mixture was then poured into water (100 ml) and extracted with three portions (100 ml each) of dichloromethane. The combined extracts were dried ($MgSO_4$) and concentrated at reduced pressure, leaving 1.32 g (72%) of a clear oil with spectra (ir, near ir, nmr) identical with those described for authentic 5-*exo*-methoxy-3-*exo*,*endo*-carbomethoxynortricyclene (**3d**): glpc 47:53 endo:exo.

In a control experiment, a solution of **1b** (1.53 g, 10 mmol) in methanol (10 ml) was allowed to stir at room temperature for nearly 7 days. Vacuum evaporation of the solvent left 1.45 g (95%) of product with an nmr spectrum identical with that of unreacted starting material.

Uncatalyzed Methanolysis of 1b.—A solution of **1b** (1.50 g, 10 mmol) in methanol (10 ml) was refluxed mildly over a period of 4 days. Reduced pressure evaporation of the solvent left 1.61 g of crude product found by nmr analysis to consist primarily of diene **2b** (14%), nortricyclene **3d** (72%), and unreacted **1b** (13%). The product ratios were estimated by integration of appropriate carbomethoxy proton resonances. However, owing to significant peak overlap, they may be somewhat in error.

Registry No.—**1a**, 38739-89-8; **1b**, 24161-47-5; **2a**, 38739-91-2; **2b**, 3604-36-2; *endo*-**3a**, 38739-93-4; *exo*-**3a**, 38822-43-4; *endo*-**3b**, 38822-44-5; *exo*-**3b**, 38822-45-6; *endo*-**3c**, 38822-46-7; *exo*-**3c**, 38734-70-2; *endo*-**3d**, 28298-03-5; *exo*-**3d**, 35193-30-7; bis(dimethylamino)benzophenone, 90-94-8.

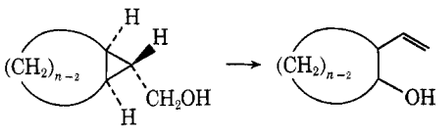
Synthesis of Cyclodec-3-en-1-ols by Acid-Catalyzed Two-Carbon Ring Expansion

RICHARD W. THIES* AND JAMES E. BILLIGMEIER

Department of Chemistry, Oregon State University, Corvallis, Oregon 97331

Received December 12, 1972

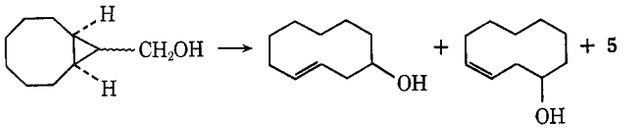
Acid-catalyzed rearrangement of bicyclo[*n*.1.0]alkyl methanols (**1**) represents an effective synthetic route to 2-vinylcycloalkanols (**2**) for certain ring sizes.[1]



1 **2**

$n = 4, 5, 6$

In an effort to use this reaction with an eight-membered ring (**3**), we discovered that the major products



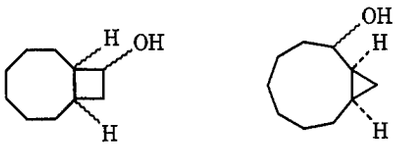
3 *trans*-**4** *cis*-**4**

of the reaction are not analogous to **2** but rather are the result of an interesting two-carbon ring expansion.[2,3] The rearrangement provides a convenient synthetic route to 3-cyclodecenols.

Compound **3** is readily prepared from cyclooctene by addition of ethyl diazoacetate followed by hydride reduction. This results in a 66:34 mixture of exo and endo isomers. Acid-catalyzed rearrangement of the mixture gave a 74:19:7 ratio of *trans*-**4**, *cis*-**4**, and **5** in an overall yield of 95%. Products *cis*-**4** and *trans*-**4** were identified by retention time comparisons of the alcohols and their trimethylsilyl derivatives and by spectral comparisons with authentic samples. The minor component (**5**) is an isomeric alcohol of unknown structure.

The isomers of **3** (*syn*-**3** and *anti*-**3**) were separated by gas chromatography and examined separately. Acid-catalyzed rearrangement of *anti*-**3** gave only the trans ring-expanded product, *trans*-**4**. Rearrangement of *syn*-**3** gave a 46:40:9:4 ratio of *trans*-**4**, *cis*-**4**, **5**, and another unknown compound.

No cyclobutanol products **6** were detected. A mixture of cyclobutanols (**6**) was prepared and coinjected



6 **7**

on gc and was found not to enhance any of the product peaks. It was also established that the cyclobutanols are stable to the acid catalysis conditions.

It should be noted that a stereospecific synthesis of *cis*-**4** or *trans*-**4** is best accomplished by the Winstein–Poulter method[4] involving stereospecific rearrangement of bicyclo[7.1.0]decan-2-ols, **7**. Although the syntheses of *cis*,*syn*- or *cis*,*anti*-**7** are lengthy, they are formed with high stereoselectivity and require no difficult separations. Although *anti*-**3** rearranges cleanly to *trans*-**4**, the synthesis of *anti*-**3** is nonselective and the separation is difficult.

The rearrangement of **3** is more useful where the stereochemistry of the double bond is not crucial, *e.g.*, in making compounds where the double bond is to be removed.[5] For those cases the sequence requires fewer steps than the Winstein–Poulter method and gives a higher overall yield (35% *vs.* 19%).

Experimental Section

Spectral measurements utilized Beckman IR-8, Varian Associates A-60 or HA-100, and Atlas CH7 instruments. Analyses were performed by Alfred Bernhardt Microanalytisches Laboratorium or Galbraith Laboratories, Analytical gas chromatography (gc) was carried out with a Wilkens Aerograph Model 1200 instrument with flame ionization detector and the 0.01-in. capillary columns listed: (A) 125 ft UCONLB550X, (B) 75 ft DEGS, (C) 100 ft Apiezon N. Samples were collected using an

(1) (a) T. L. Bond, *Tetrahedron Lett.*, 4255 (1965); (b) K. B. Wiberg and A. J. Ashe, *J. Amer. Chem. Soc.*, **90**, 63 (1968).

(2) Solvolysis of the analogous seven-membered ring dinitrobenzoate has recently been reported: K. B. Wiberg and T. Nakihara, *ibid.*, **93**, 5193 (1971).

(3) Unpublished work of E. Walton in these laboratories has shown that the analogous [5.1.0] bicyclic system does not give this two-carbon ring expansion. The syn (endo) isomers of the analogous [3.1.0] and [2.1.0] systems favor the ring expansion while the anti (exo) isomers show none of that process.[1a]

(4) S. Winstein and C. D. Poulter, *J. Amer. Chem. Soc.*, **92**, 4282 (1970), and references cited therein.

(5) Hydrogenation of the 3-cyclodecenols in ether over Adams catalyst is essentially quantitative (determined by internal glc standard).

Aerograph A90-P instrument using the 0.25-in. columns listed: (D) 10 ft, 5% KOH-5% Carbowax 4000 on Chromosorb W, (E) 10 ft, 5% UCONLB550X on Chromosorb G.

Preparation of the *cis*-Bicyclo[6.1.0]nonane-9-methanols (*syn*-3 and *anti*-3).—To 165 g (1.5 mol) of cyclooctene was added 4.0 g of anhydrous cupric sulfate. The mixture was heated and stirred at 70–80° under nitrogen while 28.5 g (0.25 mol) of ethyl diazoacetate[6] was added dropwise (*ca.* 1 hr for addition). The solution was heated and stirred at 55–60° overnight. The cupric sulfate was removed by filtration. Analysis by gc on column B at 110° showed essentially two volatile products in a ratio of 34:66.

To 140 ml of Vitride in 100 ml of dry ether was slowly added (*ca.* 2 hr) the crude reaction mixture at reflux. The mixture was allowed to cool to room temperature and stir overnight. To the crude reaction solution was added dropwise 100 ml of saturated sodium carbonate solution. The organic and aqueous layers were separated, and the organic layer was washed with two 50-ml portions of saturated sodium carbonate solution, four 50-ml portions of water, and one 50-ml portion of saturated salt solution. The organic layer was dried over anhydrous magnesium sulfate and filtered, and all of the volatile solvent was removed on a rotary evaporator. The crude, dark mixture was vacuum distilled to give 18.6 g (48.3%) of light yellow liquid, bp 96–100° (0.6 mm). Gc analysis on column C at 135° showed essentially two components in a ratio of 66:34 which were separated by gc using column D at 140°. Collection of the first component gave *anti*-3 (100% pure by gc): ir (neat) 3325, 3000, 2920, 2870, 1470, 1440, 1140, 1103, 1075, 1030, 1020 cm^{-1}; nmr (CCl_4, 100 MHz) δ 0.31–0.68 (m, 3), 0.75–2.23 (m, 13), 3.35 (d, $J = 6$ Hz, 2).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.66. Found: C, 77.72; H, 11.88.

Collection of the second peak gave 35% *anti*-3 and 65% *syn*-3. A more effective separation was obtained by converting the 66:34 *syn*- and *anti*-3 mixture to trimethylsilyl ethers and separating the mixture on column E at 115°. Hydrolysis[7] of the second gc fraction gave *syn*-3 (still contained 12% *anti*-3): ir (neat) 3375, 3000, 2920, 2870, 1470, 1440, 1160, 1145, 1105, 1090, 1015 cm^{-1}; nmr (CCl_4, 100 MHz) δ 0.57–2.30 (m, 16), 3.57 (d, $J = 7$ Hz, 2).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.66. Found: C, 77.68; H, 11.74.

The trimethylsilyl derivative was prepared by shaking for 10 min a mixture of 100 μl of **3**, 200 μl of Tri-sil,[8] and 400 μl of dimethyl sulfoxide. The mixture was extracted twice with 2-ml portions of pentane. The pentane solution was washed with 10% sulfuric acid and water and dried over sodium sulfate.

Acid-Catalyzed Rearrangement of *anti*-3.—To 0.11 g (0.73 mmol) of *anti*-3 was added 0.84 ml of 0.23 *M* perchloric acid and 4 ml of dioxane. The mixture was heated and stirred at 80° for 15 hr, whereupon all of the starting material was shown to be gone by gc on column C. To the mixture was added 30 ml of ether. The ether solution was washed with two 20-ml portions of 10% sodium carbonate, one 20-ml portion of water, and one 20-ml portion of saturated salt solution. The organic layer was dried over anhydrous magnesium sulfate and filtered, and the ether was removed on a rotary evaporator to yield 0.10 g (95%) of clear, viscous **4** (>95% pure on column C at 135°): ir (neat) 3320, 2900, 2700, 1450, 1350, 1260, 1170, 1120, 1053, 1015, 985, 860, 705 cm^{-1}; nmr (CCl_4, 100 MHz) δ 1.06–1.83 (m, 10), 1.83–2.28 (m, 3), 2.32–2.69 (m, 1), 3.21 (OH, 1), 3.73, (m, 1), 5.45 (m, 2). The ir and nmr spectra of an authentic sample of *trans*-cyclodec-3-en-1-ol and those of the major component were identical.

Further gc analysis was conducted on the trimethylsilyl ether of the reaction product (prepared as above). Analysis by gc on column A at 130° showed essentially one peak (>98%, 6.8 min). Coinjection of this major component with the trimethylsilyl derivative of *trans*-cyclodec-3-en-1-ol on two different columns gave one peak. The minor component (<2%, 10.0 min) was shown not to be the trimethylsilyl ether of *cis*-cyclodec-3-en-1-ol by coinjection with an authentic sample.

Acid-Catalyzed Rearrangement of *syn*-3.—A solution of 0.011 g of *syn*-3 (containing 12% *anti*-3), 2 ml of dioxane, and 84 μl of 0.23 *M* perchloric acid was heated at 80–85° for 20.5 hr and then worked up as described above. A portion of the reaction products was converted to trimethylsilyl derivative (as above) and analyzed on column A at 130° which showed four products in a ratio of 9:4:46:40. The latter two components were shown to be *trans*-4 and *cis*-4, respectively, by coinjection on columns A and C with authentic samples and by mass spectral comparison with these samples.

Acid-Catalyzed Rearrangement of a Mixture of *syn*-3 and *anti*-3.—To 6.5 g (0.042 mol) of **3** (66:34 mixture of *anti*-3 and *syn*-3) was added 220 ml of dioxane, 48 ml of water, and 1.6 g of 70% perchloric acid. The mixture was stirred, heated for 12 hr at 85–90°, and worked up as described above, which gave 6.2 g (95%) of products. A portion was converted to the trimethylsilyl derivative (as above) and analyzed on column A at 130° which gave four peaks in a ratio of 6:64:16:14. The first peak corresponds to the 9% unknown component observed from rearrangement of *syn*-3. The next two peaks correspond to *trans*-4 and *cis*-4; the last peak is unreacted *syn*-3 (coinjection on column A and C and mass spectral comparison).

Bicyclo[6.2.0]decan-9-ols (6).—The method of Wiberg and Nakihara[2] was used to produce bicyclo[6.2.0]decan-9-one (C=O at 1760 cm^{-1}), which was reduced with lithium aluminum hydride to give a mixture of alcohols (6): ir (neat) 3430, 2980, 2860, 1465, 1440, 1325, 1190, 1135, 1095, 1065, 870, 810 cm^{-1}; nmr (CCl_4, 100 MHz) δ 1.07–2.10 (m, 16), 3.23–4.02 (m, 1), 4.93 (s, OH).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.66. Found: C, 77.78; H, 11.82.

Analysis of the trimethylsilyl derivative of the above mixture (column A) indicated four overlapping peaks in an approximate ratio of 5:50:40:5. Coinjection of this mixture with the trimethylsilylated mixture from **3** gave no enhancement of peaks.

Registry No.—*syn*-3, 38858-51-4; *anti*-3, 38858-52-5; *trans*-4, 29971-50-4; *cis*-4, 29746-36-9; 6, 38868-39-2; cyclooctene, 931-88-4; bicyclo[6.2.0]decan-9-one, 38868-40-5.

Acknowledgment.—We thank the Research Corporation for their support of this work.

(6) E. B. Womack and A. G. Nelson, "Organic Syntheses," Collect. Vol III, Wiley, New York, N. Y., 1955, p 392.

(7) S. Friedman and M. L. Kaufman, *Anal. Chem.*, **38**, 144 (1966).

(8) Pierce Chemical Co.

Christinine, a New Epoxyguaianolide from *Stevia Serrata* Cav.

MANUEL SALMÓN,* EDUARDO DÍAZ, AND ALFREDO ORTEGA

Contribution No. 367 from the Instituto de Química de la Universidad Nacional Autónoma de México, México 20, D. F.

Received September 26, 1972

Very few sesquiterpene lactones had been isolated from *Stevia* genera.[1] We now describe the structure determination of a new guaianolide from *Stevia serrata* Cav.[2] which we have named *christinine*.

Fractionation of the methanol extract with chloroform and chromatographic separation involving silica gel and alumina yielded christinine ($C_{19}H_{24}O_7$).[3] The ion *m/e* 304 [$M^+ - (CH_3COOH)$] was observed by mass spectrometry: mp 164–165°; $[\alpha]D$ + 19.72° (*c* 3.65, $CHCl_3$); uv max (95% EtOH) 215 nm (ϵ 2270); ir ($CHCl_3$) 1775 (lactone), 1730 cm^{-1} (acetate).

* Address correspondence to author at The Johns Hopkins University School of Medicine, Department of Pharmacology and Experimental Therapeutics, Baltimore, Md. 21205.

(1) T. Ríos, A. Romo de Vivar, and J. Romo, *Tetrahedron*, **23**, 4265 (1967).

(2) We are indebted to Mr. H. Quero-Rico from the Instituto de Biología, UNAM, for the classification of the plant.

(3) Cited empirical formula was supported by satisfactory analysis and/or mass spectral molecular weight. We thank Mr. Cortés for the mass spectral data.