ated IIIc changed the H-2 signal to a quartet and the double doublet at 3.86 ppm to a doublet (J = 8.6 Hz). From these results, the band at 3.86 ppm was assigned to H-7, and a multiplet at 1.57 ppm to H-2 (J_{gem} = −15.2 Hz). In conclusion, configuration and conformational structures of these lactams (IIIa,b,c) are shown in Chart III.

Experimental Section

All melting points are uncorrected. Optical rotations were measured in a 0.1-dm tube with a JASCO automatic polarimeter DIP-SL, unless otherwise noted. Nmr spectra were recorded in deuteriochloroform at 100 MHz with a Varian Associate H-100 spectrometer and tetramethylsilane was used as an internal reference. Mass spectra were taken with a Japan Electron Optics JMS-01S high-resolution spectrometer with a direct inlet system.

cis-**Tetrahydro-α-santonin Oxime (IIa).**—To a solution of hydroxylamine hydrochloride (1.0 g) in ethanol (5 ml) and pyridine (5 ml) was added 1.0 g of *cis*-tetrahydro-α-santonin (Ia) and the resulting solution was warmed under reflux for 3 hr. After evaporation of organic solvents under a reduced pressure, ice water was added and white crystals precipitated. Recrystallization from methanol afforded IIa in 80–90% yield as colorless prisms: mp 175°; ir ν_{max}^{Nujol} 3230 (OH), 1670 cm^{-1} (C=N); $[\alpha]^{26}D$ −30.0° (*c* 1.8, EtOH), −12.0° (*c* 1.5, $CHCl_3$).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 67.81; H, 8.87; N, 5.07.

trans-4β-**Tetrahydro-α-santonin Oxime (IIb).**—4β-Tetrahydro-α-santonin (Ib) was treated in the same manner as for IIa. Recrystallization from benzene gave *trans*-4β-oxime (IIb) in 70% yield as colorless plates: mp 199–202°; $[\alpha]^{20}D$ −9.1° (*c* 1.0, $CHCl_3$); tlc R_f 0.26 and 0.36 (4:1) in benzene–acetone (5:1); ir ν_{max}^{KBr} 3320 (OH), 1655 cm^{-1} (C=N); nmr (DMSO-d_6) δ 3.60 ppm (m, 1, H-4).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 67.63; H, 8.72; N, 5.14.

A mixture melting point with *trans*-4α-oxime (IIc, mp 219–224°) was depressed to 174–182°.

trans-4α-**Tetrahydro-α-santonin Oxime (IIc).**—4α-Tetrahydro-α-santonin (Ic) was treated in the same way as IIa. Recrystallization from methanol–water gave *trans*-4α-oxime (IIc) in 80% yield as colorless plates: mp 221–225° dec; $[\alpha]^{20}D$ −29.9° (*c* 1.0, $CHCl_3$); tlc R_f 0.26 and 0.36 (1:5) in benzene–acetone (5:1); ir ν_{max}^{KBr} 3440 (OH), 1635 cm^{-1} (C=N); nmr (DMSO-d_6) δ 2.46 ppm (m, 1, H-4).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 67.76; H, 8.64; N, 5.11.

Beckmann Rearrangement of *cis*-**Tetrahydro-α-santonin Oxime (IIa).**—A solution of IIa (1.0 g) and *p*-toluenesulfonyl chloride (1.0 g) in pyridine (6 ml) was warmed on a water bath at 50° for 1 hr. After evaporation of pyridine under reduced pressure, the resulting residue was treated with ice water and extracted with chloroform. Evaporation of the dried chloroform solution and recrystallization of the residue from methanol afforded 4-aza-*A*-homo-*cis*-tetrahydro-α-santonin (IIIa) in 76% yield as colorless prisms: mp 222°; $[\alpha]^{26}D$ +27.5° (*c* 1.5, $CHCl_3$); ir ν_{max}^{Nujol} 3200, 3070 (NH), 1763 (lactone), 1679 cm^{-1} (C=O); nmr δ 5.99 (d, 1, J = 4.5 Hz, NH), 4.36 (dd, 1, $J_{7,6}$ = 4.3, $J_{7,8}$ = 11.0 Hz, H-7), 3.76 (m, 1, $J_{5,4}$, = 4.5, $J_{5,6}$ = 9.0, $J_{5,\text{C-5 CH}_3}$ = 6.7 Hz, H-5), 2.05 (dd, 1, $J_{6,5}$ = 9.0, $J_{6,7}$ = 4.3 Hz, H-6), 1.24 (d, 3, J = 6.7 Hz, C-5 CH_3), 1.23 (d, 3, J = 6.75 Hz, C-12 CH_3), 1.16 ppm (s, 3, C-11 CH_3); mass *m/e* 265 (M^+).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28; mol wt, 265.169. Found: C, 68.06; H, 8.90; N, 5.20; mol wt, 265.167.

Beckmann Rearrangement of *trans*-4β-**Tetrahydro-α-santonin Oxime (IIb).**—To the warmed (70°) solution of *trans*-4β-oxime (1.0 g) in dioxane (20 ml), thionyl chloride (0.6 ml) was added dropwise during 20 min with stirring. After standing at room temperature for 30 min the reaction mixture was neutralized with sodium bicarbonate solution and then extracted with chloroform. The chloroform solution was dried and evaporated under reduced pressure. The residue was treated with methyl acetate and gave a crude lactam (IIIb + IIIc) in 30% yield, tlc R_f 0.24 and 0.43 (2:3) in chloroform–methanol (10:1). This crude lactam was chromatographed on silica gel and eluted with benzene–chloroform (3:2).

From the first eluate **4-aza-*A*-homo-*trans*-tetrahydro-α-santonin (IIIb)** was obtained as colorless plates from benzene: mp 214–218°; $[\alpha]^{24}D$ −3.92° (*c* 0.9, $CHCl_3$); ir ν_{max}^{KBr} 3240, 3090 (NH), 1770 (lactone), 1675 cm^{-1} (C=O); nmr δ 5.97 (d, 1, J = 4.0 Hz, NH), 3.75 (m, 1, $J_{5,4}$ = 4.0 Hz, $J_{5,\text{C-5 CH}_3}$ = 6.9, $J_{5,6}$ = 6.5 Hz, H-5), 3.75 (dd, 1, $J_{7,6}$ = 7.0, $J_{7,8}$ = 11.0 Hz, H-7), 2.18 (dd, 1, $J_{6,5}$ = 6.5, $J_{6,7}$ = 7.0 Hz, H-6), 1.35 (d, 3, J = 6.9 Hz, C-5 CH_3), 1.20 (d, 3, J = 6.75 Hz, C-12 CH_3), 1.09 ppm (s, 3, C-11 CH_3); mass *m/e* 265 (M^+).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28; mol wt, 265.169. Found: C, 67.95; H, 8.63; N, 5.13; mol wt, 265.167.

From the second eluate, **3-aza-*A*-homo-*trans*-tetrahydro-α-santonin (IIIc)** was obtained as colorless plates from benzene: mp 211–213°; $[\alpha]^{23}D$ +10.9° (*c* 1.0, $CHCl_3$); ir ν_{max}^{KBr} 3570, 3440, 3310 (NH), 1770 (lactone), 1655 cm^{-1} (C=O); nmr δ 6.74 (t, 1, J = 5.3 Hz, NH), 3.86 (dd 1, $J_{7,6}$ = 8.6, $J_{7,8}$ = 11.0 Hz, H-7), 2.83 (m, 1, J_5, C-5 CH_3 = 7.4, $J_{5,6}$ = 8.0 Hz, H-5), 2.25 (dd, 1, $J_{6,5}$ = 8.0, $J_{6,7}$ = 8.6 Hz, H-6), 1.27 (d, 3, J = 7.4 Hz, C-5 CH_3), 1.17 (d, 3, J = 7.0 Hz, C-12 CH_3), 1.14 ppm (s, 3, C-11 CH_3); mass *m/e* 265 (M^+).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28; mol wt, 265.169. Found: C, 67.62; H, 8.73; N, 5.11; mol wt, 265.167.

Schmidt Reaction of *cis*-**Tetrahydro-α-santonin (Ia).**—To a cooled solution of Ia (1.0 g) in chloroform (6 ml) was added dropwise concentrated sulfuric acid (2 ml), and then sodium azide (0.55 g) was added during 30 min at −10° with stirring. After stirring for 30 min at room temperature, the reaction mixture was allowed to stand overnight at room temperature. Crushed ice was added to the reaction mixture, which was neutralized with sodium carbonate and extracted with chloroform. Evaporation of dried chloroform solution left 4-aza-*cis*-lactam (IIIa) in 85% yield, mp 220°, $[\alpha]^{21}D$ +23.8° (*c* 1.0, EtOH), which was identified with the product (IIIa) of Beckmann rearrangement by comparison of their ir spectra and by mixture melting point determination.

Schmidt Reaction of *trans*-4α-**Tetrahydro-α-santonin (Ic).**—Ic (1.0 g) was treated in the same manner as Ia. Recrystallization from methanol gave 4-aza-*A*-homo-*trans*-tetrahydro-α-santonin (IIIb) in 40% yield, mp 228–229°, $[\alpha]^{23}D$ −5.0° (*c* 1.0, $CHCl_3$), which was identified with a sample described above in the Beckmann rearrangement, 4-aza compound IIIb, by comparison of their ir spectra and by mixture melting point determination.

Registry No.—IIa, 32979-73-0; IIb, 32979-74-1; IIc, 32979-75-2; IIIa, 32979-76-3; IIIb, 32979-77-4; IIIc, 32979-78-5.

Acknowledgment.—We wish to acknowledge our indebtedness to Dr. H. Kuwano, Central Research Laboratories, Sankyo Co., Ltd., for the nmr measurements, and to Dr. K. Takagi and Mrs. A. Hatano for the mass spectral measurements.

Hydrogenolysis of Mixed Ketals of Norcamphor by Dichloroalane

WALTER W. ZAJAC, JR.,* AND KEVIN J. BYRNE

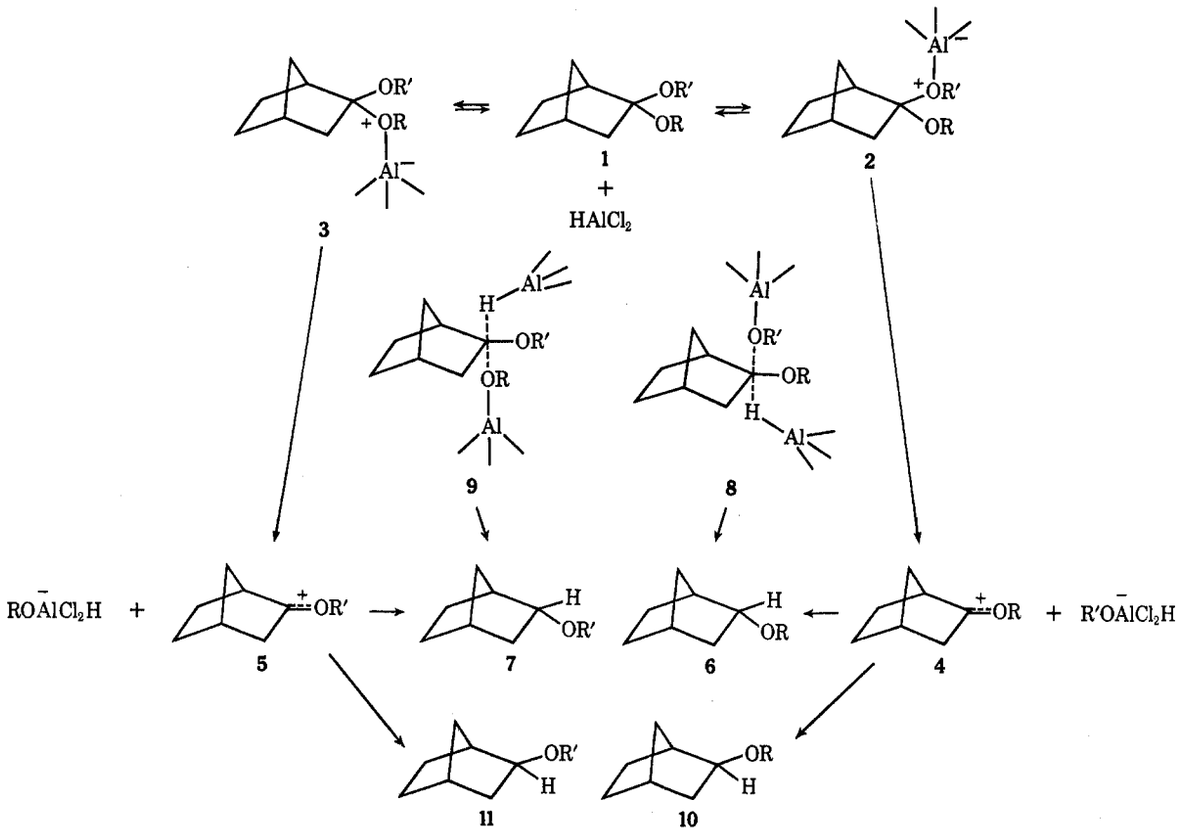
Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

Received June 29, 1971

Hydrogenolysis of ketals by "mixed hydrides" ($LiAlH_4$–$AlCl_3$) gives ethers as the products. Studies on the hydrogenolysis of 4-substituted 1,3-dioxolanes,[1] a steroidal propylene ketal,[2] and 2-substituted tetra-

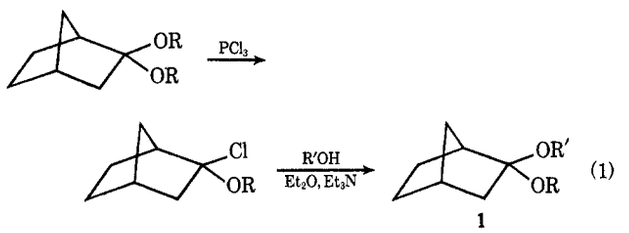
(1) B. E. Leggetter and R. K. Brown, *Can. J. Chem.*, **42**, 990 (1964).
(2) M. S. Ahmad and S. C. Logani, *Aust. J. Chem.*, **24**, 143 (1971).

SCHEME I



hydropyranyl and tetrahydrofuranyl ethers[3,4] have shown that the product which results from the more inductively stabilized oxocarbonium ion intermediate usually predominates. From the data obtained on the hydrogenolysis of cycloalkanone dimethyl ketals[5] it has been suggested that in the medium ring sizes (8–12) there is a steric hindrance, due to transannular repulsion, to the formation of a ketal–dichloroalane complex, which is the first step of the hydrogenolysis reaction. Recent evidence has led to the suggestion that ortho esters[6] and one of the two isomeric norcamphor isobutylene ketals[7] are hydrogenolyzed by back-side attack of a hydride. In an effort to better understand the steric and electronic conditions which control the mechanism of hydrogenolysis, we have synthesized a series of mixed ketals of norcamphor and subjected these compounds to hydrogenolysis by dichloroalane.

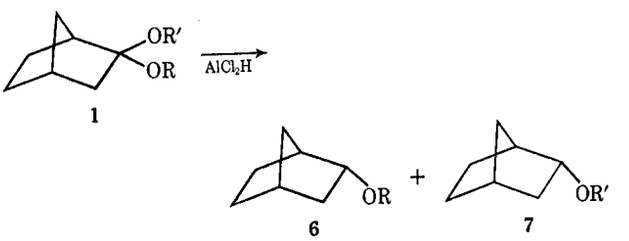
The mixed ketals are synthesized from the dimethyl, diethyl, and diisopropyl ketals of norcamphor, respectively. When these starting ketals are allowed to react with PCl_3, the corresponding 2-chloronorbornyl ethers are formed. When the chloro ethers are allowed to react with an alcohol and an organic base in a nonpolar medium, they are converted to the mixed ketals (eq 1). The addition of the alcohol is from the exo side, giving a mixed ketal (**1**) of high isomeric purity. The



(1)

mixed ketals synthesized and their hydrogenolysis products, the ethers, are tabulated in Table I.

TABLE I
HYDROGENOLYSIS OF MIXED KETALS OF NORCAMPHOR BY A 1:3 MIXTURE OF LiAlH–$AlCl_3$ IN ETHER AT ROOM TEMPERATURE



Compd	R	R′	Compd	R	Yield, %	Compd	R′	Yield, %
1a	CH_3	CD_3	**6a**	CH_3	67	**7a**	CD_3	33
1b	CH_3	Et	**6b**	CH_3	20	**7b**	Et	80
1c	CH_3	*i*-Pr	**6c**	CH_3	2	**7c**	*i*-Pr	98
1d	CH_3	*tert*-Bu	**6d**	CH_3	8	**7d**	*tert*-Bu	83[a]
1e	Et	CH_3	**6e**	Et	86	**7e**	CH_3	14
1f	*i*-Pr	CH_3	**6f**	*i*-Pr	99	**7f**	CH_3	1

[a] 9% *endo*-norborneol also isolated.

All the ethers produced by the hydrogenolysis of the mixed ketals were identified as endo ethers (Scheme I, **6** and **7**). The norbornyl ethyl ether from nor-

(3) E. L. Eliel, B. E. Nowak, R. A. Daignault, and V. G. Badding, *J. Org. Chem.*, **30**, 2441 (1965).
(4) U. E. Diner and R. K. Brown, *Can. J. Chem.*, **45**, 2547 (1967).
(5) W. W. Zajac, Jr., and K. J. Byrne, *J. Org. Chem.*, **35**, 3375 (1970).
(6) S. S. Bhattacharjee and P. A. J. Gorin, *Can. J. Chem.*, **47**, 1195 (1969).
(7) P. C. Loewen, W. W. Zajac, Jr., and R. K. Brown, *ibid.*, **47**, 4059 (1969).

TABLE II
PROPERTIES OF MIXED KETALS

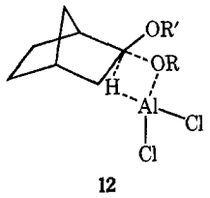
Mixed ketal	Bp, °C (mm)	Isomeric purity,[a] %	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Nmr (CCl_4),[b] cps, CH_3O
1a[c]	84–86 (30)	94					186.0
1b	103–104 (40)	97	70.55	10.66	70.33	10.60	186.4
1c	112–114 (40)	97	71.70	10.94	71.76	10.96	189.3
1d	89–90 (8.6)	99	72.68	11.18	72.60	10.92	188.4
1e	78–80 (13)	97	70.55	10.66	70.74	10.78	184.6
1f	104–108 (40)	90	71.70	10.94	71.92	11.09	187.0

[a] The isomeric purity was determined by the integration of the methoxyl signals in the nmr. [b] Positions are given downfield of TMS. The relative positions were determined in mixtures of these compounds. The positions for the endo and exo methoxyls of norcamphor dimethyl ketal are 186.0 and 184.4 cps, respectively. [c] The molecular ion peak is 159, by mass spectroscopy.

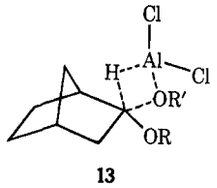
camphor *exo*-ethyl *endo*-methyl ketal (**1b**) and norcamphor *endo*-ethyl *exo*-methyl ketal (**1e**) and the norbornyl methyl ether from all the ketals had ir and nmr identical with those of the unequivocally synthesized endo ethers. The norbornyl isopropyl and *tert*-butyl ether produced by the hydrogenolysis of norcamphor *endo*-methyl *exo*-isopropyl ketal (**1c**), and norcamphor *exo*-methyl *endo*-isopropyl ketal (**1f**), and norcamphor *exo-tert*-butyl *endo*-methyl ketal (**1d**), respectively, are assigned as the endo isomers on the basis of their nmr spectra. The C-2 hydrogen of the norbornyl system is a multiplet centered around 185 and 195 ppm for the methyl and ethyl exo ethers and 215 and 220 ppm for the two endo ethers. The norbornyl isopropyl and *tert*-butyl ethers have a C-2 hydrogen signal centered around 230 ppm. Furthermore, the nmr spectra of *exo*-norbornyl methyl and ethyl ethers show that the chemical shifts of the C-1 and C-4 hydrogens are similar and give rise to a single complicated multiplet. For the endo ethers the same two hydrogens are sufficiently different to give rise to two adjacent complicated multiplets. The spectra published by Loewen, *et al.*,[7] show a similar behavior of the tertiary hydrogens of some endo and exo norbornyl ethers. Both the norbornyl isopropyl and *tert*-butyl ethers have two adjacent complicated multiplets for the C-1 and C-4 hydrogens which agree with the endo assignment. Furthermore, the norborneol which was produced during hydrogenolysis of **1d** was the endo alcohol and could only arise by the further hydrogenolysis of *endo*-norbornyl *tert*-butyl ether. A similar hydrogenolysis of a tertiary *exo*-norbornyl ether has been reported to give *exo*-norborneol.[7] The hydrogenolysis of norcamphor *endo*-methyl *exo*-methyl-d_3 ketal (**1a**) gave only one glpc peak, which was examined by mass spectroscopy to determine the ratio of products. *endo*-Norbornyl methyl ether has a molecular ion peak of 126. *endo*-Norbornyl methyl-d_3 ether with a molecular peak of 129 is easily determined. The results obtained by integrating the methoxyl group against the C-2 hydrogen downfield and against all the other hydrogens upfield together were in close agreement with the mass spectral analysis of the hydrogenolysis reaction mixture.

The hydrogenolysis of norcamphor dimethyl ketal is known to give 95% *endo*-methyl ether and 5% *exo*-methyl ether.[8] Other reactions[8-10] of the norbornyl system where C-2 is sp^2 hybridized in the rate-controlling step show high selectivity for approach from the exo side. The results of the hydrogenolysis of **1a** (Scheme I, R = CH_3; R′ = CD_3) indicate that even one atom removed from C-2 the approach to form the complexes (**2** and **3**), which are the first steps in the hydrogenolysis, is easier from the exo side because the deuterated methoxyl is lost to the extent of 67%. For the ethyl methyl ketals (**1b**, R = CH_3; R′ = Et) (**1e**, R = Et; R′ = CH_3) the methoxyl group is lost to the extent of 86% when it is exo and 80% when it is endo. For the methyl isopropyl ketals (**1c**, R = CH_3; R′ = *i*-Pr) (**1f**, R = *i*-Pr; R′ = CH_3) the methoxyl group is lost to the extent of 99% when it is exo and 98% when it is endo. This is in agreement with the principle that the more inductively stabilized oxocarbonium ion (**4** and **5**) will predominate. Clearly the stabilizing abilities of the alkoxyl groups are *tert*-BuO > *i*-Pro > EtO > MeO, whereas the ease of complexation is in the opposite order. Along with the electronic effects, then, part of the observed trend is undoubtedly due to the ease of complexing the methoxy group whether it is in an exo or endo position.

It has been suggested that hydrogenolysis can proceed through a four-center transition state resulting in net retention of configuration.[7] In this case a four-center transition state such as **12** or **13** would be required. Transition state **12** is clearly ruled out by the results since no exo ethers (**10**, **11**) are observed as products.



12



13

Furthermore, it would not be consistent to invoke a four-center transition state (**13**) to account for the endo ethers **6a–d** from the ketals **1a–d** and at the same time to invoke an oxocarbonium ion **5** to account for the other endo ether products **7a–d** resulting from hydrogenolysis of the same ketals **1a–d**.

The results of this investigation can be uniformly explained as arising from the attack of dichloroalane from the least hindered side (exo) on an intermediate oxocarbonium ion which can be formed by the decomposition of a ketal complexed with either the exo or endo alkoxy group (see Scheme I, paths **1** → **3** → **5** → **7** and **1** → **2** → **4** → **6**).

Experimental Section

Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

(8) T. G. Traylor and C. L. Perrin, *J. Amer. Chem. Soc.*, **88**, 4934 (1966).
(9) E. L. Eliel and D. Nasipuri, *J. Org. Chem.*, **30**, 3809 (1965).
(10) W. W. Zajac, Jr., B. Rhee, and R. K. Brown, *Can. J. Chem.*, **44**, 1547 (1966).

Mass spectra were obtained through the courtesy of Dr. J. F. Siuda, University of Pittsburgh.

Analytical glpc was carried out on an F and M Model 700 using a 0.25 in. × 6 ft 10% Carbowax column. Preparative glpc was done on a 0.50 in. × 12 ft 10% SE-30 column. The percentage yields reported correspond to peak area. Nmr spectra were recorded on a Varian A-60 spectrometer using tetramethylsilane as an internal standard.

Glassware used in the handling of the mixed ketals was washed with dilute sodium hydroxide and oven dried.

exo-Norbornyl methyl ether and ethyl *exo*-norbornyl ether were prepared by the acid-catalyzed addition of methanol and ethanol, respectively, to norbornene.[11] *endo*-Norbornyl methyl ether and *endo*-norbornyl ethyl ether were prepared by the reaction of *endo*-norborneol[12] and sodium hydride in dimethoxyethane with methyl iodide and ethyl iodide, respectively.

Starting Ketals.—The dimethyl, diethyl, and diisopropyl ketals of norcamphor are most easily prepared by the acid-catalyzed reaction of norcamphor and trimethyl orthoformate, triethyl orthoformate, and triisopropyl orthoformate,[13] respectively, in the appropriate alcohol. The reaction of triisopropyl orthoformate and norcamphor was followed by the appearance of the formate hydrogen and the disappearance of the orthoformate hydrogen in the nmr. The equilibrium mixture has about one-third conversion to the product.

2-Chloronorbornyl Ethers.—The preparative procedure was to add the starting norcamphor ketal to a 5% molar excess of PCl_3 which is stirring in an ice bath. The ice bath was removed and the mixture was stirred for 1.5 hr. The mixture was distilled using an oil bath which was kept below 65°. Fractionation was accomplished by reducing the pressure of the distillation. The receiving flask was in an ice–calcium chloride slurry, and the pump was protected by a Dry Ice–acetone trap and a liquid nitrogen trap. Yields were high and free of starting ketals, but norcamphor, which appears to be a thermal decomposition product, accounts for *ca.* 10% of the products.

Mixed Ketals.—The preparation of norcamphor *exo*-ethyl *endo*-methyl ketal (**1b**) is representative and is given here. To 4.60 g (100 mmol) of ethanol, 20 ml of triethylamine, and 100 ml of diethyl ether mechanically stirred in an ice bath, 11.0 g (68 mmol) of 2-chloronorbornyl methyl ether in 20 ml of diethyl ether was added over 10 min. A thick white precipitate of triethylamine hydrochloride formed. The ice bath was removed and after 15 min 80 ml of 10% sodium carbonate was added. The ether layer was separated and washed twice with 20 ml of water. The ether was dried ($CaSO_4$), concentrated, and distilled.

When the alcohol being added was isopropyl alcohol, and particularly *tert*-butyl alcohol, a larger excess of alcohol was necessary to minimize the dehydrohalogenation product, norbornenyl methyl ether.

Distillation through a vacuum-jacketed column typically gave yields of 60–70%. Physical data for the mixed ketals is tabulated in Table II.

endo-Norbornyl isopropyl ether was collected by glpc from the hydrogenolysis reaction. *Anal.* Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.70; H, 11.62.

endo-Norbornyl *tert*-butyl ether was collected by glpc from the hydrogenolysis reaction. *Anal.* Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.39; H, 11.90.

Hydrogenolysis of Mixed Ketals.—After 0.12 g of $LiAlH_4$ had refluxed for 1 hr in 20 ml of diethyl ether, the solution was added to a solution of 1.20 g of $AlCl_3$ and 15 ml of ether in an ice bath. This yields 12.0 mmol of dichloroalane, which is stirred for 0.5 hr without the ice bath. Then 6.29 mmol of a mixed ketal (1.00 g of **1a**, 1.07 g of **1b** and **1e**, 1.16 g of **1c** and **1f**, and 1.25 g of **1d**) in 5 ml of ether was added over 5 min. After 10 min of stirring 20% NaOH was added until the ether was clear and the aluminum salts were precipitated. The products were determined by glpc and all products were collected by preparative glpc. Retention times, ir spectra, and nmr spectra were obtained for all products. A mass spectrum was obtained for the hydrogenolysis product of **1a**.

(11) S. J. Cristol, W. K. Seifert, D. W. Johnson, and J. B. Jutale, *J. Amer. Chem. Soc.*, **84**, 3918 (1962).

(12) H. C. Brown and H. R. Deck, *ibid.*, **87**, 5620 (1965).

(13) Prepared by the distillation of methanol from an acid-catalyzed trimethyl orthoformate and isopropyl alcohol mixture. Dynamitnoble A.-G., Netherlands Appl. 6,500,507; *Chem. Abstr.*, **64**, 601*g* (1966).

Registry No.—**1a**, 33016-02-3; **1b**, 33016-03-4; **1c**, 33016-04-5; **1d**, 33016-05-6; **1e**, 33068-14-3; **1f**, 33016-06-7; **6f**, 33016-07-8; **7d**, 33016-08-9; $AlCl_2H$, 13497-97-7.

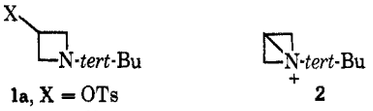
On the Mechanism of the Reaction of 1-*tert*-Butyl-3-azetidinyl Tosylate with Methanolic Potassium Cyanide and with Solvent[1]

ROBERT H. HIGGINS, FRED M. BEHLEN, DOUGLAS F. EGGLI, JAMES H. KREYMBORG, AND NORMAN H. CROMWELL*

Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68508, and Department of Chemistry, Doane College, Crete, Nebraska 68333

Received August 6, 1971

Recently Chen, *et al.*, described the synthesis[2] and some reactions[2,3] of 1-*tert*-butyl-3-azetidinyl tosylate (**1a**). Deyrup and Moyer[4] have determined the solvolysis rate of **1a** in ethanol and concluded that **1a** underwent assisted ionization, probably by transannular nitrogen participation forming intermediate **2**. A similar conclusion was drawn by Gaertner,[5] who studied the solvolysis of **1b** in 50% aqueous ethanol.



1a, X = OTs
b, X = Cl
c, X = CN
d, X = OMe
e, X = OH

2

As a continuation of our studies[6] of the reactions of functionally substituted azetidines, we have reexamined the solvolysis reactions of **1a**, since previous studies[4,5] have not clearly demonstrated the importance (or lack thereof) of direct nucleophilic attack on the substrate by solvent, nor have previous rate data been sufficiently precise for computation of activation parameters, which might be compared with those of the solvolysis reactions of cyclobutyl tosylates.

Results and Discussion

If it could be shown that the rate of the reaction of **1a** with nucleophiles, which are more nucleophilic than solvent, were independent of the concentration of nucleophile (and first order in substrate), it could safely be deduced that direct nucleophilic displacement of tosylate by the poorer nucleophile, solvent, was unimportant. Furthermore, except for a small "salt

(1) Presented in part at the 80th Annual Meeting of the Nebraska Academy of Sciences, Lincoln, Nebraska, April 1970.

(2) T.-Y. Chen, T. Sanjiki, H. Kato, and M. Ohta, *Bull. Chem. Soc. Jap.*, **40**, 2401 (1967).

(3) T.-Y. Chen, H. Kato, and M. Ohta, *ibid.*, **41**, 712 (1968).

(4) J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968).

(5) V. R. Gaertner, *J. Org. Chem.*, **35**, 3952 (1970).

(6) See, for example, (a) E. Doomes and N. H. Cromwell, *J. Heterocycl. Chem.*, **6**, 153 (1969); (b) *J. Org. Chem.*, **34**, 319 (1969); (c) R. M. Rodebaugh and N. H. Cromwell, *J. Heterocycl. Chem.*, **6**, 439 (1969); (d) **8**, 19 (1971).