Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.40; H, 4.91; N, 13.77.

1-(Phenylcarbamoyl)-L-azetidine-2-carbomorpholide (5b).—The intermediate **4b** was prepared from 220 mg (1.0 mmol) of **2b** and 206 mg (1.0 mmol) of DCC in 25 ml of CH_3CN as above. Morpholine (0.50 g) was added after 3 min. The reaction time and work-up followed the procedure for **5a**. The product was purified by preparative tlc on 1 mm silica gel PF_{254} using $CHCl_3$–HOAc (95:5) (5–7 passes) and recrystallized from CH_2Cl_2–petroleum ether, 73 mg (25% yield), mp 186–187°. After recrystallization twice from CH_2Cl_2–petroleum ether, the product had mp 188–189°; $[\alpha]^{28}D$ −201° (*c* 1.11, CH_3CN); ir (KBr) 3260 (NH), 1665, 1640 (amide C=O's), 1535 cm^{-1} (amide II).

5b was obtained in 53% yield when 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride[14] was substituted for DCC in this reaction. The crude product was recrystallized directly without prior purification by tlc after removal of the water-soluble urea: mp 186–188°, $[\alpha]^{28}D$ −197° (*c* 1.05, CH_3CN).

Anal. Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.62; N, 14.52. Found: C, 62.19; H, 6.91; N, 14.61.

1-(2,4-Dinitrophenyl)-L-azetidine-2-carboxylic Acid.—This DNP derivative of **1** was prepared in 80% yield according to the dinitrophenylation procedure of Rao and Sober,[15] and recrystallized from H_2O-saturated CH_2Cl_2–hexane, mp 119–120°.

Anal. Calcd for $C_{10}H_9N_3O_6$: C, 44.95; H, 3.40; N, 15.73. Found: C, 44.87; H, 3.26; N, 15.57.

1-(5-Dimethylaminonaphthalene-1-sulfonyl)-L-azetidine-2-carboxylic Acid, Cyclohexylammonium and Piperidinium Salts.—The dansyl derivative of **1** was prepared in the same manner as for the higher ring homologs[8] except that the free imino acid instead of the methyl ester was used. Recrystallization of the dansyl derivative from EtOH containing excess cyclohexylamine afforded the cyclohexylammonium salt in 80% yield, mp (broad) 170–181° after recrystallization from EtOH. Tlc[5] indicated that this product was homogeneous.

Anal. Calcd for $C_{22}H_{31}N_3O_4S$: C, 60.95; H, 7.21; N, 9.69. Found: C, 61.08; H, 7.02; N, 9.71.

The piperidinium salt was prepared in 89% yield by substituting piperidine for cyclohexylamine in the above procedure, and recrystallized from CH_2Cl_2–petroleum ether, mp 117–123°.

Anal. Calcd for $C_{21}H_{29}N_3O_4S$: C, 60.12; H, 6.97; N, 10.02. Found: C, 59.94; H, 7.17; N, 9.79.

Registry No.—**2b**, 32970-20-0; **3a**, 32970-21-1; **5a**, 32970-22-2; **5b**, 32970-23-3; **7a**, 32970-24-4; **7b**, 32970-25-5; 1-(2,4-dinitrophenyl)-L-azetidine-2-carboxylic acid, 32970-26-6; 1-(5-dimethylaminonaphthalene-1-sulfonyl)-L-azetidine-2-carboxylic acid, 32970-27-7 (cyclohexylammonium salt), 32970-28-8 (piperidinium salt).

Acknowledgment.—We are indebted to Mrs. O. Hamerston for the ir spectra, Miss F. N. Shirota for the nmr spectra, and Mr. J. McMahon for the mass spectra.

(14) J. C. Sheehan, J. Preston, and P. A. Cruickshank, *J. Amer. Chem. Soc.*, **87**, 2492 (1965).

(15) K. R. Rao and H. A. Sober, *J. Amer. Chem. Soc.*, **76**, 1328 (1954).

Beckmann Rearrangements of Tetrahydro-α-santonin Oximes

HARUO OGURA,* HIROAKI TAKAYANAGI, AND CHIEKO MIYAHARA

School of Pharmaceutical Sciences, Kitasato University, Shirogane, Minato-ku, Tokyo 108, Japan

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The Beckmann rearrangement[1,2] of cis- and trans-fused tetrahydro-α-santonin oximes has been carried out. Cis- and trans-fused tetrahydro-α-santonins (I) were prepared by the reported method,[3] and converted to their oximes (II) by the usual method.

The Beckmann rearrangement of *cis*-tetrahydro-α-santonin oxime (IIa) with *p*-toluenesulfonyl chloride at 50° afforded only 4-aza-*A*-homo-*cis*-tetrahydro-α-santonin (IIIa). No other isomeric products were found by tlc or by ir spectral examination of the mother liquor after separation of IIIa. This indicates that the cis-fused tetrahydro-α-santonin oxime (IIa) has the *E* configuration (anti form) (Chart I).

The oxime from *trans*-4β-tetrahydro-α-santonin oxime (IIb), mp 199–202°, showed two spots on tlc at R_f 0.36 and 0.26 (1:4 ratio). The oxime from *trans*-4α-tetrahydro-α-santonin oxime (IIc), mp 221–225°, showed two spots with the same R_f value of 0.36 and 0.26 but in a different ratio (5:1). Mixture melting point determination of these trans oximes (IIb and IIc) showed a depression. Therefore, the trans-fused tetrahydro-α-santonin oximes (IIb and IIc) are two different syn–anti mixtures, with IIb having the 4β configuration (H-4, δ 3.60 ppm) and IIc having the 4α configuration (H-4, δ 2.46 ppm).[4] This was further confirmed by the observed ratio of Beckmann rearrangement products. Although IIb and IIc did not react under the conditions described for IIIa, they did react with thionyl chloride in dioxane at 70° (Chart II).

The product of the Beckmann rearrangement of *trans*-4β-oxime (IIb) showed two spots on tlc (R_f 0.43 and 0.24, chloroform–methanol). The product from IIb was chromatographed on silica gel and yielded a 4-aza lactam (IIIb, R_f 0.43) and a 3-aza lactam (IIIc, R_f 0.24) in a ratio of 2:3. On the other hand, the Beckmann rearrangement product of *trans*-4α-oxime (IIc) gave a mixture of 4-aza lactam (IIIb) and 3-aza lactam (IIIc) in the ratio of 2:1.

The Schmidt reaction of *cis*-tetrahydro-α-santonin (Ia) produced 4-aza-*A*-homo-*cis*-tetrahydro-α-santonin (IIIa) in good yield, while *trans*-4α-tetrahydro-α-santonin (Ic) gave 4-aza-*A*-homo-*trans*-tetrahydro-α-santonin (IIIb) in 40% yield. These lactams were identical with those obtained from the Beckmann rearrangement.

The stereochemistry of the Beckmann rearrangement products (IIIa, b, and c) was confirmed by analysis of their nmr spectra. In the case of 4-aza-*A*-homo-*cis*-tetrahydro-α-santonin (IIIa), a doublet at δ 5.99 ppm (J = 4.5 Hz) could be assigned to the amide hydrogen. The angle between the amide hydrogen and H-5 should be approximately 53° (a)[5] from the Karplus equation.[6] When the amide hydrogen was irradiated, the multiplet (1 H) at 3.76 ppm changed to a double quartet ($J_{5,14}$ = 6.7 and $J_{5,6}$ = 9.0 Hz), and could therefore be attributed to the H-5. Irradiation of the H-7 at 4.36 ppm (1 H, dd, $J_{7,6}$ = 4.3 and $J_{7,8}$ = 11.0

(1) S. D. Levine, *J. Org. Chem.*, **35**, 1064 (1970).

(2) K. Oka and S. Hara, *Chem. Ind. (London)*, 168 (1969).

(3) M. Yanagita and A. Tahara, *J. Org. Chem.*, **20**, 959 (1955); M. Yanagita and H. Ogura, *ibid.*, **22**, 1092 (1957).

(4) H. Saito, I. Terasawa, M. Ohno, and K. Nukada, *J. Amer. Chem. Soc.*, **91**, 6696 (1969).

(5) In this case, a value of the vicinal coupling constant was obtained by parameters in the equations

$$J = 6.6\cos^2\phi + 2.6\sin^2\phi \quad (0° \leq \phi \leq 90°)$$
$$J = 11.6\cos^2\phi + 2.6\sin^2\phi \quad (90° \leq \phi \leq 180°)$$

[E. W. Garbish, *J. Amer. Chem. Soc.*, **86**, 5561 (1964)].

(6) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, London, 1969, p 280.

CHART I

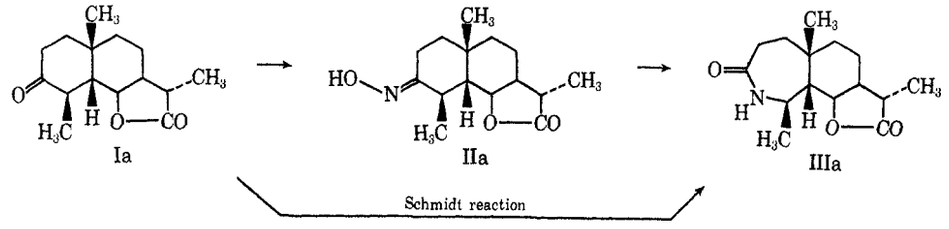


CHART II

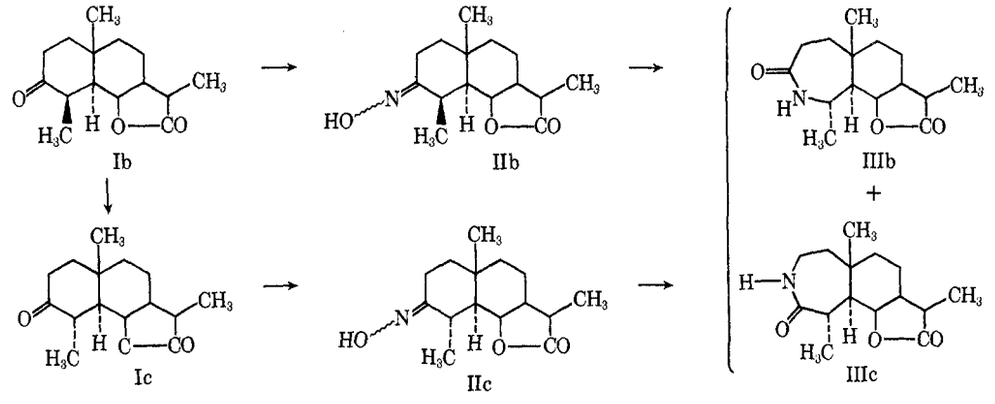
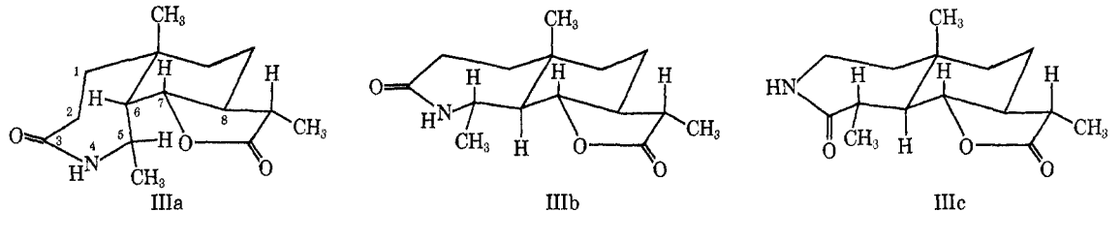
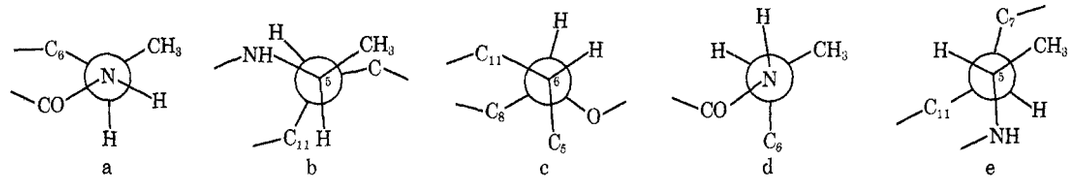


CHART III





Hz) resulted in simplification of a signal at 2.05 ppm (dd, $J_{6,7}$ = 4.3 and $J_{6,5}$ = 9.0 Hz) to a doublet (J = 9.0 Hz); hence the proton at 2.05 ppm was assigned to H-6 whose coupling to H-5 (J = 9.0 Hz) indicated a trans configuration (b). On the other hand, the value of $J_{6,7}$ = 4.3 Hz suggested a cis relationship between H-6 and H-7 (c)[6] (Chart III).

The stereochemistry of 4-aza-*A*-homo-*trans*-tetrahydro-α-santonin (IIIb) was also confirmed by nmr measurements. A doublet at 5.97 ppm (J = 4.0 Hz) was assigned to an amide hydrogen; the relationship of the amide and H-5 hydrogen is therefore as shown in d. Irradiation of the amide hydrogen changed a multiplet (2 H) at 3.75 ppm. This showed that one proton in this multiplet is H-5. Irradiation of H-5 resulted in collapse of the amide hydrogen resonance (5.97 ppm) and a methyl doublet at 1.35 ppm to singlets. Moreover, on double decoupling of the amide hydrogen (5.97 ppm) and the C-5 methyl, the band at 3.75 ppm changed to a doublet ($J_{5,6}$ = 6.5 Hz) and a double doublet (J = 7.0 and 11.5 Hz, H-7). This shows that the C-5 methyl group occupies the quasi-equatorial configuration. By analogy with the H-6,-H-7 and the H-7,H-8 splitting in the cis compound (IIIa), the splitting of 7.0 Hz was assigned to the coupling between H-6 and H-7, and the splitting of 11.0 Hz to that between H-7 and H-8. Values near 11 Hz are generally characteristic for $J_{7,8}$ in the santonin series (α-santonin 9.0 Hz, β-santonin 10.9 Hz, artemisin 11.6 Hz).[7] On the basis of these results, the conformation of N–C_5–C_6 is considered to be that shown in d and e (Chart III).

In the case of 3-aza-*A*-homo-*trans*-tetrahydro-α-santonin (IIIc), a triplet at 6.74 ppm (J = 5.3 Hz) was attributed to the amide hydrogen and a band of 2.83 ppm (multiplet) was attributed to the H-5. This was confirmed by the change in the band at 2.83 ppm on addition of deuterium oxide. When the H-5 was irradiated, a methyl doublet at 1.27 ppm (J = 7.4 Hz) changed to a singlet; decoupling at 1.27 ppm changed the band at 2.83 ppm to a doublet (J = 8.0 Hz).

Decoupling of the band at 1.57 ppm (m) in deuter-

(7) J. T. Pinhey and S. Sternhell, *Aust. J. Chem.*, **18**, 543 (1965).

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.

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Hydrogenolysis of Mixed Ketals of Norcamphor by Dichloroalane

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

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

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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).