Cr^{II}(en) Reduction of Cholesterol α-Oxide.—To a solution of cholesterol α-oxide (100 mg) in dimethylformamide (30 ml) under purified nitrogen, Cr^{II} solution (3 ml) and ethylenediamine (0.15 ml) were added. The solution was kept at 90° for 5 hr and then poured into 2 *N* HCl (20 ml). The aqueous solution was extracted with ether (20 ml, three times) and the combined ether extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to dryness. The crystalline residue was chromatographed on silica gel with a mixture of chloroform, acetone, and ethanol (96:4:1, vol) to give 37 mg (39%) of crystals. Recrystallization of the product from ethanol gave cholesterol (23 mg).

Registry No.—**1**, 20071-52-7; **2**, 20071-53-8; **4**, 28180-56-5; **5**, 10191-01-2; **6**, 10215-89-1; **8**, 20071-51-6; **9**, 20071-54-9; **10**, 13017-11-3; **11**, 28180-62-3; **12**, 28180-63-4; **14**, 28291-99-8; **15**, 28180-64-5; **16**, 20230-31-3; **18**, 28312-59-6; **19**, 28180-66-7; styrene oxide, 96-09-3; *cis*-stilbene oxide, 1689-71-0; *trans*-stilbene oxide, 1439-07-2; 1-octene oxide, 2984-50-1; 2-*cis*-octene oxide, 23024-54-6; 2-*trans*-octene oxide, 28180-70-3; 3-*cis*-octene oxide, 28180-71-4; 3-*trans*-octene oxide, 28180-72-5; 4-*cis*-octene oxide, 1439-06-1; 4-*trans*-octene oxide, 1689-70-9.

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The Acetylation of Cyclononene

THOMAS S. CANTRELL,* JAMES M. HARLESS, AND BURT L. STRASSER[1]

Department of Chemistry, Rice University, Houston, Texas 77001

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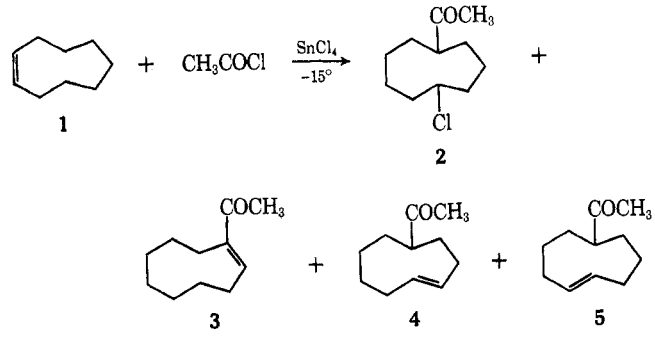
The acetylation of *cis*-cyclononene with acetyl chloride in the presence of stannic chloride yields 50–60% of 1-acetyl-5-chlorocyclononane and ~20% of 4- and 5-acetylcyclononenes, the products of 1,5-transannular hydride transfer. Use of acetic anhydride–trifluoroacetic acid gave similar results. Acetylation in the presence of active aluminum chloride led to ring contraction, with six- and seven-membered ring compounds being formed. The major (35%) product was shown to be a chloro derivative of 1-acetyl-4-isopropylcyclohexane. The other products are chlorine-bearing derivatives of 4-ethyl-1-acetylcycloheptane and, possibly, 4- or 5-methyl-1-acetylcyclooctane.

The Lewis acid catalyzed acylation of cyclic olefins and polyolefins containing seven- and eight-membered rings, including cycloheptene,[2] cycloheptatriene,[3] cyclooctene,[4,5] and 1,3- and 1,5-cyclooctadiene,[6] has been the subject of considerable recent investigation. Transannular hydride transfers were frequently observed as well as ring contraction and ring-bridging reactions. Thus, acetylation of cyclooctene in the presence of stannic chloride or added deactivated aluminum chloride gave predominantly 1-acetyl-4-chlorocyclooctane, the product of a sequence of steps which includes a 1,5-transannular hydride transfer.[5,6] When fresh, active aluminum chloride was employed, the acetylation gave a mixture of 1-acetyl-4-chloro-4-ethylcyclohexane and 1-acetyl-4-methylcycloheptane, products of ring-contraction reactions. Since of the medium rings, the nine-membered ring appears to possess the most severe transannular interactions,[7] it was considered worthwhile to extend our previous investigations to nine-membered ring olefins. We present herewith the results of our studies on the acetylation of *cis*-cyclononene.

Results

Our initial experiments were of acetylations employing acetyl chloride in the presence of stannic chloride, performed in methylene chloride as solvent. This system might, by analogy with cyclooctene, favor the formation of products resulting from transannular hydride transfer, with ring-contraction and bridging reactions being avoided. In fact, acetylation of *cis*-cyclononene (**1**) in the presence of stannic chloride in methylene chloride at −15° gave as the major product 1-acetyl-5-chlorocyclononane (**2**, 42–55%) and a mixture of 1-, 4-, and 5-acetylcyclononene (**3**, **4**, and **5**, 20–25%). The yields were erratic and depend particularly on the purity of the catalyst. Larger amounts of the unsaturated ketones **3** and **4** were obtained when stannic chloride from a freshly opened bottle was used. The structures of **2**, **3**, **4**, and **5** were assigned initially on the bases of analytical and spectral data. The mass spectrum of chloro ketone **2** showed molecular ion peaks at *m/e* 202 and 204; its infrared spectrum displayed bands for a

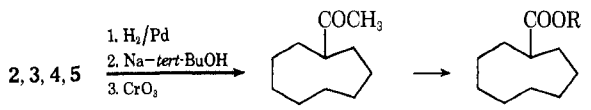


saturated ketone function at 1709 cm^{-1}. The nmr spectrum of **2** exhibited, *inter alia*, a one-hydrogen multiplet at τ 5.83 attributable to the hydrogen on the chlorine-bearing carbon (C-5) and an acetyl methyl singlet at τ 7.85; no signals in the τ 8.6–9.2 region which might be attributable to *C*-methyl groups were present. The lower boiling fraction from the acetylation of **1** showed two partially resolved peaks on several gas chromatography columns. The infrared spectrum

(1) NDEA Fellow, 1965–1968.
(2) (a) N. Jones, H. T. Taylor, and E. Rudd, *J. Chem. Soc.*, 1342 (1961); (b) L. Rand and R. J. Dolinski, *J. Org. Chem.*, **31**, 3063 (1966).
(3) J. A. Blair and C. J. Tate, *Chem. Commun.*, 1506 (1969).
(4) T. S. Cantrell, *J. Org. Chem.*, **32**, 1669 (1967).
(5) J. K. Groves and N. Jones, *J. Chem. Soc. C*, 1718 (1969).
(6) T. S. Cantrell and B. L. Strasser, *J. Org. Chem.*, **36**, 670 (1971).
(7) V. Prelog, "Perspectives in Organic Chemistry," A. R. Todd, Ed., Wiley–Interscience, New York, N. Y., 1956.

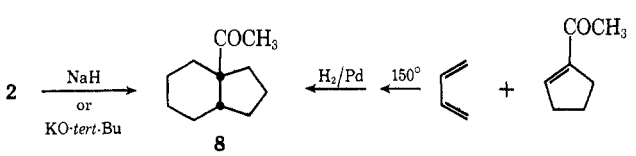
of the mixture displayed carbonyl stretching bands at 1662 and 1708 cm^{-1}; the nmr spectrum of the mixture showed vinyl hydrogen signals at τ 3.11 (hydrogen β to carbonyl) and 4.3 (unconjugated vinyl) and singlets indicative of conjugated and nonconjugated acetyl groups at τ 7.71 and 7.90. The intensities of the infrared bands suggest a **3**:**4** + **5** ratio of 55:45. The products exhibiting the 1708-cm^{-1} band are assigned structures **4** and **5** by analogy, since they are the result of pathways involving a 1,5 hydride transfer, shown to be important in acylations of cyclooctene.[5,6] In studies on cyclooctene, no 3-acetylcyclooctene was found.

That all of these compounds did possess an intact nine-membered ring was confirmed by conversion of the total reaction mixture to methyl cyclononanecarboxylate. The mixture of **2**, **3**, **4**, and **5** obtained by rapid distillation (without fractionation) of the acetylation reaction mixture was subjected to catalytic hydrogenation and was then reduced with sodium borohydride. Dechlorination of the material thus obtained, using sodium–*tert*-butyl alcohol–tetrahydrofuran, gave crude methyl cyclononylcarbinol. Oxidation with Jones reagent gave acetylcyclononane (**6**) in 41% overall yield. For positive identification the acetylcyclononane was



subsequently oxidized under haloform conditions and the crude product esterified directly with diazomethane. The methyl cyclononanecarboxylate (**7**) thus obtained was identical (ir, gc, nmr) with an authentic sample prepared from cyclodecanone according to Schenker and Prelog.[8]

The relative positions of the acetyl group and chlorine atom of **2** were established by base-effected ring closure to 1-acetylbicyclo[4.3.0]nonane (**8**), *via* intramolecular alkylation. Distillation of **2** from 1,5-diazabicyclo[5.4.0]undecene gave mainly unchanged starting material. However, treatment of **2** with sodium hydride in dimethoxyethane afforded a chlorine-free product (**8**) which showed no olefinic absorption in its infrared or nmr spectrum. The absence of signals due to cyclopropyl hydrogens in its nmr spectrum eliminated the possibility of a bicyclo[6.1.0]nonane skeleton having been formed. Compound **8** was conclusively identified as 1-acetyl-



cis-bicyclo[4.3.0]nonane by comparison with a sample prepared by an unambiguous synthesis.[9] Thus, Diels–Alder addition of butadiene to 1-acetylcyclopentene, followed by subsequent hydrogenation, gave a saturated ketone identical with the product of intramolecular alkylation of **2**. Use of potassium *tert*-butoxide as the base in the intramolecular alkylation of **2** gave a 70:30 mixture of two products, **8** and **9**. The minor component was identified as hydrindan **8** by direct comparison. The major component exhibits an infrared spectrum very similar to, but not identical with, that of **8**. The nmr spectrum of **9** shows no signals attributable to vinyl hydrogens, and the mass spectra of **8** and **9** show parent and major fragment ions of the same mass. It seems most likely that **9** is the trans-fused isomer of **8**, rather than 1-acetylbicyclo[5.2.0]nonane. One explanation for the behavior of **2** on treatment with the different bases begins with the observation that **2** appears to be a single isomer; many other processes involving transannular hydride transfer have been found to be stereospecific.[10] On treatment of **2** with sodium hydride a concerted transannular elimination is effected, producing the *cis*-hydrindan **8**. The weaker base, *tert*-butoxide, on the other hand, effects prior epimerization of **2** to a mixture of cis and trans isomers *via* a reversibly formed enolate; the cis and trans isomers of **2** undergo 1,5 elimination to give both acetylbicyclo[4.3.0]nonanes. Very recently Jones and Groves have employed potassium *tert*-butoxide to effect a similar conversion of 1-acetyl-4-chlorocyclooctane to 1-acetylbicyclo[4.2.0]octane.[11] Only the cis product was obtained; however, the trans-fused bicyclo[4.2.0]octanes are appreciably less stable than the cis isomers, whereas in the bicyclo[4.3.0]nonane series, the trans isomer is actually slightly more stable (~1 kcal).[12]

Acetylation of cyclononene with acetic acid–trifluoroacetic anhydride without additional solvent gave a mixture of acetylcyclononenes, **3**, **4**, and **5**, and an acetyltrifluoroacetoxycyclononane, presumably the 1,5 isomer. Attempted hydrolysis of the trifluoroacetoxy group afforded only the elimination product, **4**, or 5-acetylcyclononene, identical with the material obtained in the stannic chloride catalyzed acetylation of cyclononene.

Attention was then turned to acylations employing the more active catalyst, aluminum chloride, with the expectation of observing deep-seated changes in the nine-membered ring. In fact, acetylation of *cis*-cyclononene in the presence of aluminum chloride in methylene chloride at −20° gave a mixture of five products which appeared to contain (as shown by nmr) *C*-methyl groups, indicative of rings smaller than nine-membered. This mixture was not resolvable on any of wide variety of gas chromatography columns, with exception of the peak of shortest retention time, which amounted to 2% of the mixture. For determination of the carbon skeleton, a mixture of the four chlorine-containing products was subjected to a chemical degradative sequence in order to remove the chlorine atoms and convert the acetyl groups to ring ketone functions. Thus, Baeyer–Villiger oxidation followed by lithium aluminum hydride reduction gave a mixture of alcohols which was dechlorinated with sodium–*tert*-butyl alcohol. Oxidation with Jones reagent gave a mixture of cyclanones which could be separated and was found to consist of

(8) K. Schenker and V. Prelog, *Helv. Chim. Acta*, **36**, 896 (1953).

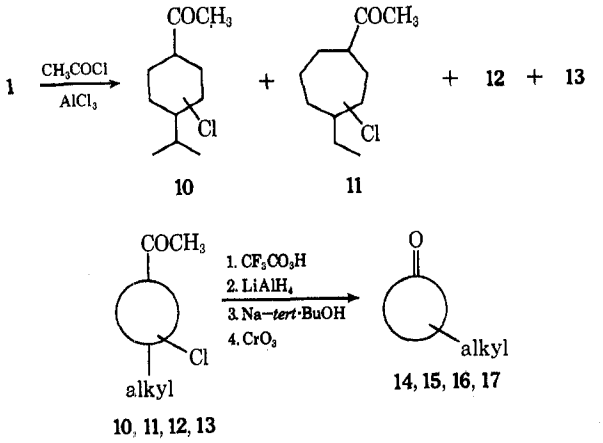
(9) R. L. Kronenthal and E. I. Becker, *J. Amer. Chem. Soc.*, **79**, 1095 (1957).

(10) See, for example, A. C. Cope, S. W. Fenton, and C. F. Spencer, *ibid.*, **74**, 5884 (1952); for further references, see J. G. Traynham and V. Prelog in "Molecular Rearrangements," Vol. I, Wiley, New York, N. Y., 1963, Chapter VIII.

(11) J. K. Groves and N. Jones, *J. Chem. Soc. C*, 2350 (1969).

(12) (a) E. L. Eliel, N. L. Allinger, H. Angyal, and H. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, pp 225–226; (b) E. L. Eliel, "The Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, pp 274–275.

4-isopropylcyclohexanone (**14**, 63%), 4-ethylcycloheptanone (**15**, 12%), and two components of unknown



structure, which may be 4- or 5-methylcyclooctanone (**16** or **17**). The first two compounds were positively identified (ir, gc, nmr) by comparison with samples prepared by unambiguous routes.[13] That neither the third nor the fourth components are cyclononanone was established by comparison with an authentic sample of that compound. The two unidentified products seem unlikely to be hydrindanones, since C-methyl absorption is present.

The acylation of cyclononene follows a course similar to that of cyclooctene, in that the milder catalyst systems such as stannic chloride lead to products resulting from 1,5-hydride transfers, albeit containing intact nine-membered rings. The stronger Lewis acid aluminum chloride induced ring contraction, with a cyclohexane derivative predominating among the products.

Experimental Section

General.—The aluminum chloride used was from a freshly opened bottle of Baker and Adamson sublimed reagent grade material, unless stated otherwise. Stannic chloride was Baker and Adamson Reagent Grade. The methylene chloride and carbon disulfide were reagent grade materials, used without further purification. Magnesium sulfate was used for all drying operations. The infrared spectra were obtained on a Beckman IR-8 instrument and the nmr spectra on a Varian A-56/60-A instrument operating at 46°. Gas chromatographic work was performed on a Varian Aerograph Model 202-1 instrument (thermal conductivity detector) utilizing the following columns: column A, 5 ft × 0.25 in. 20% SE-30 on Chromosorb P; column B, 6 ft × 0.25 in., 10% QF-1 fluorosilicone on Chromosorb W; column C, 5 ft × 0.25 in. 15% Carbowax 20M on Chromosorb P; column D, 5 ft × 0.25 in., 20% diethylene glycol succinate on Chromosorb W; column E, 10 ft × 1/8 in. Carbowax 20M on Chromosorb P; and column F, 20 ft × 1/8 in. SE-30 on Chromosorb W. Elemental analyses were performed by Elek Laboratories, Torrance, Calif.

Acetylation of *cis*-Cyclononene with Acetyl Chloride in the Presence of Stannic Chloride.—To a solution of stannic chloride (12.5 g, 0.05 mol) in methylene chloride (50 ml) was added dropwise a solution of cyclononene (6.1 g, 0.05 mol) and acetyl chloride (3.9 g, 0.05 mol) in 20 ml of methylene chloride at −25° over 0.5 hr. The reaction mixture was stirred at −15° for an additional 1 hr, allowed to warm to 0°, and then poured onto crushed ice. The organic layer was combined with an ethereal extract (40 ml) of the water layer and the combined organic phases were washed with water (three 50-ml portions), dried ($MgSO_4$), and evaporated under reduced pressure to give a yellow oil (7.9 g). Analysis of this material on column A at 175° indicated the presence of seven components. Distillation of the yellow oil gave three fractions.

Fraction A, bp 25–60° (0.3 mm) (1.8 g), appeared to be a mixture of unchanged cyclononene and chlorocyclononanes; the infrared spectrum showed bands indicative only of C–H and C–Cl bonds at 2940 and ~700 cm^{-1}.

Fraction B, bp 75–95° (0.3 mm) (2.1 g), appeared to be a mixture of **3**, **4**, and **5**, the acetylcyclononene isomers: ir (film) max 1710, 1662, and 1620 cm^{-1}; nmr (*inter alia*) (CCl_4) τ 3.10 (t, 1 H, H-2 of 3), 3.9 (2 H, m, vinyl hydrogens of 4 and 5), 7.72 and 7.90 (3 H each, s, $COCH_3$). Analysis on column E showed the presence of three components in the ratio 55:25:20. From the nmr and infrared spectra of the mixture, the conjugated ketone was the major isomer. The mixture was not sufficiently well resolved on other gc columns to allow collection of pure samples.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.52; H, 10.92. Found: C, 79.36; H, 10.63.

Fraction C, bp 96–101° (0.2 mm), was ~92% 1-acetyl-5-chlorocyclononane (**2**). A sample collected from column B exhibited ir (film) 1711 (C=O) and 665 cm^{-1} (CCl); nmr (CCl_4) τ 5.8 (1 H, pentet, $J \sim 5$ Hz, CHCl), 7.6 (1 H, broad, CHCO), 7.85 (3 H, s, $COCH_3$), and 8.3–8.7 (14 H, multiplet). Ketone **2** darkened on storage, even at 0°, and an accurate analysis could not be obtained. The compound was characterized as the semicarbazone. This derivative, obtained in the usual fashion, was recrystallized twice from ethanol to give shiny white leaflets, mp 159–160°.

Anal. Calcd for $C_{12}H_{22}ON_3Cl$: C, 55.49; H, 8.54. Found: C, 56.05; H, 8.69.

Degradation of the Cyclononene Acylation Mixture.—A reaction mixture obtained as described above, distilled once without fractionation, was employed here. The ketone mixture (5.0 g, 75% of **2** present by gc) in 75 ml of methanol was shaken with 100 mg of 10% palladium on charcoal under 15 psig of hydrogen for 3 hr; 96% of 1 molar equiv was absorbed. The catalyst was removed by filtration and washed with methanol, and the filtrates were concentrated to *ca.* 25 ml. To this solution, cooled to 10–15°, was added, with stirring, a solution of sodium borohydride (0.8 g) in methanol (30 ml) over 0.5 hr. The solution was stirred at ambient temperature for 1 hr and poured into excess ice and water, and the whole solution extracted with three 50-ml portions of ether. The ethereal extracts were combined, washed twice with saturated sodium chloride solution, dried ($MgSO_4$), and evaporated under reduced pressure to give the carbinol mixture as a faintly yellow oil (4.2 g): ir (film) 3360 (br) cm^{-1}; no carbonyl absorption was present.

The alcohol mixture thus obtained was dechlorinated by the addition of sodium (10 g, 0.43 g-atom) in small pieces to a stirred refluxing solution of the crude alcohol mixture as obtained above (6.5 g, 0.034 mol) and *tert*-butyl alcohol (100 ml) in tetrahydrofuran (400 ml). The reaction mixture was stirred and refluxed an additional 15 hr. The bulk of the solvents was removed by evaporation under reduced pressure leaving a yellow slurry which was poured into ice water. The resulting mixture was extracted with ether; the combined extracts were washed with 5% hydrochloric acid and twice with water, dried, and concentrated under reduced pressure. Distillation of the residue gave 1-cyclononylethanol (3.5 g, 58%) as a colorless oil: bp 93–95° (0.3 mm); ir (film) 3360 and 1152 cm^{-1}; analysis on column C indicated the alcohol sample to be about 91% pure.

The entire sample of 1-cyclononylethanol obtained above (3.5 g) was oxidized with Jones reagent (2.8 ml, 8 *N* in oxygen) in dry acetone at 20–30° and worked up by the usual procedure involving evaporation of solvent, treatment with water, and repeated extraction with ether. Distillation gave 3.0 g (85%) of acetylcyclononane: bp 82–85° (0.2 mm); ir (film) 1705 cm^{-1}. Analysis on column C indicated the material to be *ca.* 90% pure. A semicarbazone was prepared and recrystallized twice from ethanol to give white leaflets, mp 172°.

Anal. Calcd for $C_{12}H_{23}N_3O$: C, 63.96; H, 10.29. Found: C, 63.77; H, 10.40.

For positive identification, the ketone was oxidized to cyclononanecarboxylic acid as described below.

Haloform Oxidation of Acetylcyclononane.—To a solution of acetylcyclononane (1.6 g, 90% pure, 0.008 mol) and 20 ml of 10% sodium hydroxide in 60% aqueous dioxane (100 ml) was added dropwise 10% aqueous iodine–potassium iodide until an excess was indicated (50 ml). The reaction mixture was stirred overnight at room temperature, filtered to remove iodoform, acidfied,

(13) (a) R. L. Frank, R. E. Berry, and O. L. Shotwell, *J. Amer. Chem. Soc.*, **71**, 3889 (1949); (b) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

and extracted with three 40-ml portions of ether. The combined ether extracts were washed with 20% sodium thiosulfate solution and with water, dried, and concentrated to give 0.94 g of crude cyclononanecarboxylic acid; ir (film) 3400–2900 (broad) and 1702 cm^{-1}. Analysis on columns A and B showed only one peak. This material was esterified directly by treatment at 0° with ethereal diazomethane prepared from *N*-nitrosomethylurea (10 g). After the solution had been stirred overnight at room temperature, the ether was evaporated and the residue distilled to give methyl cyclononanecarboxylate: bp 90° (0.3 mm); ir (film) 1736, 1250 cm^{-1}. The infrared and nmr spectra, as well as gc retention times on columns A and B, were identical with those of an authentic sample prepared from cyclodecanone (bromination followed by Favorskii rearrangement) as previously described.[8]

Intramolecular Alkylation of 1-Acetyl-5-chlorocyclononane (2) with Sodium Hydride. Preparation of *cis*-1-Acetylbicyclo[4.3.0]nonane.—To a cold (0°) suspension of sodium hydride (0.8 g of a 52% dispersion in mineral oil) in dry dimethoxyethane (100 ml) under nitrogen was added a solution of chloro ketone **2** (2.0 g, 0.01 mol) in dry dimethoxyethane (40 ml). The solution was stirred for 1.5 hr while warming to room temperature and was then poured into water. The resulting mixture was extracted with ether (three 30-ml portions); the ether extracts were washed with saturated sodium chloride solution, dried, and concentrated to give an orange oil (1.1 g) which showed on column D at 148° three small peaks of short retention time which appeared to possess the same retention times as the impurities in the sample of **2** used. The major peak (retention time 4.2 min, 75% of total area) was collected and identified as 1-acetylbicyclo[4.3.0]nonane: ir (film) 1705 cm^{-1}; nmr (CCl_4) τ 7.91 (3 H, s, CH_3CO) and 8.2–8.8 (15 H, multiplets); mass spectrum: *m/e* (parent) 166. The infrared and nmr spectra were identical with those of an authentic sample (*vide infra*).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 16.92. Found: C, 79.19; H, 10.93.

Intramolecular Alkylation of 1-Acetyl-5-chlorocyclononane (2) with Potassium *tert*-Butoxide. Preparation of 8 and 9.—To a solution of potassium (0.40 g) in dry *tert*-butyl alcohol (50 ml) was added a solution of **2** (0.62 g, 90% pure) in *tert*-butyl alcohol. The reaction mixture was stirred and refluxed for 1 hr under nitrogen and was then concentrated under reduced pressure; water was added to the residue and the resulting suspension was extracted with ether (three 30-ml portions). The ether extracts were washed three times with water, dried, and concentrated to give an orange oil which was distilled to give 0.29 g of colorless oil: bp 55–65° (bath) (0.2 mm); ir (film) 1704 cm^{-1}. Analysis on column C at 145° indicated the material to be a 70:30 mixture of two components: the major component, of shorter retention time, was collected from this column and exhibited the following spectral parameters: ir (film) 1704 cm^{-1}; nmr (CCl_4) τ 8.02 (3 H, s, CH_3CO) and 8.2–8.8 (15 H, m); no signals at 2–6; mass spectral parent peak at 166.

The minor peak was collected and found to be identical with the ketone **8** obtained using sodium hydride as base.

The infrared spectrum of ketone **9** was very similar to that of **8** but exhibited definite differences. It seems likely that **9** is the trans-fused 1-acetylbicyclo[4.3.0]nonane.

Preparation of Authentic 8.—The cis-fused ketone **8** was prepared according to a modified procedure of Kronenthal and Becker. A mixture of butadiene (24 g, 0.44 mol) and 1-acetylcyclopentene[14] (11 g, 0.10 mol) and hydroquinone (0.5 g) was placed in a steel tube and heated to 170–180° for 12 hr. Rapid distillation of the black residue gave 6.8 g, bp 55–60° (0.5 mm), of crude product, in addition to a large amount of black tar. Fractionation of the crude product through a helice-packed column gave 1-acetyl-*cis*-bicyclo[4.3.0]non-3-ene: bp 52–54° (0.5 mm); ir (film) 1705 cm^{-1}. The 2,4-dinitrophenylhydrazone crystallized from ethanol as orange flakes, mp 131–132° (lit.[8] mp 130–131°).

A solution of the above ketone (1.8 g) in 95% ethanol (100 ml) was shaken with 10% palladium on charcoal under 2 atm of hydrogen pressure until uptake had ceased (15 min). Filtration of the catalyst, evaporation of the solvent, and distillation of the residue gave authentic 1-acetyl-*cis*-bicyclo[4.3.0]nonane (**8**), bp 52–55° (0.5 mm). This sample showed ir and nmr spectra identical with those of the sample obtained by intramolecular alkylation of **2** (*vide supra*).

Acylation of *cis*-Cyclononene with Trifluoroacetic Anhydride–Acetic Acid.—To a mixture of trifluoroacetic anhydride (3.5 g) and acetic acid (1.0 g) was added dropwise cyclononene (2.0 g) over 15 min at 25–28°, according to the procedure of Henne and Tedder.[15] The dark brown solution was stirred at this temperature for an additional 1.5 hr, poured into ice water, and worked up in the manner described for previous acylations to give 3.7 g of a yellow oil. Analysis on column A indicated this material to be composed of two major components and three minor ones, the latter comprising *ca.* 12% of the total area. Fractional distillation of the oil through a Vigreux column gave first 89% pure 5- (or 6-) acetylcyclononene (**4** or **5**) as a colorless liquid, bp 68–74° (0.6 mm); the infrared spectrum of this material was essentially identical with that of the sample obtained in the acetylation of **1** using stannic chloride. A second fractionation, bp 100–130° (0.5 mm), appeared to be, on the basis of gc analysis on column A, a 1:4 mixture of **4** or **5** and an isomer of acetyltrifluoroacetoxycyclononane, probably the 1,5 isomer. The infrared spectrum of the mixture showed bands at 1760, 1708, and 1245 cm^{-1}; the nmr spectrum exhibited signals at τ 5.8 (1 H, m, $-CHOOCCF_3$), 7.3 (1 H, m CHCOR), and 7.6–8.9 (16 H, m).

Acetylation of Cyclononene Using Aluminum Chloride.—Aluminum chloride (from a freshly opened bottle of sublimed reagent grade material, 13.5 g, 0.1 mol) was added to methylene chloride and acetyl chloride (7.8 g, 0.1 mol) and swirled at 0°. The solution was decanted from the insoluble solid and cooled to −15 to −20°. To the stirred solution at this temperature was added dropwise a solution of cyclononene (11.2 g, 0.10 mol) in methylene chloride (100 ml) over 20 min. The solution was allowed to warm to 0° and was then poured onto crushed ice. The organic layer was separated and the aqueous layer extracted once with methylene chloride (50 ml). The combined organic layers were washed with water (three 50-ml portions), dried ($MgSO_4$), and concentrated. The residual liquid was distilled to give the product mixture as an almost colorless liquid, bp 85–100 (0.5 mm) (9.7 g, 56%). Attempts at analysis by gc were inconclusive due to decomposition of the chloro compounds at the temperatures required. Analysis on column A showed the presence of five poorly resolved components. The reaction was repeated, using aluminum chloride from a bottle which had been opened and exposed to the air several weeks previously. The composition of the reaction mixture was very similar, with the exception that the smallest peak (*ca.* 3% of total area) was absent.

Degradation of the Aluminum Chloride Produced Acetylation Mixture.—Sodium (10 g, 0.43 g-atom) was added in small pieces to a stirred, refluxing mixture of the aluminum chloride produced acetylation mixture, obtained as described above (8.7 g, 0.042 mol), *tert*-butyl alcohol (90 ml), and tetrahydrofuran (200 ml). The reaction mixture was stirred and refluxed for 24 hr and the bulk of the solvent was evaporated. The residue was poured into an ice–water slurry and the resulting suspension extracted with ether (four 50-ml portions). The combined extracts were washed with 2% hydrochloric acid and with water, dried, and concentrated. Distillation of the residue gave 4.7 g (64%) of a chlorine-free (negative Beilstein test) oil, bp 86–98° (1.0 mm), whose infrared spectrum indicated it to be composed of alcohols (relative intensities of bands at *ca.* 1710 and 3500 cm^{-1}). This mixture, dissolved in reagent grade acetone (30 ml), was treated with Jones reagent (8 *N* in oxygen, 3 ml) at room temperature over 40 min. After being stirred at room temperature for an additional 2 hr, the solvent was evaporated under reduced pressure and the residue treated with water. Repeated ether extraction of the resulting mixture, followed by washing of the extracts with 5% sodium bicarbonate and with water, drying, and concentration, gave a ketone mixture which was used directly in the Baeyer–Villiger reaction. A solution of the ketone mixture obtained above (4.3 g), disodium phosphate (25 g), and methylene chloride (100 ml) was treated dropwise with trifluoroperacetic acid (from 1 g of 90% hydrogen peroxide and 7 g of trifluoroacetic anhydride in cold methylene chloride) and then stirred and refluxed for an additional 1 hr. The salts were filtered and washed twice with methylene chloride; the combined filtrates were dried and evaporated. The residue was distilled to give the acetate mixture as a faintly yellow oil: bp 78–95° (1.0 mm); infrared absorption at 1708 and 1730 cm^{-1} indicated the acetate mixture contained *ca.* 10% unchanged ketone. The product was treated with Girard's reagent T (0.8 g) by the standard procedure. The acetate mixture recovered from this treatment was ketone

(14) N. Jones and H. T. Taylor, *J. Chem. Soc.*, 4017 (1959).

(15) A. L. Henne and J. M. Tedder, *ibid.*, 3628 (1953).

free as shown by the absence of infrared absorption maxima or shoulders at 1700–1720 cm^{-1}.

A solution of the acetate mixture obtained above (4.0 g) in ether (40 ml) was added dropwise to a stirred suspension of lithium aluminum hydride (0.8 g) in ether (50 ml); after completion of the addition, the reaction mixture was refluxed 2 hr more. The reaction mixture was cooled and treated slowly with water (0.7 ml), 15% sodium hydroxide (1.0 ml), and water (3 ml), and stirred for 1 hr. The white salts were filtered and washed well with ether; the combined filtrates were dried and concentrated to give the mixture of ring alcohols and as a colorless, slightly cloudy oil (1.2 g); ir (film) 3450–3500 cm^{-1}.

The mixture of ring alcohols (1.2 g) in reagent grade acetone (30 ml) was treated with Jones reagent (1.3 ml, 8 *N* in oxygen at 25–30° and stirred at ambient temperature for 5 hr. Evaporation of the solvent, treatment with water, and extraction as usual gave, after evaporation of the solvent and distillation, 0.82 g (16% overall) of colorless liquid, ir (film) 1712 cm^{-1}. This mixture of ring ketones showed four peaks on column E at 170°. The retention times of these and the per cent of total peak area represented by each are (a) 5.5 (63%); (b) 6.5 (12%); (c) 7.4 (16%); and (d) 8.3 min (9%). Peaks a and b were collected from column C, on which they were partially resolved. Rechromatography on column A afforded first 4-isopropylcyclohexanone, identical (ir, gc on two columns, mixture melting point of 2,4-DNP) with material prepared from authentic 4-isopropylphenol by a hydrogenation–oxidation sequence. Peak b was identical with a sample of 4-ethylcycloheptanone prepared by ring expansion with diazomethane of authentic 4-ethylcyclohexanone. Peaks c and d both exhibited gc retention times which were significantly different from that of authentic cyclononanone and of 4-*n*-propylcyclohexanone. It seems most likely that at least one of these compounds is 4- or 5-methylcyclooctanone; however, samples of these isomers were not available for comparison.

Registry No.—**2**, 27921-40-0; 2 semicarbazone, 27921-41-1; **3**, 27921-42-2; **4**, 27921-43-3; **5**, 27921-44-4; *cis*-cyclononene, 933-21-1; acetylcyclononane, 19207-40-0; acetylcyclononane semicarbazone, 27921-46-6.

Acid-Catalyzed Cyclization of 4-(2,6,6-Trimethylcyclohexenyl)-2-methylbutanal. X-Ray Structure Analysis of the Major Product

GABRIEL SAUCY*

Chemical Research Department, Hoffmann-La Roche Incorporated, Nutley, New Jersey 07110

ROBERT E. IRELAND,[1] JON BORDNER, AND RICHARD E. DICKERSON

Contribution No. 4052 from the Norman W. Church Laboratories of Chemical Biology, California Institute of Technology, Pasadena, California 91109

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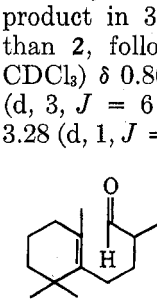
The cyclization of 4-(2,6,6-trimethylcyclohexenyl)-2-methylbutanal (luciferin aldehyde) with phosphoric acid has been found to give (±)-1,2,3,4,4a,7,8,8a-octahydro-2α,4aβ,5,8aβ-tetramethylnaphthalen-1β-ol as the major product. The structure and stereochemistry of this bicyclic alcohol, the formation of which involves an interesting Wagner–Meerwein rearrangement, was established by X-ray analysis of the 4-bromobenzoate derivative. The alcohol is probably identical with a product obtained (cyclization and degradation) from β-monocyclofarnesic acid by Kitahara, *et al.*

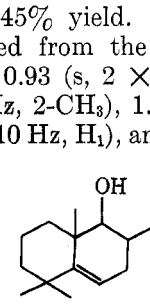
Some time ago, we became interested in the cyclization of the aldehyde **1** which is readily available from the "β-C_{14}-aldehyde"[2] by partial hydrogenation with palladium on charcoal in acetone solution. The same aldehyde (**1**, "luciferin aldehyde") has recently been obtained[3] upon hydrolysis of luciferin, which is the enol formate derived from **1**, and by subsequent synthesis[4,5] from dihydro-β-ionone. It was hoped that the aldehyde **1** might cyclize to give the bicyclic alcohol **2**, thus offering a new approach to the preparation of certain sesqui- and higher terpenoids. A precedent for this type of reaction is the well-known cyclization of citronellal, which affords isopulegol.[6]

Results

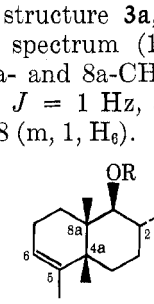
Upon mixing the aldehyde **1** with 85% phosphoric acid, a solid mass was produced in an exothermic reaction. After alkaline work-up and crystallization, the bicyclic alcohol **3a** was obtained as the major product in 35–45% yield. The structure **3a**, rather than **2**, followed from the nmr spectrum (100 mc, $CDCl_3$) δ 0.86, 0.93 (s, 2 × 3, 4a- and 8a-CH_3), 0.94 (d, 3, J = 6 Hz, 2-CH_3), 1.60 (t, J = 1 Hz, 5-CH_3), 3.28 (d, 1, J = 10 Hz, H_1), and 5.38 (m, 1, H_6).



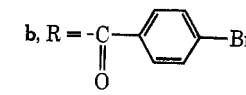
1



2



3a, R = H

b, R = 

In order to assign the stereochemistry unambiguously, the alcohol **3a** was converted into its 4-bromobenzoate **3b** and the latter subjected to single crystal X-ray structure analysis. As a result, proof for the relative stereochemistry shown in formula **3a** was obtained. A product with the same structure and "tentative" relative stereochemistry was recently described by Kitahara, Kato, and Kanno.[7] These authors obtained **3a** *via* its acetate by lead tetraacetate oxidation of the bicyclic acid **6**. The latter was formed as a

(1) The portion of this work carried out at the California Institute of Technology was made possible by a grant from the Hoffmann-La Roche Foundation, and this support is gratefully acknowledged.

(2) Intermediate of the technical synthesis of vitamin A; *cf.* O. Isler, W. Huber, A. Ronco, and M. Kofler, *Helv. Chim. Acta*, **30**, 1911 (1947).

(3) O. Shimomura and F. H. Johnson, *Biochemistry*, **7**, 1734 (1968).

(4) M. G. Fracheboud, O. Shimomura, R. K. Hill, and F. H. Johnson, *Tetrahedron Lett.*, 3951 (1969).

(5) F. Nakatsubo, Y. Kishi, and T. Goto, *ibid.*, 381 (1970).

(6) A. R. Pinder, "The Chemistry of the Terpenes," Wiley, New York, N. Y., 1960, p 38.

(7) Y. Kitahara, T. Kato, and S. Kanno, *J. Chem. Soc. C*, 2397 (1968).