Journal of Organometallic Chemistry, 70 (1974) 121—132

STEREOCHEMISTRY OF HALOGENATION OF SOME ENYL COMPLEXES OF PALLADIUM(II)

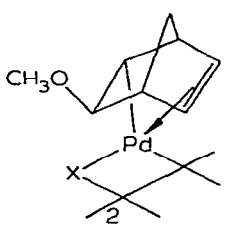
P.K. WONG and J.K. STILLE*
Department of Chemistry, University of Iowa, Iowa City, Iowa 52242 (U.S.A.)
(Received October 9th, 1973)

Summary

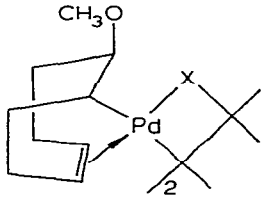
The halogenation of some enyl complexes of palladium(II) in dichloromethane was found to proceed with predominant retention of configuration at the carbon bearing palladium but with overall inversion of configuration in the presence of added halide ion in methanol. The results are interpreted in terms of an oxidative addition—reductive elimination mechanism.

Introduction

The stereochemical course of halogen cleavage of carbon—transition metal σ bonds varies with the nature of the metal. Predominant inversion of stereochemistry has been observed in halogenolysis of an alkyliron complex [1] and several alkylcobalt complexes [2]. However, halogenation of carbon—metal σ bonds with retention of configuration has been reported in both alkylmanganese [3] and alkylpalladium [4] complexes. This work reports the stereochemistry of halogenation of enyl complexes (I) and (II) and the effect of nucleophiles on the stereochemical course of the reaction.



(Ia), X = Cl
(Ib), X = Br



(IIa) X = Cl
(IIb) X = Br

Results

The halogenation of (Ia) and (Ib) in dichloromethane afforded a mixture of 3-*exo*-methoxy-5-halonortricyclene epimers, in all cases (Table 1). The *endo*

* Author to whom correspondence should be addressed.

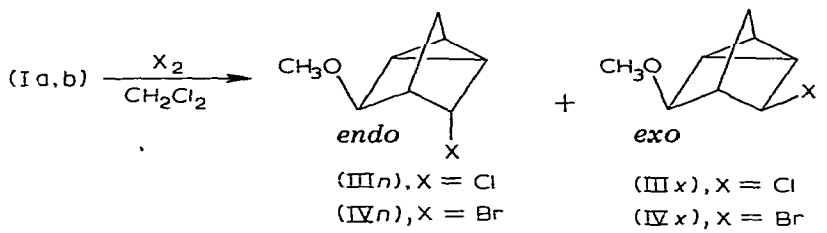
TABLE 1

HALOGENATION OF (I) IN DICHLOROMETHANE[a]

Complex	Halogen	(III) ($\frac{endo}{exo}$) (%)	(IV) ($\frac{endo}{exo}$) (%)
(Ia)	Cl_2	100(83/17)	
(Ia)	Br_2	22(70/30)	78(80/20)
(Ib)	Br_2		100(82/18)
(Ib)	Cl_2	77(75/25)	23(70/30)

[a] These reactions were carried out at room temperature. Essentially no difference in product or product ratio was observed when the reactions were carried out at —78°.

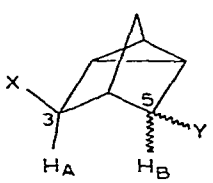
epimers, (III*n*) and (IV*n*), were identified by comparison with authentic samples [4a].



The assignment of the geometry at the 5-position is further supported by NMR chemical shift data. It has been well documented [4,5] that in 3,5-disubstituted nortricyclenes, *endo*-substitution at the 5-position produces a paramagnetic shift of the 3-*endo* proton, whereas *exo*-substituents at the 5-position have negligible effect on the chemical shift of the 3-*endo* proton. The chemical shift data in Table 2 show that the 3-*endo* protons in (III*n*) and (IV*n*) were shifted down-

TABLE 2

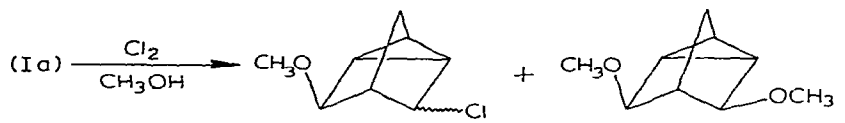
CHEMICAL SHIFT DATA OF 3-*exo*-OXY-5-HALONORTRICYCLENES



Compound	Substituents	δ (ppm)	
		H_A	H_B
(III*n*)	X = OCH_3, Y = Cl	4.16	3.98
(III*x*)	X = OCH_3, Y = Cl	3.40	3.89
(IV*n*)	X = OCH_3, Y = Br	4.15	3.96
(IV*x*)	X = OCH_3, Y = Br	3.39	3.91
(V*n*)	X = OAc, Y = Cl	5.30	3.95
(V*x*)	X = OAc, Y = Cl	4.62	3.99

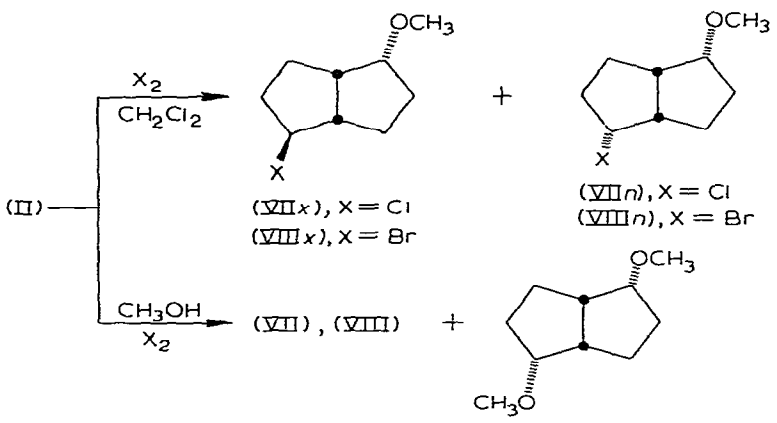
field relative to the corresponding protons in (III*x*) and (IV*x*) owing to this "nearest neighbor" deshielding effect. Such a deshielding effect has also been observed in the analogous 3-*exo*-acetoxy-5-chloronortricyclene isomers, (V*n*) and (V*x*) [4b].

Chlorination of (Ia) in methanol gave a diether (VI) in addition to (III*n*) and (III*x*). The products were shown to be stable under reaction conditions. The diether (VI) was identified as 3,5-*exo*,*exo*-dimethoxynortricyclene on the basis that a single NMR resonance at δ 3.33 ppm was observed for the C_3 and C_5 methine protons. The alternative *exo*,*endo* structure would result in two signals for the C_3 and C_5 methine protons due to the "nearest neighbor" paramagnetic shift effect.



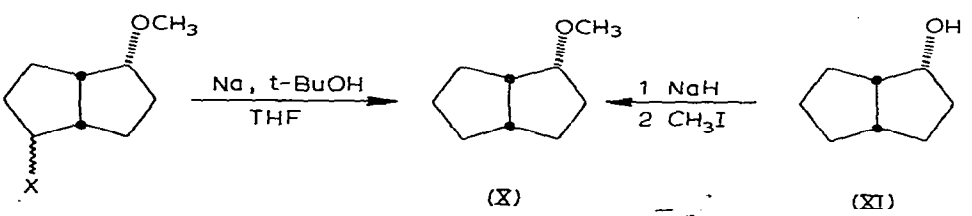
(III) (*n*/*x* = 60/40) 62% (VI) 38%

The reaction of (II) with halogen in dichloromethane gave a mixture of epimeric 2-*endo*-methoxy-6-halo-*cis*-bicyclo[3.3.0]octanes (Table 3). In methanol, 2,6-*endo*,*endo*-dimethoxy-*cis*-bicyclo[3.3.0]octane, (IX), was obtained in addition to the bicyclic halides (VII) and (VIII).



(VII*x*), X = Cl
(VIII*x*), X = Br
(VII*n*), X = Cl
(VIII*n*), X = Br
(VII), (VIII)
(IX)

The *endo* geometry of the methoxy group in (VII) and (VIII) was assigned from the following evidence. Dehalogenation of either (VII) or (VIII) with sodium-tert-butanol/tetrahydrofuran gave a single product which was identical to the methyl ether (X) obtained from the methylation of 2-*endo*-hydroxy-*cis*-bicyclo[3.3.0]octane, (XI) [6].



(X) (XI)

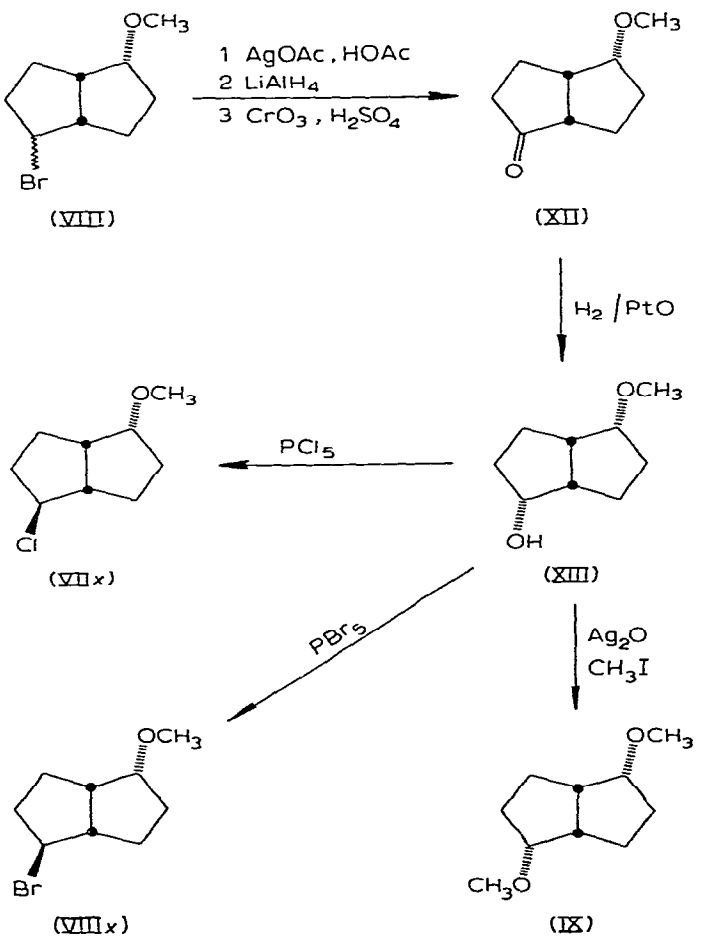
TABLE 3

HALOGENATION OF (II)

Complex (II)	X_2	Solvent	(VII)(x/n)(%)	(VIII)(x/n)(%)	(IX)(%)
a	Cl_2	CH_2Cl_2	100(72/28)		
b	Br_2	CH_2Cl_2		100(95/5)	
a	Cl_2	CH_3OH	77(17/83)		23
b	Br_2	CH_3OH		58(45/55)	42
a	Cl_2,Cl^{-a}	CH_3OH	98(14/86)		2
b	Br_2,Br^{-a}	CH_3OH		100(10/90)	
a	Br_2,Cl^{-a}	CH_3OH	70(14/86)	29(80/20)	1
b	Cl_2,Br^{-a}	CH_3OH	3	97(10/90)	

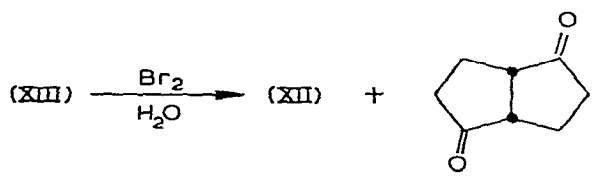
[a] Saturated methanolic solutions of lithium chloride and sodium bromide were employed.

SCHEME 1



The stereochemistries of the halogen and methoxy substitutents in (VII), (VIII) and (IX) were established by the reactions shown in Scheme 1. The halide (VIII) was converted to the corresponding alcohol by treatment with silver acetate in acetic acid and subsequent reduction with lithium aluminum hydride. The resulting alcohol was oxidized to the ketone (XII) with Jones reagent. Hydrogenation of (XII) gave 2-*endo*-methoxy-6-*endo*-hydroxy-*cis*-bicyclo[3.3.0]-octane, (XIII). The structural assignment of (XIII) was supported by the fact that both catalytic hydrogenation and hydride reduction of *cis*-bicyclo[3.3.0]-octan-2-one and substituted *cis*-bicyclo[3.3.0]octan-2-one afforded the corresponding *endo*-alcohol [7]. Treatment of (XIII) with phosphorus pentachloride and phosphorus pentabromide gave the corresponding halides which were identical to (VII*x*) and (VIII*x*), respectively. The conversion of alcohol to halide with phosphorus pentahalide has been shown to proceed with inversion of configuration [8]. Methylation of (XIII) with silver oxide/methyl iodide gave a diether identical to (IX).

The presence of halogen at the 6-position was confirmed by the reaction shown below. Oxidation of (XIII) by aqueous bromine gave two major products, one of which was identified as (XII). The other product was shown to be identical to an authentic sample of *cis*-bicyclo[3.3.0]octan-2,6-dione, (XIV) [9].



(XIV)

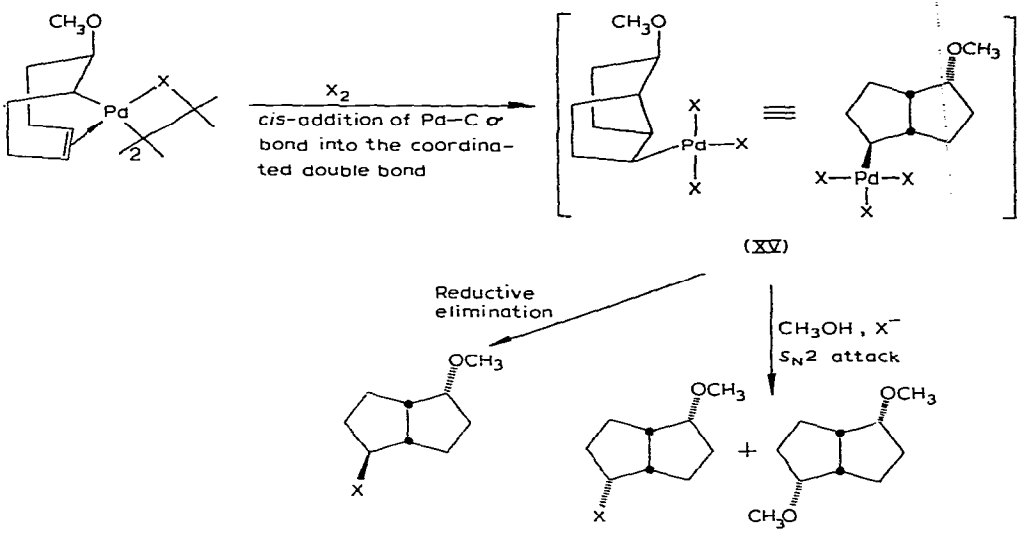
When the halogenation of (II) was carried out in the presence of added halide ion, the formation of (IX) was suppressed and that of (VII*n*) and (VIII*n*) enhanced (Table 3). Control experiments showed that no interconversion between reaction products occurred during halogenation of (II) in the presence of added halide ion and no reactions of (II) were observed in methanol containing added halide ion. Variable amounts of the corresponding diene complexes were isolated from most of the halogenation reactions of (I) and (II)*.

Discussion

In all of these halogenation reactions, the insertion of a coordinated double bond into the Pd—C σ bond took place in addition to (prior to) the cleavage of the Pd—C σ bond. Alkyl halides of opposite stereochemistry were obtained from the halogenation of (II) in dichloromethane and in methanol with added halide ion. These results are best accomodated by an oxidative addition—reductive elimination mechanism, as shown in Scheme 2, with (II). A similar mechanism has been proposed for the acid cleavage of Pt^{II}—C σ bonds [10].

* The yields of diene complexes depended on the work-up. The isolated yields ranged from 55% for the bromination of (Ib) in methanol to trace amount for the bromination of (Ib) in dichloromethane. Yields of organic products fell typically in the range of 30—60%.

SCHEME 2



The first step in Scheme 2 involves the oxidative addition of halogen to (II) with either concomittant or subsequent *cis*-insertion of the coordinated double bond into the Pd—C σ bond to give a Pd^{IV} intermediate (XV). Oxidative addition of halogens to d^8 transition metal complexes has been well documented [11]. Even though stable adducts of Pd^{II} complexes with halogens have not been isolated, a Pt^{II}—alkyl complex has been reported to react with chlorine to form a stable Pt^{IV} complex [12].

The insertion of a coordinated double bond into a Pd—C σ bond as observed in the halogenation of (I) is not surprising since closure of (I) to the nortricyclenic structure can be effected by various coordinating ligands [4a,5,13]. Similar insertion reactions of enyl complexes of 1,5-cyclooctadiene to give bicyclo[3.3.0]octane derivatives can be induced by the action of light or strong base [14]. The proposed oxidatively induced insertion of coordinated double bonds has not previously been observed but oxidatively induced carbonyl insertion reactions of several transition metal complexes have recently been reported using various oxidants [15].

The Pd^{IV} intermediate (XV) can undergo either reductive elimination or nucleophilic attack at the α-carbon with inversion owing to the enhanced leaving group ability of the metal*. This is supported by the isolation of diether (IX) in methanol and the predominant inversion of configuration found in halides (VII) and (VIII) obtained from the halogenation of (II) in the presence of added halide ion. The trapping of (XV) with bromide ion was particularly effective. Chlorination of (IIb) in the presence of added bromide ion gave 3% of the chloroether

* Oxidation products of alkylcobalt(III) complexes were found to readily undergo nucleophilic attack at the α-carbon. It was thus suggested that the inversion of stereochemistry observed in the halogenolysis of alkylcobalt(III) complexes might be the result of an initial oxidation of the complex followed by nucleophilic attack at the α-carbon [2c].

(VII) and 97% of the bromoether (VIII) with an *endo/exo* ratio of 90/10.

Reductive elimination of (XV) apparently proceeds with overall retention of configuration at carbon. The inversion products obtained in dichloromethane might arise from S_N2 attack of (XV) by halide ion generated during the reaction. A possible source of such halide ion could be the reaction of halogen with the alkoxy-enyl complex reversing the methoxypalladation reaction and giving the corresponding diene complex. The possibility that some of the products are formed from the reaction of (XV) with additional halogen can not be discounted.

It is interesting to note that the Pd^{IV} intermediate (XV) did not yield any olefinic products. The oxidation of ethylene by Pd^{II} in acetic acid to give vinyl acetate was proposed to proceed via a Pd^{II} σ-bonded intermediate. The same reaction carried out in the presence of various oxidants afforded mostly 1,2-disubstituted ethanes [16]. Apparently, the facile β palladium—hydride elimination pathway in Pd^{II} chemistry is a relatively high energy process for palladium complexes in higher oxidation states.

Experimental

General procedure for halogenation in dichloromethane

To a vigorously stirred solution of the alkoxy complex in dichloromethane was added an equivalent amount of bromine or a titrated solution of chlorine in carbon tetrachloride. The mixture was stirred at room temperature for 5 min. The precipitated palladium salt was removed by gravity filtration and rinsed with ether. Addition of pentane to the combined filtrates caused the precipitation of the corresponding diene complex which was collected by gravity filtration and washed with ether. The filtrate was concentrated under reduced pressure and the residue was extracted with several small portions of pentane. The combined pentane extracts were washed with dilute hydrochloric acid, aqueous sodium bicarbonate and dried over magnesium sulfate. The solvent was removed under reduced pressure and the products were analyzed by VPC and NMR. Separation of products was achieved by means of preparative VPC using a 10 ft × 0.375 in. 30% DEGS/Chromsorb W column.

Products from chlorination of di-μ-chloro-bis(6-methoxybicyclo[2.2.1]-hept-2-ene-endo-5σ,2π)dipalladium(II), (Ia). Chlorination of 2.2 g (4.2 mmol) of (Ia) in 75 ml of dichloromethane with 42 ml of a 0.206 *M* solution of chlorine in carbon tetrachloride (8.6 mmol) afforded 0.9 g of organic products consisting of two components. The major component (83%) was identified as (III*n*): NMR ($CDCl_3$) δ 4.16 (t,1, CH_3OCH), 3.98 (t,1, $ClCH$), 3.33 (s,3, OCH_3), and 2.2-1.2 ppm (6). The minor component was identified as (III*x*): NMR ($CDCl_3$) δ 3.89 (t,1, $ClCH$), 3.40 (t,1, CH_3OCH), 3.26 (s,3, OCH_3), and 2.4-1.4 ppm (6). (Found: C, 60.44; H, 7.05. $C_8H_{11}ClO$ calcd.: C, 60.57; H, 6.99%.)

Products from bromination of di-μ-bromobis(6-methoxybicyclo[2.2.1]-hept-2-ene-endo-5σ,2π)dipalladium(II), (Ib). Bromination of 1.8 g (2.9 mmol) of (Ib) in 75 ml of dichloromethane with 0.92 g (5.8 mmol) of bromine gave 1.0 g of organic material consisting of two components. The major component (82%) was identified as (IV*n*): NMR ($CDCl_3$) δ 4.15 (t,1, CH_3OCH), 3.96 (t,1, $BrCH$), 3.31 (s,3, OCH_3), and 2.3-1.2 ppm (6). The minor component (18%)

was identified as (IVx): NMR ($CDCl_3$) δ 3.91 (t,1, BrC*H*), 3.39 (t,1, CH_3OCH), 3.26 (s,3, OCH_3) and 2.3-1.3 ppm (6). (Found: C, 47.13; H, 5.43. $C_8H_{11}BrO$ calcd.: C, 47.31; H, 4.92%.)

Products from chlorination of di-μ-chlorobis(1-methoxycyclooct-4-ene-8σ, 4π)dipalladium(II), (IIa). Chlorination of 2.9 g (5.2 mmol) of (IIa) in 150 ml of dichloromethane with 30 ml of a 0.335 *M* solution of chlorine in carbon tetrachloride (10 mmol) gave 0.65 g of organic products consisting of two components. The major component (72%) was identified as (VIIx) by comparison with an authentic sample: NMR ($CDCl_3$) δ 4.04 (m,1, ClC*H*), 3.71 (m,1, CH_3OCH), 3.33 (s,3, OCH_3), 2.75 (m,2) and 2.2-1.1 ppm (8). The minor component (28%) was identified as (VII*n*) by comparison with an authentic sample: NMR ($CDCl_3$) δ 4.33 (m,1, ClC*H*), 3.77 (m,1, CH_3OCH), 3.32 (s,3, OCH_3), 2.64 (m,2) and 2.2-1.1 ppm (8). (Found: C, 62.11; H, 8.51. $C_9H_{15}ClO$ calcd.: C, 61.89; H, 8.66%.)

Products from bromination of di-μ-bromobis(1-methoxycyclooct-4-ene-8σ, 4π)dipalladium(II), (IIb). Bromination of 1.6 g (2.4 mmol) of (IIb) in 100 ml of dichloromethane with 0.75 g (4.8 mmol) of bromine yielded 0.65 g of organic products consisting of two components. The major component (95%) was identified as (VIIIx) by comparison with an authentic sample: NMR ($CDCl_3$) δ 4.03 (m,1, BrC*H*), 3.69 (m,1, CH_3OCH), 3.29 (s,3, OCH_3), 2.78 (m,2), and 2.3-1.1 ppm (8). The minor component (5%) was identified as (VIII*n*) by comparison with an authentic sample: NMR ($CDCl_3$) δ 4.29 (m,1, BrC*H*), 3.74 (m,1, CH_3OCH), 3.27 (s,3, OCH_3), 2.59 (m,2) and 2.2-1.1 ppm (8). (Found: C, 49.33; H, 7.05. $C_9H_{15}BrO$ calcd.: C, 49.33; H, 6.90%.)

General procedure for halogenation in methanol

A rapidly stirred suspension of the alkoxy complex was halogenated by the addition of an equimolar amount of chlorine or bromine dissolved in methanol of chlorine over the suspension. The reaction mixutre was allowed to stir at room temperature for 5 min. The precipitated diene complex was collected by gravity filtration and washed with methanol. The combined filtrates were evaporated under reduced pressure and the residue was extracted with several small portions of pentane. The combined pentane extracts were washed with dilute hydrochloric acid, aqueous sodium bicarbonate and dried over magnesium sulfate. The pentane was removed under reduced pressure and the products were analyzed by VPC and NMR. Reactions involving added halide ion were carried out using saturated methanolic solutions of sodium bromide and lithium chloride.

Products from chlorination of di-μ-chlorobis(6-methoxybicyclo[2.2.1]-hept-2-ene-endo-5σ,2π)dipalladium(II), (Ia). Chlorination of 3.1 g (11.7 mmol) of (Ia) in 1.75 ml of methanol gave 0.8 g of organic material consisting of three components, two of which were identified as (III*n*) (37%) and (IIIx) (25%). The third component (38%) was identified as (VI): NMR ($CDCl_3$) δ 3.33 (t,2, CH_3OCH), 3.26 (s,6, OCH_3), 2.25 (m,1), 1.69 (m,2) and 1.42 ppm (bs,3); mass spectrum (70 eV) *m/e* 154 (M^+). (Found: C, 69.70; H, 9.08. $C_9H_{14}O_2$ calcd.: C, 70.10; H, 9.15%.)

Products from bromination of di-μ-bromobis(1-methoxycyclooct-4-ene-8σ, 4π)dipalladium(II), (IIb). Bromination of 1.3 g (2.0 mmol) of (IIb) in 75 ml of

methanol with 0.6 g (3.8 mmol) of bromine afforded 0.4 g of organic material consisting of three components, two of which were identified as (VIIIx) (26%) and (VIII*n*) (32%). The third component was identified as (IX): NMR ($CDCl_3$) δ 3.72 (m,2, CH_3OCH), 3.29 (s,6, OCH_3), 2.56 (m,2) and 2.1-1.2 ppm (8); mass spectrum (70 eV) *m/e* 170 (M^+). (Found: C, 69.53; H, 10.57. $C_{10}H_{18}O_2$ calcd.: C, 70.55; H, 10.66%.)

Control experiments

To insure that the products obtained were primary products, a number of control experiments were carried out by running the halogenation reactions in the presence of one or more of the reaction products. All reaction products were found to be stable under reaction conditions. To test the possibility that some of the products arose from reactions between complex (II) and nucleophiles, (II) was allowed to react with halide ions in methanol. No reaction was observed.

Debromination of 2-endo-methoxy-6-bromo-cis-bicyclo[3.3.0]octane, (VIII); formation of 2-endo-methoxy-cis-bicyclo[3.3.0]octane, (X)

To a solution of 1.7 g (7.8 mmol) of (VIII) in 10 ml of tert-butyl alcohol and 40 ml of tetrahydrofuran was added 1.8 g (78 mmol) of sodium in small pieces. The mixture was heated at reflux for 40 h under an atmosphere of nitrogen. The cooled mixture was poured into water and extracted with 3 × 100 ml of ether. The combined ether extracts were washed with water, dried over magnesium sulfate and concentrated under reduced pressure. Short path distillation afforded 0.5 g (3.6 mmol, 46%) of (X): b.p. 33-34°/2 mm; NMR ($CDCl_3$) δ 3.66 (m,1, CH_3OCH), 3.32 (s,3, OCH_3), 2.7-2.2 (2) and 2.2-1.0 ppm (10); mass spectrum (70 eV) *m/e* 140 (M^+). (Found: C, 76.77; H, 11.16. $C_9H_{16}O$ calcd.: C, 77.08; H, 11.50%.)

Dechlorination of 2-endo-methoxy-6-chloro-cis-bicyclo[3.3.0]octane, (VII); formation of 2-endo-methoxy-cis-bicyclo[3.3.0]octane, (X)

Treatment of 0.45 g (2.57 mmol) of (VII) in 5 ml of tert-butyl alcohol and 20 ml of tetrahydrofuran with 0.6 g (26 mmol) of sodium in a manner described above yielded 0.15 g (1.05 mmol, 41%) of (X).

Methylation of 2-endo-hydroxy-cis-bicyclo[3.3.0]octane, (XI); formation of 2-endo-methoxy-cis-bicyclo[3.3.0]octane, (X)

A solution of 0.4 g (3.2 mmol) of (XI) in 10 ml of anhydrous ether was added dropwise to a suspension of 1 g (21 mmol) of 50% sodium hydride suspension in 20 ml of dry ether under an atmosphere of nitrogen. The reaction mixture was heated at reflux for 1 h. A solution of 1.0 g (7.0 mmol) of methyl iodide in 10 ml of dimethyl sulfoxide was added dropwise and the resulting mixture was heated at reflux for 30 min. The cooled reaction mixture was hydrolysed by 20 ml of water and the organic layer was separated. The aqueous layer was extracted with 2 × 100 ml of ether. The combined organic layers were washed with aqueous sodium bicarbonate, dried over magnesium sulfate and concentrated under reduced pressure to give 0.3 g of an oil. VPC analysis showed two components. The minor component (40%) was identified as the unreacted alcohol (XI). The major component (60%) was collected by preparative

VPC using a 10 ft × 0.375 in. 20% SE30/Chromsorb W column. VPC and NMR comparison showed it to be identical to (X).

Conversion of 2-endo-methoxy-6-bromo-cis-bicyclo[3.3.0]octane, (VIII), to 2-endo-methoxy-cis-bicyclo[3.3.0]octan-6-one, (XII)

To a solution of 3.4 g (15.5 mmol) of (VIII) in 60 ml of acetic acid was added 4.1 g (24.6 mmol) of silver acetate. The resulting suspension was heated at reflux for 16 h. The reaction mixture was filtered through Celite and rinsed with ether. The solvent was evaporated under reduced pressure. Short path distillation gave 1.5 g (7.6 mmol, 49%) of a mixture of 2-*endo*-methoxy-6-acetoxy-*cis*-bicyclo[3.3.0]octane epimers: b.p. 76-84°/0.2 mm; NMR ($CDCl_3$) δ 4.82 (m,1, AcOC*H*), 3.56 (m,1, CH_3OCH), 3.27 (s,3, OCH_3), 2.00 (s,3, $OCOCH_3$) and 2.9-1.15 ppm (10).

A solution of 1.5 g (7.6 mmol) of the acetates was added dropwise to a suspension of 0.5 g (13.2 mmol) of lithium aluminum hydride in 20 ml of anhydrous ether at 0°. The reaction mixture was stirred at room temperature for 24 h and then hydrolysed by the addition of 0.5 ml of water, 0.5 ml of 15% sodium hydroxide and 1.5 ml of water successively. The precipitated salt was removed by vacuum filtration and washed with ether. The combined ether filtrates were washed with aqueous potassium bicarbonate and dried over magnesium sulfate. The ether was removed under reduced pressure and the residue was distilled using a short path system to give 1.0 g (6.4 mmol, 84%) of a mixture of 2-*endo*-methoxy-6-hydroxy-*cis*-bicyclo[3.3.0]octane isomers: b.p. 76-78°/0.12 mm; NMR ($CDCl_3$) δ 4.1-3.4 (m,2, HOC*H* and CH_3OCH), 3.28 (s,3,OCH_3), 2.48 (s,1, OH) and 2.9-1.1 ppm (10).

A solution of 1.0 g (6.4 mmol) of the alcohols in 10 ml of reagent grade acetone was titrated with Jones reagent (8 *N* in oxygen). The reaction mixture was stirred at room temperature for 2 h. The green aqueous layer was diluted with 20 ml of water and extracted with 3 × 50 ml of Skelly B. The organic layers were combined and washed with saturated aqueous sodium chloride, sodium bicarbonate, and sodium chloride successively. After being dried over magnesium sulfate, the solvent was removed under reduced pressure. Short path distillation afforded 0.7 g (4.5 mmol, 70%) of (XII): b.p. 48.5-50°/0.12 mm; IR (film) 1740 cm^{-1} (C=O); NMR ($CDCl_3$) δ 3.78 (m,1, CH_3OCH), 3.27 (s,3, OCH_3) and 2.0-1.5 ppm (10).

Hydrogenation of 2-endo-methoxy-cis-bicyclo[3.3.0]octan-6-one, (XII); formation of 2-endo-methoxy-6-endo-hydroxy-cis-bicyclo[3.3.0]octane, (XIII)

A mixture of 0.7 g (4.5 mmol) of (XII) and 0.2 g of platinum oxide in 20 ml of absolute ethanol was placed in a glass-lined autoclave, which was pressurized with 35 atm. of hydrogen and stirred at room temperature for 16 h. The precipitated platinum metal was removed by gravity filtration and rinsed with ether. The solvent was removed under reduced pressure. Short path distillation gave 0.6 g (3.8 mmol, 85%) of (XIII): b.p. 60-61°/0.3 mm; NMR ($CDCl_3$) δ 3.88 (m,1, HOC*H*), 3.52 (m,1, CH_3OCH), 3.30 (s,3, OCH_3), 3.22 (s,1, O*H*), 2.5 (m,2) and 2.2-1.2 ppm (8).

Chlorination of 2-endo-methoxy-6-endo-hydroxy-cis-bicyclo[3.3.0]octane, (XIII); formation of 2-endo-methoxy-6-exo-chloro-cis-bicyclo[3.3.0]octane, (VIIx)

To a solution of 0.1 g (0.64 mmol) of (XIII) in 2 ml of dichloromethane was added 0.2 g (0.96 mmol) of phosphorus pentachloride. The reaction mixture was stirred at room temperature for 6 h and poured into water. The water layer was extracted with 3 × 20 ml of dichloromethane. The combined organic layers were washed with aqueous sodium bicarbonate and dried over magnesium sulfate. Removal of solvent under reduced pressure gave a material which was identical to (VIIx) by VPC and NMR comparison.

Bromination of 2-endo-methoxy-6-endo-hydroxy-cis-bicyclo[3.3.0]octane, (XIII); formation of 2-endo-methoxy-6-exo-bromo-cis-bicyclo[3.3.0] octane, (VIIIx)

A solution of 0.3 g (1.85 mmol) of bromine in 10 ml of dichloromethane was added to a solution of 0.5 g (1.85 mmol) of phosphorus tribromide in 10 ml of dichloromethane with cooling. To the resulting mixture was added a solution of 0.2 g (1.28 mmol) of (XIII) in 2 ml of dichloromethane. After stirring at room temperature for 1 h, the reaction mixture was poured into water and extracted with 2 × 50 ml of dichloromethane. Removal of solvent under reduced pressure followed by distillation using a micro-distillation apparatus gave a material which was identical to (VIIIx) by VPC and NMR comparison.

Methylation of 2-endo-methoxy-6-endo-hydroxy-cis-bicyclo[3.3.0]octane, (XIII); formation of 2,6-endo,endo-dimethoxy-cis-bicyclo[3.3.0]octane, (IX)

To a solution of 0.1 g (0.64 mmol) of (XIII) in 5 ml of methyl iodide was added 0.4 g of calcium sulfate and 0.4 g (1.6 mmol) of silver oxide. The resulting suspension was heated at reflux for 24 h. The reaction mixture was filtered through Celite, and washed with ether. The filtrate was evaporated under reduced pressure. VPC analysis of the residue showed the presence of two components. The minor component (30%) was identified as the unreacted alcohol (XIII). The major component (70%) was isolated by preparative VPC using a 10 ft × 0.375 in. 30% DEGS/Chromsorb W column. VPC and NMR comparison showed it to be identical to (IX).

Oxidation of 2-endo-methoxy-6-endo-hydroxy-cis-bicyclo[3.3.0]octane, (XIII); formation of cis-bicyclo[3.3.0]octan-2,6-dione, (XIV)

To a suspension of 0.2 g (1.28 mmol) of (XIII) in 15 ml of a 0.6 *M* acetate buffer at pH 5 was added 1.2 g (12.5 mmol) of bromine. The reaction mixture was stirred in the dark for 12 h. The excess bromine was reduced by the addition of sodium bisulfite. The resulting mixture was extracted with 3 × 50 ml of dichloromethane. The combined organic extracts were washed with aqueous sodium bicarbonate, dried over magnesium sulfate and concentrated under reduced pressure. VPC analysis showed the presence of two components contaminated by a minor amount of impurities. The two components were separated using a 10 ft 30% DEGS column. The minor component (30%) was identified as (XII).

The major component (70%) was shown to be identical with an authentic sample of (XIV)* by IR and VPC comparison.

Acknowledgement

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

References

1 G.M. Whitesides and D.J. Boschetto, J. Amer. Chem. Soc., 93 (1971) 1529.
2 (a) F.R. Jensen, V. Madan and D.H. Buchanan, J. Amer. Chem. Soc., 93 (1971) 5283;
(b) D. Dodd and M.D. Johnson, J. Chem. Soc., Chem. Commun., (1971) 571;
(c) S.N. Anderson, D.H. Ballard, J.Z. Chrzatowski, D. Dodd and M.D. Johnson, ibid., (1972) 685.
3 R.W. Johnson and R.G. Pearson, Chem. Commun., (1970) 986.
4 (a) D.R. Coulson, J. Amer. Chem. Soc., 91 (1969) 200;
(b) E. Vedejs and M.F. Salomon, J. Org. Chem., 37 (1972) 2075.
5 L.F. Hines and J.K. Stille, J. Amer. Chem. Soc., 94 (1972) 485, and references therein.
6 A.C. Cope, H-H. Lee and H.E. Petree, J. Amer. Chem. Soc., 80 (1958) 2849.
7 (a) A.C. Cope, M. Brown and H.E. Petree, J. Amer. Chem. Soc., 80 (1958) 2852;
(b) H.C. Brown and W.J. Hammer, ibid., 89 (1967) 6378;
(c) I. Tabushi, K. Fujita and R. Oda, J. Org. Chem., 35 (1970) 2376.
8 (a) C.W. Shoppe, T.E. Bellas and R. Lack, J. Chem. Soc., (1965) 6450;
(b) E.L. Eliel and R.G. Haber, J. Org. Chem., 24 (1959) 143.
9 T.S. Cantrell and B.L. Strasser, J. Org. Chem., 36 (1971) 670.
10 (a) U. Belluco, U. Croatto, P. Uguagliati and R. Pietropaolo, Inorg. Chem., 6 (1967) 718;
(b) U. Belluco, M. Giustiniani and M. Graziani, J. Amer. Chem. Soc., 89 (1967) 6494.
11 J.P. Collman and W.R. Roper, Advan. Organometal. Chem., 7 (1968) 53.
12 J. Chatt and B.L. Shaw, J. Chem. Soc., (1959) 705.
13 E. Vedejs and M.F. Salomon, J. Amer. Chem. Soc., 92 (1970) 6965.
14 (a) C.B. Anderson and B.L. Burreson, Chem. Ind. (London), (1967) 620;
(b) H. Takahashi and J. Tsuji, J. Amer. Chem. Soc., 90 (1968) 2387.
15 (a) S.N. Anderson, C.W. Fong and M.D. Johnson, J. Chem. Soc., Chem. Commun., (1973) 163;
(b) K.M. Nicholas and M. Rosenblum, J. Amer. Chem. Soc., 95 (1973) 4449.
16 P.M. Henry, J. Org. Chem., 38 (1973) 1681.

* We wish to thank Dr. T.S. Cantrell [9] for a gift of a sample of *cis*-bicyclo[3.3.0]octan-2,6-dione.