$ from olefin, followed by the addition of the produced hydrogen chloride to olefin, because excess $SbCl_5$ is present in the solution when olefin has been added. Such hydride abstraction by $SbCl_5$ from alkane and alkene to form hydrogen chloride has previously been reported.[2] Although the 1,4-chlorination with $PbCl_4$ has been known,[14] $SbCl_5$ is superior to $PbCl_4$ in its yield and in its selectivity for the formation of the *cis*-1,4-isomer. This seems to be another feature of the chlorination of olefin with $SbCl_5$. As a part of our study of the chlorination of olefins with various chlorinating agents,[5,11,14] we have examined their behavior toward *cis*-cyclooctene and found that 1,4-chlorination also occurred with $PhICl_2$ (ionic condition), VCl_4, $SeCl_4$, and PCl_5, although the selectivities and the yields were low compared to those in the cases of $SbCl_5$ and $PbCl_4$. The chlorinations with $CuCl_2$, SO_2Cl_2 (radical condition), and $PhICl_2$ (radical condition) gave almost only the 1,2-somers, **10** and **11**.

Experimental

All the organic and inorganic materials were commercial products. The IR and NMR spectra were recorded with a Hitachi EPI-S2 and a Varian A-60 (CCl_4 as solvent) apparatus respectively. The GLC analyses were carried out on Shimadzu 4BMPF apparatus, using EGSS-X(15%)-Chromosorb-W (3 m), PEG 6000(25%)-Chromosorb-W (3 m), and Apiezon-L(30%)-Celite (1 m) columns (N_2 as carrier gas).

Chlorination of 1,5-COD with $SbCl_5$. To a CCl_4 (200 ml) solution of 1,5-COD (16.2 g), we slowly added a solution of $SbCl_5$ (45 g, 150 mmol) in CCl_4 (100 ml) at −20 °C under N_2 for 30 min. Aqueous NaOH was then added, and the organic layer was separated after the usual work-up. Distillation gave 13.2 g of a mixture of **1** and **2** (**1** : **2**=*ca.* 70 : 30), contaminated by a trace amount of **6**; bp 117—119 °C/22 Torr. Found: C, 53.30; H, 7.06; Cl, 39.75%. Calcd for $C_8H_{12}Cl_2$: C, 53.64; H, 6.76; Cl, 39.60%.

When 1,5-COD (5.4 g, 50 mmol) was added, all at once, to a CS_2 (100 ml) solution of $SbCl_5$ (7.5 g, 25 mmol) at a refluxing temperature, an isomeric mixture of four dichloroalkanes which contained **6** and **7** besides **1** and **2** was obtained (18 mmol, **1** : **2** : **6** : **7**=29 : 11 : 40 : 20 by GLC). Although it was not possible to isolate both **6** and **7** in a pure state by fractional distillation, two fractions (**A** and **B**) which contain mainly **6** and **7** respectively were obtained by the distillation of the combined reaction products of several runs. The NMR spectrum of Fraction **A** (bp 110—114 °C/21 Torr, **1** : **2** : **6** : **7**=7 : 4 : 14 : 75 by GLC) showed two multiplet peaks at δ 4.7—4.3 and δ 4.3—3.8 which could be assigned to *exo*- and *endo*-hydrogen in **7** respectively. Found: C, 53.37; H, 7.07%. Calcd for $C_8H_{12}Cl_2$: C, 53.64; H, 6.76%. The NMR spectrum of Fraction B (bp 118—122 °C/21 Torr, **1** : **2** : **6** : **7**=30 : 12 : 55 : 3 by GLC) showed a broad multiplet peak at δ 4.65—4.0 which could be assigned to two *exo*-hydrogen in **6**. Found: C, 52.93; H, 7.22%. Calcd for $C_8H_{12}Cl_2$: C, 53.64; H, 6.76%.

*Dehydrochlorination of **1** and **2**.* A mixture of **1** and **2** (25 g, 140 mmol) was added, drop by drop, to a DMSO (200 ml) solution of *t*-BuOK (50 g, 446 mmol) at room temperature, and then the mixture was heated to 60 °C for 10 h. The reaction mixtures were worked up by the following successive treatments: dilution with water, extraction with ether, and then the evaporation of the ether. After the fractional distillation of the residue, the monochloride (**3**; 2.8 g, 20 mmol, bp 78—81 °C/22 Torr) and the dichloride (**1**; 8.7 g, 49 mmol, bp 123—124 °C/25 Torr) were both purely isolated. **3**, NMR: δ 6.0—5.2 (m, 2H), 4.23 (s, 1H), 2.8—1.2 (m, 8H); mass: *m/e* 142 (M^+), 144 (M^++2). **1**, NMR: δ 4.1—3.85 (m, 1H), 3.85 (s, 1H), 2.7—1.2 (m, 10H); mass: *m/e* 178 (M^+), 180 (M^++2), 182 (M^++4). Found: C, 53.51; H, 7.01%. Calcd for $C_8H_{12}Cl_2$: C, 53.64; H, 6.76%. **2**, NMR: δ 4.60 (s, 1H); the other absorptions overlap those of **1** and have not been clarified.

*Acetolysis of **3**.* The reaction of **3** (2.9 g, 20.3 mmol) with AgOAc (4.0 g, 24.0 mmol) in acetic acid (40 ml) at a refluxing temperature for 10 h gave 2.1 g of **4**; bp 101—102 °C/18 Torr (lit,[9] 69—73 °C/5 Torr), *m/e* 166 (M^+). The NMR spectrum (in $CDCl_3$) of **4** was identical with that of *exo-cis*-bicyclo[3.3.0]oct-7-en-2-yl acetate reported by Fujita *et al.*;[9] δ 5.6 (s, 2H), 4.9—4.7 (m, 1H), 1.94 (s, 3H), 3.1—1.2 (m, 8H).

*Isomerization of a Mixture of **6** and **7** to a Mixture of **1** and **2** with $SbCl_5$.* A CCl_4 (10 ml) solution containing a

mixture of the dichlorides (0.14 g, 0.76 mmol; **1** : **2** : **6** : **7**= 29 : 11 : 40 : 20) and $SbCl_5$ (0.65 g, 2.2 mmol) was kept at 0 °C for 30 min. A GLC analysis of the CCl_4 layer after a usual work-up revealed the presence of a mixture of **1** (63%) and **2** (37%); yield of the mixture, 65%.

Chlorination of cis-*Cylooctene with* $SbCl_5$. To a solution of *cis*-cyclooctene (5.5 g, 50 mmol) in CCl_4 (40 ml), we added $SbCl_5$ (7.5 g, 25 mmol) in CCl_4 (10 ml) at −30 °C under N_2 for 30 min; aqueous NaOH was then added to stop the reaction. After the usual work-up, the distillation of the organic layer afforded 2.3 g of **13** in an almost pure state; bp 115—118 °C/8 Torr (lit,[13] 116—119 °C/10 Torr). NMR: δ 4.5—3.9 (m, 2H), 2.4—1.8 (m, 12H). The NMR spectrum was identical with that of *cis*-1,4-dichlorocyclooctane reported by Havinga *et al.*[13]

When the reverse addition was carried out at 20—30 °C under N_2——namely, the addition of *cis*-cyclooctene (5.5 g, 50 mmol) to a solution of $SbCl_5$ (7.5 g, 25 mmol) in CCl_4 (100 ml), chlorocyclooctane (1.2 g, bp 98—104 °C/30 Torr, lit,[15] 82—90 °C/21 Torr) was the sole product; none of dichlorocyclooctane was formed.

The chlorinations with other metal salts were carried out by almost the same method as those previously reported.[5,11,14]

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