The Dehydration of Some Triterpenoid Epoxides with Pyridinium Chloride. A Method for the Conversion of Tetrasubstituted Triterpenoid Olefins into Unrearranged Dienes

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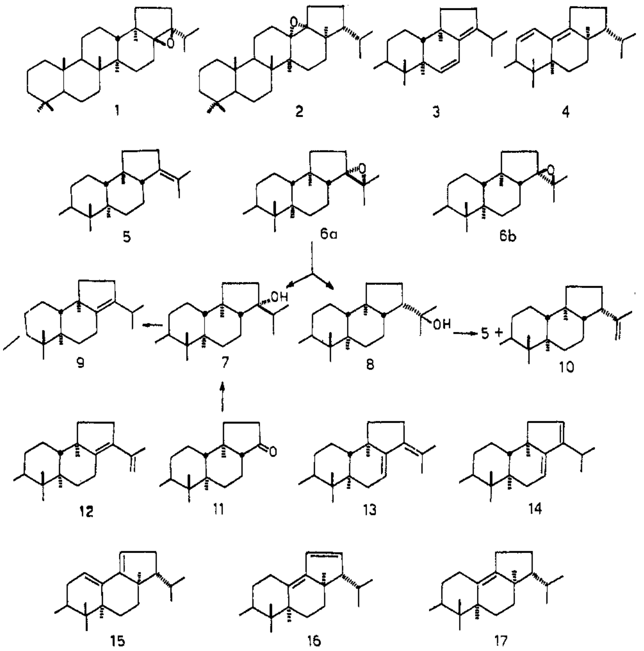
Whereas, on treatment with hydrochloric acid in ethanol, 17,21β-epoxy-A′-neogammacerane (1) and 21,22-epoxy-A′-neogammaceranes 6a and 6b afford A′-neogammacera-15,17(21)-diene (3) and 13,18α-epoxy-B′:A′-neogammacerane (2) gives B′:A′-neogammacera-11,13(18)-diene (4), different results were obtained in the dehydration of the same epoxides with pyridinium chloride. In this reaction the following dienes were isolated: from 1, A′-neogammacera-16,21-diene (13), 3, and A′-neogammacera-16,20-diene (14); from 2, B′:A′-neogammacera-12,18-diene (15), 4, and B′:A′-neogammacera-13(18),19-diene (16); from 6, A′-neogammacera-17(21),22-(29)-diene (12).

17,21β-Epoxy-A′-neogammacerane (**1**)[1] and 13,18α-epoxy-B′:A′-neogammacerane (**2**), when treated with hot ethanolic hydrochloric acid, afford, respectively, A′-neogammacera-15,17(21)-diene (**3**)[2] and B′:A′-neogammacera-11,13(18)-diene (**4**).[3] More extensive rearrangements take place when boron trifluoride is used as the isomerizing agent.[4]

Since the dienes **3** and **4** could conceivably have been formed by further rearrangement of isomeric diene intermediates under the action of the acid, the present work was undertaken in order to find milder dehydration conditions that would permit isolation of the primary dienes. Pyridinium chloride proved to be a fairly good reagent for this purpose.

Results

Treatment of A′-neogammacer-21-ene (hopene a, **5**)[5] with *p*-nitroperoxybenzoic acid resulted in formation of a 33:67 mixture of two epoxides, which were separated by column chromatography. The α configuration **6a** was attributed to the minor component on the following evidence. It is known that epoxidation of steroid and triterpene olefins is usually sensitive to steric hindrance.[6] Dreiding models show that the double bond in **5** is more hindered on the α side, because of the presence of the α-methyl group at C-18; thus, attack by the peroxy acid on the β side should be more favored. Therefore the β oxide should form preferentially to the α one **6a**. This assumption was confirmed by treating the two epoxides with lithium aluminum hydride; whereas the major component did not react even in boiling tetrahydrofuran, the other one was smoothly reduced to give mainly 21α-hydroxy-A′-neogammacerane (**7**), formed by hydride attack on C-22, accompanied by a small amount of a second alcohol. Although the latter one could not be identified by tlc or glpc, it certainly was 22-hydroxy-A′-neogammacerane (**8**),[5,7] since dehydration of the crude mixture of alcohols gave, beside A′-neogammacer-17(21)-ene (hopene I, **9**)[8] and **5**, a small amount of **10**. It is known that **8** gives about a 75:25 mixture of **5** and **10** on dehydration.[5,7b] Compound **7** was also obtained on treatment of bisnoradiantone (**11**)[9] with isopropylmagnesium bromide; attack by the Grignard reagent should be more favored on the less hindered β side of **11**. Treatment of the resulting alcohol with phosphorus oxychloride gave the olefin **9**, containing only a trace of **5**, in agreement with a *trans* arrangement of the hydroxyl group at C-21 (α) and the hydrogen atom at C-17 (β).



Whereas **6a** and **6b**, on treatment with hydrochloric acid in ethanol solution at reflux temperature, afforded exclusively the diene **3**, when the same epoxides were heated in pyridine containing pyridinium chloride, the unrearranged diene **12** was formed as the sole product. The structure of this compound was confirmed (see Experimental Section) by ir, uv, and nmr and easy hydrogenation to **9**. Treatment of **12** with hydrochloric acid in ethanol resulted in quantitative conversion into the diene **3**.

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(1) For the nomenclature of triterpenes, see S. Allard and G. Ourisson, *Tetrahedron*, **1**, 277 (1957).

(2) G. Berti, F. Bottari, A. Marsili, and I. Morelli, *Tetrahedron Lett.*, 979 (1966).

(3) Y. Tsuda and K. Isobe, *ibid.*, 3337 (1965).

(4) G. Berti, F. Bottari, A. Marsili, I. Morelli, and A. Mandelbaum, *ibid.*, 529 (1968).

(5) R. E. Corbett and H. Young, *J. Chem. Soc., C*, 1556 (1966).

(6) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 292.

(7) (a) H. Ageta, K. Iwata, and Y. Ôtake, *Chem. Pharm. Bull.* (Tokyo), **11**, 407 (1963); (b) W. J. Dunstan, H. Fazakerley, T. G. Halsall, and E. R. H. Jones, *Croat. Chem. Acta*, **29**, 173 (1957).

(8) H. Fazakerley, T. G. Halsall, and E. R. H. Jones, *J. Chem. Soc.*, 1877 (1959).

(9) G. Berti, F. Bottari, A. Marsili, J. M. Lehn, P. Witz, and G. Ourisson, *Tetrahedron Lett.*, 1283 (1963).

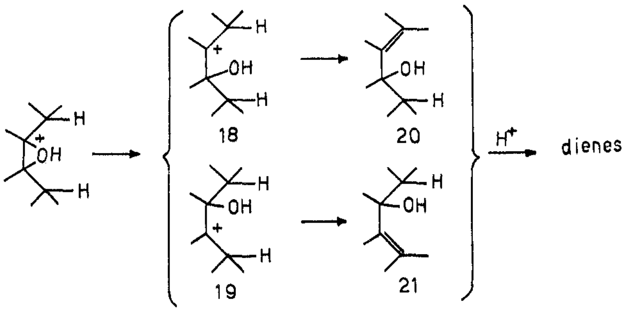
Heating of the epoxide **1** with pyridinium chloride led to a mixture containing three dienes, one of which was identical with **3**. The relative amounts of these dienes, as determined by glpc, depended upon heating times, the reaction mixture containing after 30 min 26, 27, and 47% and after 7 hr 47, 17, and 36% of compounds **3**, **13**, and **14**, respectively. Separation was effected by fractional crystallizations and chromatography over silica gel impregnated with silver nitrate. Structures **13** and **14** were attributed to the two unknown dienes mainly on the basis of their nmr (one olefinic hydrogen and two allylic methyl groups in **13**; two olefinic hydrogens in **14**) and uv spectra; moreover, ozonization of **13** afforded acetone. Treatment of the two dienes with hydrochloric acid in boiling ethanol caused transformation into the diene **3**. Whereas **14**, on catalytic hydrogenation, gave **9** (1,4 addition), from **13** a complex mixture containing at least two saturated hydrocarbons and an olefin was formed. Glpc analysis showed that the latter was **9**; one of the saturated hydrocarbons was 21βH-A′-neogammacerane (hopane)[5,10] and the other one its 21 epimer (moretane);[5,10] and a fourth component was not identified.

The epoxide **2** also afforded three dienes on treatment with pyridinium chloride. One of these was identified as **4**, its relative amount increasing with reaction time. Structures **15** and **16** were assigned to the other two dienes on the following grounds. The nmr spectrum of **15** shows two olefinic hydrogens and its uv spectrum is very similar to that of cholesta-7,14-diene,[11] whose chromophore is analogous to that present in **15**. Moreover, an adduct was obtained by heating this compound with maleic anhydride. Signals attributable to two olefinic hydrogens (AB part of an ABX system) are present in the nmr spectrum of **16**, whose uv spectrum is typical of a heteroannular diene.[12] Both **15** and **16** gave, on hydrogenation, B′:A′-neogammacer-13(18)-ene (hopene II, **17**)[8] and diene **4** on treatment with hydrochloric acid in ethanol.

Discussion

The above reported results constitute, in our opinion, a fairly good proof that dehydrations of the hindered epoxy neogammaceranes **1** to give **3** and **2** to give **4**, by action of acids in solvents of low basicity are, at least in part, stepwise reactions. Moreover, the conversion of **6** into **3** must be completely stepwise. Yet, when the reactions were carried out in boiling ethanol, owing to the low basicity of the solvent, isolation of any other compound except the rearranged dienes **3** and **4** was never possible. Only the use of pyridinium chloride and a strongly basic solvent such as pyridine also permitted isolation, from epoxides **1**, **2**, and **6**, of dienes in which migration of the double bonds to the most stable positions had not yet occurred.

Clearly, the first step of the reaction is protonation of the epoxide oxygen; opening of the three-membered ring may then occur from either of the two carbon-oxygen bonds, to give ions **18** and **19**.



The formation of unrearranged dienes in a basic solvent may be due to two facts: (1) the base shortens the life of cations **18** and **19** by rapidly extracting a proton, to give the allylic alcohols **20** and **21**, which dehydrate very easily; and (2) it makes more difficult the protonation of the unrearranged dienes **12**, **13**, **14**, and **15**, a necessary step for their conversion into the more stable ones.

Since dehydration of **1** and **2** with pyridinium chloride yields, besides the unrearranged, also the rearranged dienes **3** and **4**, the possibility exists that their formation may occur, at least in part, by a concerted process. Indeed, in the dehydration of **1** the amount of **3** formed shows a relatively small increase with time. However, we believe that in all cases the processes leading from **1** to **2** and from **3** to **4** are completely nonconcerted.

The case of **2** is also interesting because the rearranged, but not the most stable diene **16** is isolable from the reaction mixture obtained after treatment of the epoxide with pyridinium chloride. Moreover, **16** was obtained, together with **4**, by chromatography of diene **15** over silica gel. This indicates that rearrangement of **15** may occur from each side of the conjugated system, but only when the reaction medium is not strongly acidic is it possible to isolate **16**, since rapid protonation of the compound by action of mineral acids in solvents of low basicity leads to complete conversion into **4**.

Experimental Section

Melting points were determined with a Kofler apparatus and are uncorrected. Ir spectra were recorded on Nujol mulls with a Perkin-Elmer Infracord, Model 137 spectrophotometer. Uv spectra were determined in cyclohexane solutions with a Beckman DU spectrophotometer. Nmr spectra were registered in deuteriochloroform solutions (tetramethylsilane as internal standard) at 60 MHz with a Varian DA-60-IL spectrometer. Specific rotations were measured in 1% chloroform solutions at 25° with a Perkin-Elmer, Model 141, photoelectric polarimeter. Glpc analyses were performed with a Carlo Erba Fractovap, Model G.V. Columns were 1% neopentyl glycol succinate (NPGS) on Chromosorb W 80–100 mesh, temp 220°, injection block temp 250°, carrier gas nitrogen, flow rate 65 ml/min; 3% SE-52 silicone rubber on Chromosorb W 80–100 mesh, temp 250°, injection block temp 270°, carrier gas nitrogen, flow rate 50 ml/min. Petroluem ether refers to the fraction of boiling range 30–60°. *Isolated in the usual way* means that the mixture was diluted with water, extracted with ether or with petroleum ether; the extract was washed with 2 *N* sulfuric acid and 2 *N* sodium carbonate, dried ($MgSO_4$), and evaporated. The residue, dissolved in petroleum ether, was chromatographed over neutral alumina (Fluka, grade II–III).

Silica gel impregnated with silver nitrate (SiO_2–$AgNO_3$) was prepared by adding silica gel for adsorption chromatography (Woelm, grade I, 150 g) to a solution of silver nitrate (15 g) in water (15 ml) and ethanol (200 ml). After 15 min of continued stirring the solvent was evaporated at reduced pressure and the residue dried at 120°; during all operations the material was protected from light. Comparison between compounds were made on the basis of mixture melting points, ir spectra, and glpc

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[10] (a) Y. Tsuda, K. Isobe, S. Fukushima, H. Ageta, and K. Iwata, *Tetrahedron Lett.*, 23 (1967); (b) M. N. Galbraith, C. J. Miller, J. W. L. Rawson, E. Ritchie, J. S. Shannon, and W. C. Taylor, *Aust. J. Chem.*, **18**, 226 (1965).

[11] D. H. R. Barton, *J. Chem. Soc.*, 512 (1946).

[12] L. Dorfman, *Chem. Rev.*, **53**, 47 (1953).

retention times. 22-Hydroxy-A′-neogammacerane (**8**) was obtained from *Cyathea manniana* Hook[13] or by reaction of adiantone[9] with methyl magnesium iodide.

Dehydration of 8 to A′-Neogammacer-21-ene (5) and A′-Neogammacer-22(29)-ene (10).—The alcohol **8** (3.35 g) was dissolved in pyridine (35 ml) containing phosphorus oxychloride (4.7 ml) and the mixture was heated on a steam bath for 2.5 hr. The mixed olefins were isolated in the usual way; these (3.05 g) were dissolved in petroleum ether and chromatographed over SiO_2–$AgNO_3$ (350 g, 2.8 × 92 cm column). Petroleum ether (1600 ml) eluted **5** (2.30 g) which, after crystallization from chloroform–methanol, gave needles: mp 193–196°; $[\alpha]_D$ +30°; nmr δ 1.57 (3 H, s) and 1.70 (3 H, s) ppm (lit.[5] mp 178–180°).

Anal. Calcd for $C_{30}H_{50}$: C, 87.73; H, 12.27. Found: C, 87.56; H, 12.45.

Elution was continued with benzene (400 ml) to obtain **10** (0.70 g), mp 207–210° (prisms, from chloroform–methanol); $[\alpha]_D$ +62° (lit.[14] mp 210–211°; $[\alpha]_D$ +61°).

21,22α-Epoxy-A′-neogammacerane (6a) and 21,22β-Epoxy-A′-neogammacerane (6b).—The olefin **5** (0.40 g) was dissolved in chloroform (25 ml) and treated at 5°, under stirring, with 98% *p*-nitroperoxybenzoic acid (0.22 g). After 10 min the mixture was filtered and the filtrate was washed with 2 *N* sodium hydroxide and water, dried ($MgSO_4$), and evaporated. The residue (0.39 g) was chromatographed over neutral alumina (Fluka, grade II–III, 100 g, 1.8 × 37 cm column), using petroleum ether as eluent and collecting 50-ml fractions. Fractions 31–32 contained **6a** (0.12 g) which, after crystallization from petroleum ether gave plates: mp 225–228°; $[\alpha]_D$ −5.3°.

Anal. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.20; H, 11.76.

Fractions 33–35 contained mixtures of **6a** and **6b** (25 mg) and fractions 36–38 pure **6b** (0.24 g): mp 233–236° (prisms, from petroleum ether); $[\alpha]_D$ +50°.

Anal. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.70; H, 11.60.

Structure Proof of 6a.—A mixture of **6a** (50 mg) and lithium aluminum hydride (0.18 g) in anhydrous ether (20 ml) was refluxed for 8 hr. Excess hydride was decomposed with water and the filtered ethereal solution, on evaporation, afforded a residue (35 mg), whose ir spectrum was only slightly different from that of **7**. Attempts to analyze this mixture (as trimethylsilyl ethers) by glpc failed, since dehydration to **9**, **5**, and **10** occurred. Thus, the mixture was dissolved in pyridine (3 ml) containing phosphorus oxychloride (0.5 ml) and heated for 2 hr on a steam bath. The composition (glpc, SE-52 column) of the mixed olefins so obtained (20 mg), isolated in the usual way, was 95% of **9** and 5% of **5** + **10** (these have equal retention times). The ir spectrum of the mixture showed a weak band at 11.25 μ, typical of **10**. This product can be formed only by dehydration of **8**, present in a very small amount in the reduction mixture. Except for this band, the spectrum was superimposable on that of **9**.

When **6b** was heated with lithium aluminum hydride in ether or in tetrahydrofuran for 15 hr, no reduction was observed.

21α-Hydroxy-A′-neogammacerane (7).—Bisnoradiantone[9] (0.12 g) was treated with an excess of isopropylmagnesium bromide in ethereal solution and the mixture was refluxed for 8 hr. After hydrolysis with ammonium chloride the ethereal layer was dried ($MgSO_4$) and evaporated to give **7** (90 mg), which was crystallized twice from chloroform–methanol to give plates: mp 285–293° dec; $[\alpha]_D$ +33°.

Anal. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.23. Found: C, 83.75; H, 12.00.

Dehydration of 7.—The above product (25 mg) was heated for 2 hr on a steam bath with pyridine (4 ml) containing phosphorus oxychloride (0.4 ml). The dehydration mixture (15 mg), isolated in the usual way, consisted (glpc, SE-52 column) of 97% of **9** and 3% of **5**. No band at 11.25 μ was present in the ir spectrum.

Treatment of 6 with Hydrochloric Acid.—The mixed epoxides (50 mg) were refluxed for 1 hr with ethanol (50 ml) containing 36% hydrochloric acid (5 ml). Diene **3** (40 mg) was isolated in the usual way: mp 154–157° (plates, from chloroform–methanol); $[\alpha]_D$ +81° (lit.[2] mp 155–157°; $[\alpha]_D$ +80°).

Treatment of the Various Epoxides with Pyridinium Chloride.—The epoxide (1 part by weight) was dissolved in a 0.35 *M* solution of pyridinium chloride in pyridine (100 parts by volume) and the mixture was refluxed for the given time. The reaction product was isolated in the usual way. Dienes were rapidly eluted by petroleum ether; unreacted epoxide (if present) was recovered by eluting with ether.

(a) **Epoxides 6a and/or 6b.**—Reflux time was 3 hr. Diene **12** (90% yield) was purified by crystallization from chloroform–methanol: plates, mp 183–185°; $[\alpha]_D$ +57°; uv, λ_{max} (ϵ) 241 (15,400), 249 (15,600), 257 (9,600, sh) nm; ir λ(>C=CH$_2$) 6.11, 11.15 μ; nmr δ 1.81 (3 H, m), 4.72 (2 H, m) ppm.

Anal. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84. Found: C, 88.33; H, 12.05.

(b) **17,21β-Epoxy-A′-neogammacerane** (**1**).[2,3]—Reflux of 0.5 hr gave, from 70 mg of **1**, 35 mg of dienes (26% of **3**, 27% of **13**, 47% of **14**, by glpc), recovered oxide 30 mg; 2.5 hr gave, from 200 mg of **1**, 180 mg of dienes (32% of **3**, 21% of **13**, 47% of **14**), recovered oxide 10 mg; 7 hr gave, from 70 mg of **1**, 60 mg of dienes (47% of **3**, 17% of **13**, 36% of **14**). Retention times relative to cholestane: **3**, 2.26; **14**, 3.16; **13**, 4.73 (NPGS); **3**, 1.71; **14**, 2.03; **13**, 2.66 (SE 52).

(c) **13,18α-Epoxy-B′:A′-neogammacerane** (**2**).[3]—It was not possible to analyze the mixed dienes by glpc, since only one peak was obtained, having the same retention time as that of **4**, possibly owing to low thermal stabilities of **15** and **16**. Qualitative information about the composition was obtained by measuring the rotations of the mixtures (diene **15** has a negative, dienes **16** and **4** have positive rotations). Reflux time 0.25 hr: from 600 mg of **2**, 200 mg of dienes, $[\alpha]_D$ −69°, recovered oxide 370 mg; 1.5 hr: from 200 mg of **2**, 190 mg of dienes, $[\alpha]_D$ −20°; 4 hr: from 200 mg of **2**, 180 mg of dienes, $[\alpha]_D$ +34°. Retention time relative to cholestane, 2.16 (SE-52).

Separation of A′-Neogammacera-15,17(21)-diene (3) and A′-Neogammacera-16,20-diene (14).—A mixture (0.40 g) containing 30% of **3**, 22% of **13** and 48% of **14** was chromatographed over SiO_2–$AgNO_3$ (180 g, 1.8 × 65 cm column) using petroleum ether as eluent and collecting 50-ml fractions. Fractions 11–13 contained pure **3** (0.10 g); 14–19 mixtures of **3**, **13** and **14**; 20–23 mixtures of **3** and **14**. From 24–33 pure **14** was obtained (0.13 g): mp 193–196° (plates, from chloroform–methanol); $[\alpha]_D$ +44.7°; uv, λ_{max} (ϵ), 242 (12,700) nm; nmr δ 5.34 (2 H, m) ppm.

Anal. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84. Found: C, 88.43; H, 12.10.

Separation of A′-Neogammacera-16,21-diene (13).—The mixed dienes (0.5 g, 31% of **3**, 24% of **13**, 45% of **14**) were fractionally crystallized from acetone, the compositions of the various fractions being checked up by glpc. A fraction (45 mg) containing 81% of **13**, was recrystallized from chloroform–methanol to obtain pure **13** as needles: mp 188–191°; $[\alpha]_D$ −134°; uv, λ_{max} (ϵ), 244 (13,300) nm; nmr δ 1.68 (3 H, m), 1.85 (3 H, m), 5.43 (1 H, m) ppm.

Anal. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84. Found: C, 88.40; H, 11.99.

Ozonization of 13.—Ozonized oxygen was bubbled for 45 min at 0° through a solution of **13** (60 mg) in sulfuric acid washed pentane (50 ml). The solvent was evaporated at 20° under reduced pressure and the residue, dissolved in acetic acid (30 ml), was steam distilled into a solution of 2,4-dinitrophenylhydrazine (7 ml).[15] The precipitate which formed (10 mg) was identified as acetone 2,4-dinitrophenylhydrazone, mp 124–126°.

Separation of B′:A′-Neogammacera-11,13(18)-diene (4) and B′:A′-Neogammacera-13(18),19-diene (16).—The mixture (0.40 g) obtained by 4-hr reflux of **2** with pyridinium chloride was chromatographed over SiO_2–$AgNO_3$ (180 g, 1.8 × 65 cm column). Petroleum ether (1750 ml) eluted **4** (0.30 g): mp 210–213° (plates, from chloroform–methanol); $[\alpha]_D$ +31.5° (lit.[3] mp 213–215°). Benzene (750 ml) eluted **16** (70 mg): mp 212–215° (plates, from chloroform–methanol); $[\alpha]_D$ +145°; uv, λ_{max} (ϵ), 248 (18,200), 255 (21,500), 264 (15,800) nm; nmr, AB part of an ABX system, centered at δ 6.06 ppm, J_{AB} = 6 cps.

Anal. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84. Found: C, 88.30; H, 11.99.

Separation of B′:A′-Neogammacera-12,18-diene (15).—The mixed dienes (0.2 g) obtained by 0.25-hr reflux of **2** with pyridinium chloride, were fractionally crystallized from chloroform–methanol. Two fractions (35 and 55 mg) having, respectively, $[\alpha]_D$ −128° and −120° were combined and recrystallized from chloroform–methanol to give pure **15** as prisms: mp 164–167°;

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[13] Unpublished results from this laboratory.

[14] H. Ageta, K. Iwata, and S. Natori, *Tetrahedron Lett.*, 3413 (1964).

[15] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, John Wiley & Sons, New York, N. Y., 1956, p 219.

$[\alpha]_D$ −129°; uv, λ_{max} (ϵ), 247 (11,800), 255 (13,100), 264 (8,800, sh) nm; nmr δ 5.59 (1H, m), 5.80 (1 H, m) ppm.

Anal. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84. Found: C, 88.40; H, 12.10.

When this compound was chromatographed over SiO_2–$AgNO_3$, it was transformed into **4** and **16**.

Maleic Anhydride Adduct from 15.—The diene (50 mg) and maleic anhydride (50 mg) were dissolved in xylene (0.5 ml) and the mixture was heated for 8 hr at 135° in a sealed tube. The solvent was then evaporated under reduced pressure and the residue refluxed for 2 hr with 1.5 *M* methanolic potassium hydroxide (6 ml). After cooling the undissolved material (10 mg, diene **4**) was filtered off and the filtrate, diluted with water and acidified with 2 *N* hydrochloric acid, was extracted with ether. Evaporation of the dried ($MgSO_4$) extract afforded 38 mg of residue, which was dissolved in ether and precipitated with methanol to obtain an amorphous powder, mp 150–155°, $[\alpha]_D$ +43°.

Anal. Calcd for $C_{34}H_{52}O_4$: C, 77.82; H, 9.99. Found: C, 78.55; H, 9.78.

Isomerization of Dienes with Hydrochloric Acid in Ethanol.—Each diene (50 mg) was dissolved in ethanol (50 ml) containing 36% hydrochloric acid (5 ml). The solution was refluxed for 1.5 hr and the reaction product was isolated in the usual way. Yields were almost quantitative. Dienes **12**, **13**, and **14** afforded **3**; dienes **15** and **16** afforded **4**.

Catalytic Hydrogenations.—Each diene (50 mg) was dissolved in a mixture of cyclohexane (30 ml) and acetic acid (10 ml) and the solution was stirred under hydrogen in the presence of 5% Pt–C catalyst (0.15 g), for the given time. The catalyst was then filtered off, the filtrate was diluted with water, and the product was isolated in the usual way. Diene **3** (stirring time 0.5 hr) afforded **9** and A′-neogammacer-16-ene.[2] Diene **3** (stirring time 7 hr) and diene **14** (stirring time 3 hr) afforded **9**. Diene **13** (stirring time 7 hr) afforded a mixture containing (glpc) 20% **9**, 50% 21αH-A′-neogammacerane (moretane), 16% 21βH-A′-neogammacerane (hopane), and 14% unidentified product. Dienes **4**, **15**, and **16** (stirring time 5 hr) afforded **17**.

Registry No.—**4**, 3608-05-7; **5**, 1615-92-5; **6a**, 22847-67-2; **6b**, 22847-68-3; **7**, 22922-40-3; **12**, 22847-69-4; **13**, 22847-70-7; **14**, 22847-71-8; **15**, 22847-72-9; **16**, 22847-73-0; maleic anhydride adduct of **15**, 22847-74-1.

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Experiments Directed toward the Total Synthesis of Terpenes. XIV. An Interpretation of the Transmogrification of 4β,7aα-Dimethyl-1α-hydroxy-4α-phenyl-4,5,6,7-tetrahydro-2-indanone by Base[1]

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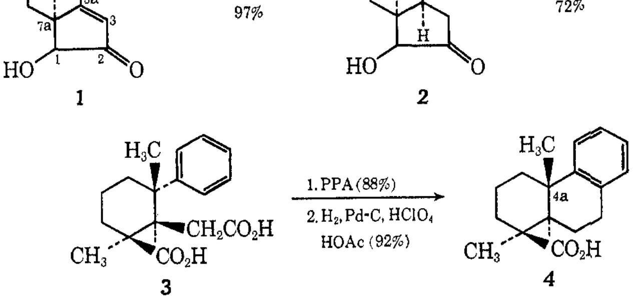
The base-catalyzed rearrangement of the unsaturated hydroxy ketone **1** has been shown to generate the diosphenol **31** in virtually quantitative yield. The process involves epimerization of the tetrasubstituted C-7a carbon of the tetrahydro-2-indanone ring system and probably entails initial reverse aldolization and subsequent recombination to the epimeric unsaturated hydroxy ketone **30** prior to diosphenol formation. The structure of the diosphenol **31** was determined by degradation to the hexahydro-2-indanone **22**, which was, in turn, synthesized independently. Oxidation of the diosphenol **31** and then polyphosphoric acid catalyzed cyclization of the resulting anhydride **35** produced the benzobicyclo[3.3.1]nonane skeleton **36**. Evidence in favor of this structure was obtained by degradation of the acid **36** to the hydrocarbon **38**. Single-crystal X-ray structural analyses of the *p*-bromobenzoates of the unsaturated hydroxy ketones **1** and **30** and the diosphenol **31** are reported, and the driving force of the rearrangement reaction is discussed in terms of the steric crowding in the hydroxy ketone **1**.

In the recently described stereoselective synthesis of deoxypodocarpic acid (**4**)[3] from these laboratories,[4] the unsaturated hydroxy ketone **1** was a key intermediate. Catalytic hydrogenation of the conjugated double bond served to introduce the last required center of asymmetry at C-3a and generate the saturated hydroxy ketone **2** in good yield. The further transformation of this saturated ketone **2** to the desired deoxypodocarpic acid (**4**) and its derivatives was then unexceptional and the sequence that was developed provides an excellent route for the synthesis of these tricyclic acids. During the course of this investigation and before the catalytic hydrogenation of the unsaturated ketone **1** had been



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[3] The structural formulas containing one or more asymmetric carbon atoms depict one diastereoisomer, but refer to racemic compounds throughout. Each racemate is arbitrarily represented by the diastereoisomer that has the C-4 (hydroindan series) or C-4a (phenanthrene series) methyl group in the β configuration. In the text the (±) prefix will be omitted and intermediates are to be assumed to be racemic.

[4] F. Giarrusso and R. E. Ireland, *J. Org. Chem.*, **33**, 3560 (1968).