CHART I

$$\begin{tikzcd}
\mathrm{I\,(R = H)}^{9a} \arrow[r, "Br_2", "(68\%)"'] & \mathrm{I\,(R = Br)}^{a} \arrow[r, "CH_2{=}CHBr", "{AlBr_3,\ -60^\circ\ (40\%)}"'] & \mathrm{I\,(R = CH_2CHBr_2)} \arrow[d, "{NaOH\ (HOCH_2CH_2)_2O^{b}}", "(95\%)"'] \\
\mathrm{II} \arrow[r, "AlCl_3", "(92.5\%)"'] & \mathrm{I\,(R = C_2H_5)} & \mathrm{I\,(R = C{\equiv}CH)} \arrow[l, "H_2"', "(79\%)"]
\end{tikzcd}$$

[a] H. Koch and J. Franken, *Ber.*, **96**, 213 (1963). [b] Following H. Stetter and P. Goebel, *ibid.*, **95**, 1039 (1962).

pounds.[8,9,15] Other tricyclic sesquiterpenes besides cedrene will likely serve as well as starting materials for the preparation of I (R = C_2H_5).

Experimental Section

Rearrangement of Dihydrocedrene (II) to 1-Ethyl-3,5,7-trimethyladamantane (I, R = C_2H_5).—Cedrene, $[\alpha]^{22}D$ −84.6° (CCl_4) (Aldrich Chemical Co.), was hydrogenated in acetic acid solution with PtO_2 to give dihydrocedrene (II), $[\alpha]^{22}D$ −6.2°.[12] The product showed only one peak on gas chromatography, using a 300-ft capillary column coated with SE-30. To 37 g of II, 18.5 g of powdered $AlCl_3$ was added, and the mixture stirred at room temperature. After 48 hr, gas chromatography showed that the starting material had completely disappeared and five new components had formed. One of these comprised *ca.* 75% of the mixture. The rearrangement was continued for an additional 24 hr at 50°. Analysis now showed that the major component was present in *ca.* a 25-fold excess over a single, second compound. The liquid was decanted from the catalyst and the latter was washed with several portions of petroleum ether (bp 30–60°). The combined organic material was washed with water and then with sodium bicarbonate solution, and dried over anhydrous magnesium sulfate. Distillation yielded 34.2 g (92.5%) of material, homogeneous to gas chromatography, with bp 108.5–110.5° at 12 mm, $n^{21}D$ 1.4841, $[\alpha]^{22}D$ −0.03° (neat). Naves, *et al.*,[12] starting with "artificial" cedrene, $[\alpha]D$ −86.3°, prepared dihydrocedrene, $[\alpha]D$ −6.2°, and rearranged this to "isodihydrocedrene," bp 90–92° at 1.6 mm, $n^{20}D$ 1.4831, $[\alpha]D$ −0.52°. The small, residual optical rotations are probably due to optically active impurities.

Anal. Calcd for $C_{15}H_{24}$: C, 87.38; H, 12.62. Found: C, 87.65; H, 12.60.

The structure of the compound was established by analysis of the mass and nmr spectra, in comparison with the behavior of polyalkyladamantanes of known composition. The base peak in the mass spectrum at *m/e* 177 represented loss of the ethyl group. A peak at *m/e* 191 (loss of methyl) was also prominent (16% of base). The parent peak itself at *m/e* 206 was only present in 0.5% abundance. Other peaks with greater than 10% abundance were at *m/e* 121 (45%), 107 (20%), 55 (16%), and 41 (27%). The base peaks of 1-alkyladamantanes are also those formed by loss of the substituent, ethyl groups being lost more readily than methyl.[16] 1-Ethyl-3-methyladamantane and 1-ethyl-3,5-dimethyladamantane gave mass spectral peaks representing parent, loss of methyl, and loss of ethyl in the ratio 3:1:30 for the former compound, and 1:1:10 for the latter.[9a] The similar ratios found here for I (R = C_2H_5) were 0.03:1:6.3 and for 1-ethyl-3,5-dimethyladamantane were 0.12:1:17.5 under similar instrumental conditions.

The nmr spectrum of I (R = C_2H_5) would be expected to be similar to the two-peak spectrum of tetramethyladamantane, I (R = CH_3), which has methyl resonances at τ 9.20 and methylene resonances at τ 8.99.[17] The two major nmr peaks of I (R = C_2H_5) had almost the same chemical shifts (τ 8.99 and 9.19), but, as anticipated, the area of the methylene proton peak was greater. The ethyl group appeared as a rather diffuse multiplet; this feature was also expected, since ethyladamantane derivatives showed A_2B_3 and not simple A_2X_3 patterns.[9]

1-Bromo-3,5,7-trimethyladamantane (I, R = Br).—1,3,5-Trimethyladamantane I (R = H) was brominated after the literature procedure.[18a] From 7.5 g of I (R = H) 7.9 g (68%) of I (R = Br), mp 100.5–101.5°, was obtained: lit.[18a] mp 101–102°.

1-(2′,2′-Dibromoethyl)-3,5,7-trimethyladamantane (I, R = CH_2CHBr_2).—The procedure used was based on similar reactions described for adamantyl bromide.[18b] I (R = Br), 7.0 g, in 15 ml of vinyl bromide was cooled to −60° in a Dry Ice–acetone bath. A total of 3.0 g of aluminum bromide was added carefully. After 3 hr the suspension was poured intoa beaker containing 30 ml of ether and 30 ml of water. The organic layer was separated and the aqueous layer extracted with several portions of ether. The combined ether layers were washed with water, saturated sodium carbonate, and water, and dried over calcium chloride. Distillation yielded 4.0 g (40%) of I (R = CH_2CHBr_2), bp 130–135° at 0.5 mm.

Anal. Calcd for $C_{15}H_{24}Br_2$: C, 49.45; H, 6.59; Br, 43.96. Found: C, 49.71; H, 6.68; Br, 43.52.

The nmr showed a triplet centered at τ 4.20 (-C*H*Br_2), a doublet at τ 7.46 (side chain CH_2), two singlets at τ 8.80 and τ 8.94 for the two types of ring CH_2 groups, and a singlet at τ 9.17 for the methyl groups. The peak area ratios were 1:2:6:6:9, as expected for I (R = CH_2CHBr_2).

1-Ethynyl-3,5,7-trimethyladamantane (I, R = HC≡C).—The dehydrohalogenation of 3.0 g of I (R = CH_2CHBr_2) was carried out in a refluxing solution of 3 g of sodium hydroxide in 15 ml of diethylene glycol.[18b] After 12-hr reaction time, 30 ml of water was added and the organic material was extracted with petroleum ether. The organic material was washed twice with water and dried over calcium chloride. Distillation gave 1.6 g of I (R = HC≡C), bp *ca.* 90–29° at 10 mm. The nmr spectrum showed a singlet ethynyl resonance at τ 8.11, two CH_2 singlets at τ 8.56 and τ 8.94, and a methyl singlet at τ 9.17. The area ratio was 1:6:6:9. An infrared spectrum of the compound showed strong ≡C—H absorption at 3307 cm^{-1} and a -C≡C- peak of moderate intensity at 2100 cm^{-1}. This was hydrogenated directly.

1-Ethyl-3,5,7-trimethyladamantane (I, R = C_2H_5).—Using palladium on charcoal as catalyst, 1.5 g of I (R = HC≡C) was hydrogenated for 8 hr in ether solvent. After filtration of the catalyst, distillation gave 1.2 g (79%) of I (R = C_2H_5), bp *ca.* 94–95° at 10 mm. A careful comparison established the identity of this material with that prepared from II by rearrangement. Both materials had identical infrared and nmr spectra, and both eluted on the capillary gas chromatograph with the same retention time, singly or when mixed together.

Acknowledgments.—We wish to thank the National Science Foundation and the Donors of the Petroleum Research Fund, administrated by the American Chemical Society, for support of this research. Dr. Abraham Schneider kindly supplied information in advance of publication and provided us with reference hydrocarbons. Dr. Koert Gerzon supplied a generous sample of trimethyladamantane used in this research. The mass spectrum was run in the laboratories of the Union Carbide Corporation, courtesy of Dr. Donald Heywood.

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(15) A methyl-substituted perhydroanthracene has also been shown to rearrange to 1-ethyl-3,5,7-trimethyladamantane.[9b]

(16) Z. Dolejšek, S. Hála, V. Hanuš, and S. Landa, *Collection Czech. Chem. Commun.*, in press.

(17) R. C. Fort, Jr., and P. von R. Schleyer, *J. Org. Chem.*, **30**, 789 (1965).

(18) See Chart I: (a) ref *a*; (b) ref *b*.

Steroids. V. 2β-Carboxy-A-norcholestane[1]

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Received November 9, 1965

The subject of this Note is the synthesis of 2β-carboxy-A-norcholestane (**5**) and several of its transformation products, and the presentation of evidence in support of the stereochemistry of acid **5**.

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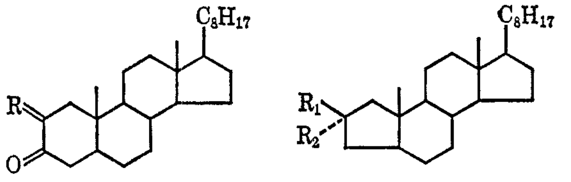
(1) Part IV of this series: M. P. Cava and B. R. Vogt, *J. Org. Chem.*, **30**, 3775 (1965).

(2) Department of Chemistry, Wayne State University, Detroit, Mich. 48202.

A 2-carbomethoxy-A-norcholestane and a 2-carboxy-A-norcholestane have been obtained as Favorskii rearrangement products of 2α-bromocholestan-3-one; these compounds were assigned the 2α configuration (structures **1** and **2**, respectively) (Chart I) on the basis of mechanistic considerations.[3]

CHART I



4, R = NOH
3, R = N_2

1, R_1 = H; R_2 = CO_2CH_3
2, R_1 = H; R_2 = CO_2H
8, R_1 = H; R_2 = CH_2OH
6, R_1 = CO_2CH_3; R_2 = H
5, R_1 = CO_2H; R_2 = H
7, R_1 = CH_2OH; R_2 = H

We have now investigated the photochemical Wolff rearrangement of 2-diazocholestan-3-one (**3**). Hydration of the ketene formed in the latter reaction was expected to take place from the less hindered α side of the molecule, giving 2β-carboxy-A-norcholestane (**5**).

The previously unreported 2-diazocholestan-3-one (**3**) was obtained by the action of chloramine on 2-oximinocholestan-3-one (**4**).[4] Photolysis of an aqueous tetrahydrofuran solution of diazo ketone **3** afforded 2β-carboxy-A-norcholestane (**5**); acid **5** was further characterized by reaction with diazomethane to give the corresponding methyl ester (**6**), and by lithium aluminum hydride reduction to give the corresponding primary alcohol (**7**).

In Table I the melting points and specific rotations ($[\alpha]_D$) of the new 2β-substituted A-norcholestanes (**5**, **6**, and **7**) are contrasted with the available data for the analogous 2α-substituted compounds (**2**, **1**, and **8**).[3]

TABLE I

PHYSICAL CONSTANTS OF 2-SUBSTITUTED A-NORCHOLESTANES

Compd	Mp, °C	$[\alpha]_D$, deg	C-19 chemical shift, τ CDCl$_3$	C-19 chemical shift, τ C$_6$H$_6$
α-Acid (**2**)	173.5–175.5[a]			
β-Acid (**5**)	186–188[a]	+13		
α-Ester (**1**)	97.5–98[b]	+29	9.30	9.33
β-Ester (**6**)	103–105[b]	+8	9.29	9.19
α-Alcohol (**8**)	118–118.5	+32		
β-Alcohol (**7**)	144–146	+29		

[a] Mixture melting point with epimer, 139–163°. [b] Mixture melting point with epimer, 68–75°.

A comparison of the nmr spectra of the epimeric esters **6** and **1** in both deuteriochloroform and benzene solution proved particularly interesting, and afforded supporting evidence for the assigned configurations at C-2. Thus, the chemical shift of the C-19 methyl protons of the β-ester **6** appear only very slightly downfield (0.01 ppm) relative to those of the α ester **1** in $CDCl_3$ solution; the same protons in **6** appear considerably further downfield (0.14 ppm) relative to those in **1** in C_6H_6 solution. This type of relative deshielding of a methyl *cis* to a nearby ester function in an aromatic solvent has ample analogy.[5]

Experimental Section[6]

2-Oximinocholestan-3-one (**4**).—This compound was prepared according to Sheehan and Erman[4] in 53–63% yield: mp 268–270° after crystallization from tetrahydrofuran (lit.[4] mp 205–207°); spectral properties, λ_{max} 3.18, 5.82, 6.18 μ, λ_{max}^{neut} 235 mμ (ϵ 8,200), λ_{max}^{basic} 310 μ (ϵ 16,000).[6] Complex formation was observed with the following metal ions: Ni^{2+} (yellow-brown), Co^{2+} (orange-red), Cu^{2+} (grass green). Both the formation of metal complexes and the bathochromic ultraviolet shift in base indicate the *anti* configuration of the oximino ketone function in **4**.[7] This oximino ketone was reported previously[4] as a crude reaction intermediate without analytical characterization. Its elemental analysis is, therefore, given below.

Anal. Calcd for $C_{27}H_{45}NO_2$: C, 78.02; H, 10.91; N, 3.37. Found: C, 78.18; H, 10.97; N, 3.07.

2-Diazocholestan-3-one (**3**).—A stirred suspension of 2-oximinocholestan-3-one (**4**) (1.05 g) in a mixture of tetrahydrofuran (10 ml), 5 *N* aqueous sodium hydroxide (20 ml), concentrated ammonium hydroxide (30 ml), and ether (300 ml) was cooled to 3–5°. Twelve 10-ml portions of 5.25% sodium hypochlorite solution ("Clorox") were added at 10-min intervals. The solution was stirred at room temperature for an additional 4 hr and then worked up in the usual manner.[7] The resulting yellow oil was chromatographed on neutral alumina (chloroform eluent), and crystallized from ether to yield diazo ketone **3** (0.45 g, 43%) as yellow-orange needles: mp 102–104°; spectral properties, λ_{max} 4.80, 6.19, 6.51 μ; $[\alpha]^{23}D$ + 33° (*c* 1.55).

Anal. Calcd for $C_{27}H_{44}N_2O$: C, 78.58; H, 10.75; N, 6.79. Found: C, 78.56; H, 10.76; N, 6.70.

2β-Carboxy-A-norcholestane (**5**).—A solution of 2-diazocholestan-3-one (**3**) (1.29 g) in a mixture of tetrahydrofuran (200 ml) and water (10 ml) was irradiated (N_2 atmosphere) for 20 min with a 450-w Hanovia L679A high-pressure mercury vapor lamp. Evaporation of the solution and trituration of the resulting solid with acetone afforded crude acid **5** (0.58 g, 45%). The pure acid, mp 195–196°, was obtained by recrystallization from acetone: spectral properties, λ_{max} 3.81, 5.89 μ; $[\alpha]^{22}D$ +12.8° (*c* 0.30).

Anal. Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.35; H, 11.37.

2β-Carbomethoxy-A-norcholestane (**6**).—Acid **5** (0.27 g) was added to an excess of ethereal diazomethane. Dilution of the ether with methanol, followed by slow concentration of the solvent, yielded crystalline ester **6** (0.15 g, 56%). The pure ester, mp 102-103°, was obtained by recrystallization from ether–methanol: spectral properties, λ_{max} 5.78 μ; $[\alpha]^{22}D$ +7.6° (*c* 0.48).

Anal. Calcd for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 81.09; H, 11.64.

2β-Hydroxymethyl-A-norcholestane (**7**).—Acid **5** (0.249 g) was added to a slurry of lithium aluminum hydride (0.7 g) in ether (25 ml). After 1.5 hr, the excess hydride was decomposed cautiously by water, and the neutral reduction product was worked up in the usual manner. Crystallization of the crude product from ether–95% methanol afforded flat white needles of **7** (0.229 g, 95%), mp 139-142°. The analytical sample, mp 142–144°, was crystallized from the same solvent: spectral properties, λ_{max} 3.00 μ; $[\alpha]^{22}D$ +28.9° (*c* 0.40).

Anal. Calcd for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.41; H, 12.49.

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(3) B. B. Smith and H. R. Nace, *J. Am. Chem. Soc.*, **76**, 6119 (1954); D. E. Evans, A. C. de Paulet, C. W. Shoppee, and F. Winternitz, *J. Chem. Soc.*, 1451 (1957); J. Beillmann and M. Rajia, *Bull. Soc. Chim. France*, 441 (1962); H. M. Hellman and R. A. Jerussi, *Tetrahedron*, **20**, 741 (1964).

(4) J. C. Sheehan and W. F. Erman, *J. Am. Chem. Soc.*, **79**, 6050 (1957).

(5) P. S. Wharton and T. I. Bair, *J. Org. Chem.*, **30**, 1681 (1965). See also D. H. Williams, *Tetrahedron Letters*, 2305 (1965).

(6) Melting points are uncorrected. Ultraviolet spectra, infrared spectra, and optical rotations were determined in dioxane, potassium bromide, and chloroform, respectively, except that the ultraviolet spectrum of **4** was determined in ethanol. The basic spectrum of **4** was obtained by the addition of 1 drop of 0.1 *N* aqueous sodium hydroxide to the neutral solution.

(7) M. P. Cava and P. M. Weintraub, *Steroids*, **2**, 41 (1964).

Acknowledgment.—This investigation was supported by Public Health Service Research Grants CY-4498 and CA-04498, National Institutes of Health. The authors wish also to thank Dr. R. A. Jerussi of the Worcester Foundation for Experimental Biology and Dr. R. Scribner of E. I. du Pont de Nemours and Company for generous samples of authentic 2α-substituted A-norcholestanes.

Four-Membered Rings by the Acyloin Condensation. A Peculiar Result in Liquid Ammonia[1,2]

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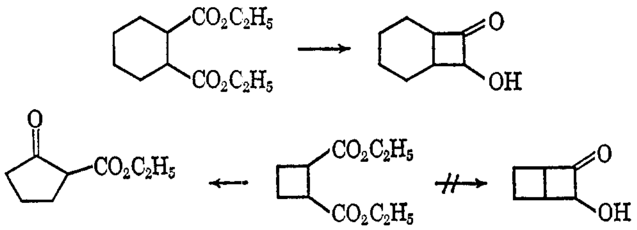
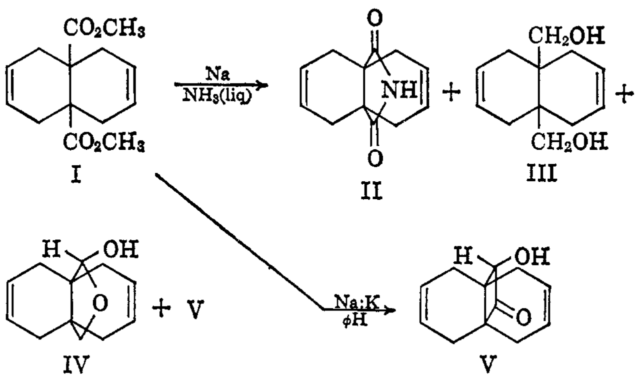
There is only one published account of the successful application of the acyloin condensation to the synthesis of a four-membered ring.[3] In that example, the cyclization of *cis*-1,2-dicarbethoxycyclohexane, the yield was 12%. In a similar attempt to cyclize *cis*-1,2-dicarbethoxycyclobutane the only identifiable product was 2-carbethoxycyclopentanone.[4]



In the course of developing a method for the introduction of a 9,10-ethano bridge into the decalin ring system we have investigated the acyloin condensation of dimethyl $\Delta^{2,6}$-hexalin-9,10-dicarboxylate, I (Chart I). When the condensation was conducted in liquid ammonia a mixture of products consisting of the cyclic imide, II (35.6%), the diol, III (21.1%), the hemiacetal, IV (6.4%), and the desired acyloin, V (10.1%) was obtained.

Although there are examples of the failure of the acyloin condensation or of competition with the Dieckmann condensation under the conditions described above[5] there are no clear examples of the formation of any products such as II, III, or IV in such a reaction. In one case,[6] an unsuccessful attempt to cyclize to a seven-membered ring in a steroid derivative, there is a suggestion that a very small amount of diol may have been formed as a side product. The imide apparently arises through an ammonolysis reaction. The hemiacetal is a logical intermediate in the formation of the diol, in what appears to be a kind of Bouveault–Blanc reduction with ammonia serving as the proton source.

Chart I



We have been able to successfully cyclize the diester in good yield when a 1:1 sodium–potassium alloy is used in refluxing benzene or xylene.[7] Sodium in refluxing toluene failed to effect cyclization.

Table I

Effect of Metal–Diester Mole Ratio on Yield of Acyloin

Diester[a]	Mole ratio Na	K	Solvent	Yield, %[b]
1 (0.05)	4.0	. . .	Toluene	c
1 (0.05)	6.1	3.6	Xylene	26[d]
1 (0.10)	7.65	4.46	Xylene	32[d]
1 (0.5)	3.07	1.84	Benzene	39[e]
1 (0.4)	3.84	2.32	Benzene	. .[f]
1 (0.3)	3.95	2.30	Benzene	61[e]
1 (0.24)	4.42	2.54	Benzene	57[e]
1 (0.10)	5.05	2.97	Benzene	70[g]
1 (0.4)	5.60	3.15	Benzene	76[g]
1 (0.3)	5.97	3.32	Benzene	70[g]
1 (0.10)	6.69	4.11	Benzene	71[g]

[a] The parenthetical number is the actual number of moles of ester used. [b] Recrystallized product free of diester by thin layer chromatography. [c] 61% of starting material recovered. No acyloin observed. [d] The crude yields were 77 and 87% for the smaller and larger runs, respectively, but the product was contaminated by unreacted diester. [e] The product contained diester. The yield is based on starting diester although considerable quantities of diester and additional acyloin were recovered by combining the residues of several runs. [f] A crude yield of 89% was obtained. The entire amount was used, however, in a subsequent reaction and a substantial amount of diester was recovered. [g] Crude yields of 91.2–93.7% were obtained. The tabular figure represents the yield after one recrystallization without attempt to work up mother liquors. The combined mother liquors from several runs were mined for additional product. That no ester was present in the *crude* product was indicated by thin layer chromatography.

The results of several runs with varying mole ratios of ester to metals are tabulated below. It appears that the amount of sodium is the critical factor and that an excess of sodium over the theoretical 4 g-atoms/mole of ester is necessary.

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[1] The work described in this paper was supported by National Science Foundation Grants GP-260 and GP-4439.

[2] Presented at the 54th Annual Meeting of the Oklahoma Academy of Science, Stillwater, Okla., Dec 3, 1965, and before the Division of Organic Chemistry at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, Abstracts, p K23.

[3] A. C. Cope and E. C. Herrick, *J. Am. Chem. Soc.*, **72**, 983 (1950).

[4] J. J. Bloomfield, R. G. Todd, and L. T. Takahashi, *J. Org. Chem.*, **28**, 1474 (1963).

[5] See the review by K. T. Finley, *Chem. Rev.*, **64**, 573 (1964).

[6] N. A. Nelson and R. N. Schut, *J. Am. Chem. Soc.*, **80**, 6630 (1958).

[7] The use of the alloy was suggested by the work of Ya. L. Goldfarb, S. Z. Taits, and L. I. Belen'kii, *Tetrahedron*, **19**, 1851 (1963).