BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 599—603 (1972)

The Rearrangement of 2α-Hydroxy-10β-pinan-3-one with Acetic Anhydride[1]

Toshifumi HIRATA

Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Hiroshima

(Received September, 6, 1971)

The reaction of (+)-2α-hydroxy-10β-pinan-3-one (**1**) with acetic anhydride afforded (+)-2α-acetoxy-10β-pinan-3-one (**2**), (−)-carvone (**3**), (−)-4α-acetoxy-10α-pinan-3-one (**4**), (+)-4β-acetoxy-10β-pinan-3-one (**5**), and (−)-4β-acetoxy-10α-pinan-3-one (**6**). The three products, **4**, **5**, and **6**, were newly identified on the basis of a combination of chemical and physico-chemical methods. By examination using the ^{14}C-labelled acetate (**2**), the formation of **4**, **5**, and **6** was shown to arise from the intramolecular rearrangement of **2**. The mechanistic implications of the reaction are given.

In connection with studies of the stereochemistry and the reaction of pinane derivatives,[3,4] we have now found it necessary to examine the rearrangement of 2α-hydroxy-10β-pinan-3-one (**1**) with acetic anhydride. This paper will deal with the structures of some isomers of an α-acetoxyketone produced newly as well as with the mechanistic implications of the reaction.

Results and Discussion

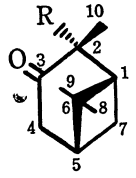
The reaction of (+)-2α-hydroxy-10β-pinan-3-one (**1**) with acetic anhydride under reflux gave an oily reaction product, which was composed of (+)-2α-acetoxy-10β-pinan-3-one (**2**) (in 14% yield based on the sample taken), (−)-carvone (**3**) (1.3%), and three unknown acetates, **4**, **5**, and **6** (39, 17, and 20% respectively). The structures of the acetates, (**4**), (**5**), and (**6**), were established on the basis of the following evidence. The hydrolysis of the acetate (**4**) gave two unknown ketols, **7** and **8**. By acetylation, the former was returned to the acetate (**4**), whereas the latter was returned to a new acetate **9**. Furthermore, the lithium aluminum hydride reduction of the tosylate (**10**) derived from **7** gave two known compounds,

1) This paper forms Part XVI[2] in the Hiroshima University series of "Stereochemical Studies of Monoterpene Compounds."

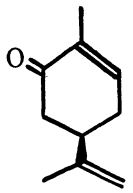
2) Part XV: T. Suga and S. Watanabe, This Bulletin, **45**, 570 (1972).

3) T. Suga, T. Shishibori, T. Hirata, and T. Matsuura, *ibid.*, **41**, 1180 (1968).

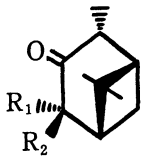
4) R. G. Carlson, J. K. Pierce, T. Suga, T. Hirata, T. Shishibori, and T. Matsuura, *Tetrahedron Lett.*, **1968**, 5941.



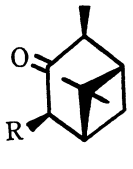
1: R=OH
2: R=OAc



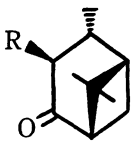
3



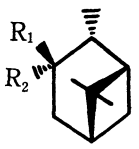
4: R_1=OAc, R_2=H
6: R_1=H, R_2=OAc
7: R_1=OH, R_2=H
10: R_1=OTs, R_2=H



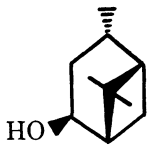
5: R=OAc
18: R=OTs
19: R=OH



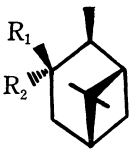
8: R=OH
9: R=OAc
13: R=OTs



11: R_1=OH, R_2=H
12: R_1=H, R_2=OH

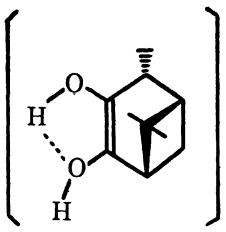


14



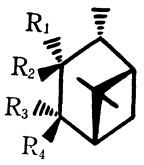
16: R_1=OH, R_2=H
17: R_1=H, R_2=OH

(−)-pinocampheol (**11**) and (+)-neopinocampheol (**12**).[5] These results showed the acetate (**4**) to be 4-acetoxy-10α-pinan-3-one. The ketol (**8**) was similarly confirmed to be 3-hydroxy-10α-pinan-4-one by the fact that its tosylate, **13**, was converted to (+)-neoverbanol (**14**)[5] on reduction with lithium aluminum hydride. It may probably be explained that the ketol (**8**) resulted from the isomerization of the ketol (**7**) through the intermediate (**15**) during the course

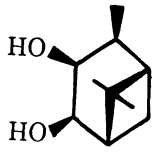


15

of the hydrolysis of the acetate (**4**). The acetate (**5**) was derived to (−)-neoisopinocampheol (**16**) and (+)-isopinocampheol (**17**)[5] on the reduction of the tosylate (**18**) derived from the hydrolyzed product, the ketol (**19**), of the original acetate (**5**) with lithium aluminum hydride. This indicates the structure of **5** to be 4-acetoxy-10β-pinan-3-one. It has been established[3,7-9] that, in the reduction of pinane derivatives with lithium aluminum hydride, the reagent approaches from the opposite side of the *gem*-dimethyl bridge and/or the polar group, because of the steric and/or the polar effects. The reduction of the hydroxyketone (**7**) with lithium aluminum hydride afforded *cis*- and *trans*-glycols, (**20**) and (**21**), in equal amounts. This can be ascribed to the competitive contribution between the *gem*-dimethyl and the hydroxyl groups to the reduction. Accordingly, the hydroxyl group of **7** should be *trans* to the *gem*-dimethyl group. On the other hand, the reduction of the acetate (**5**) with lithium aluminum hydride occurred stereospecifically to result in the formation of glycol, **22**. Therefore, the acetoxy group of **5** is surely *cis* to the *gem*-dimethyl group. This was also the case for the hydroxyketone (**8**), and **8** was converted to glycol, **23**. The acetate (**6**) was also derived to the glycol (**23**) on reduction with lithium aluminum hydride. This shows the structure of **6** to be 4β-acetoxy-10α-pinan-3-one. Consequently, all the structures of acetates, **4**, **5**, and **6**, together with those of ketol, **8**, and the diols, **20**, **21**, **22**, and **23**, were established, as is shown in the Schemes.



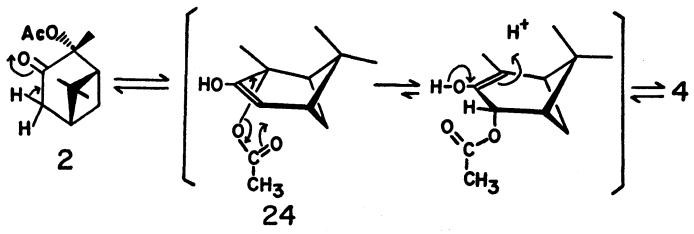
20: R_1, R_3=OH; R_2, R_4=H
21: R_1, R_4=H; R_2, R_3=OH
23: R_1, R_3=H; R_2, R_4=OH



22

Reaction Mechanism. To clarify the mechanism of the formation of the acetates, (**4**), (**5**), and (**6**), from the hydroxyketone (**1**), the ^{14}C-labeled acetate (**2**), being active at the acetoxy carbonyl group, was treated with acetic anhydride in the same manner as above to give the acetates, (**4**), (**5**), and (**6**), in 21, 7, and 10% yields respectively; all of them retained the expected radioactivity. The treatment of the ^{14}C-labeled acetate (**5**) in the same manner as above yielded the radioactive acetates, (**2**), (**4**), and (**6**), in 2, 21, and 14% yields respectively. These findings suggest that the acetate (**2**) produced from the hydroxyketone (**1**)

5) These authentic samples were prepared in our laboratory by the reduction of the appropriate ketones.[3,6,7]
6) G. Zweifel and H. C. Brown, *J. Amer. Chem. Soc.*, **86**, 393 (1964).
7) A. F. Regan, *Tetrahedron*, **25**, 3801 (1969).
8) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, **77**, 3054 (1955).
9) Y. Chretien-Bessiere, *Bull. Soc. Chem. Fr.*, **1964**, 2182.



Scheme I

by acetylation suffers intramolecular rearrangements to form **4**, **5**, and **6**. The formation of the acetates is best explained by the initial formation of the acetate (**4**) through the formation of the enolic intermediate (**24**) of the acetate (**2**) by the subsequent intramolecularly-concerted migration of the acetoxy group, and finally by the isomerization of **4** to **5** and **6** through its enolic form, as is shown in Scheme I.

Experimental

The IR spectra were measured on a Perkin-Elmer, 621, Grating Infrared Spectrometer and a Hitachi, EPI-S, Infrared Spectrophotometer. The NMR spectra were recorded on a Varian Associates, HA-100, Spectrometer and a Hitachi Perkin-Elmer, R-20, Spectrometer, using tetramethylsilane as the internal standard. Vapor-phase chromatographic analyses were made on a Perkin-Elmer, F6-D, Gas Chromatograph. Mass spectral analyses were performed on a Hitachi, RMS-4, Mass Spectrometer, ionizing at the order of 80 eV. Radioassays were carried out by converting samples to carbon dioxide by Van Slyke-Folch oxidation,[10] followed by changing the resulting carbon dioxide to barium carbonate, and by counting on planchets at an infinite thickness and with a surface area of 5.0 cm^2 by means of an Aloka, LBC-1, Low-Background 2π-Gas Flow Countmeter. The counts were corrected for the background count, and the counting error was about ±3%.

*Reaction of 2α-Hydroxy-10β-pinan-3-one (**1**) with Acetic Anhydride.* A mixture of 22.0 g of (+)-2α-hydroxy-10β-pinan-3-one [mp 33—34°C, $[\alpha]_D^{25}$ +21.0° (*c* 4.6, EtOH), prepared from (−)-α-pinene following the literature method[11]] and 35.0 g of acetic anhydride was refluxed for 6 hr at 160°C. To the mixture, after cooling, we added 30 m*l* of water, and then it was heated for 30 min at 50°C in order to degrade the remaining acetic anhydride. The reaction mixture was then extracted with ether. The separated ether solution was washed with a dilute sodium bicarbonate solution and water, and then dried over anhydrous sodium sulfate. The removal of the solvent from the ether solution gave 22.9 g of an oily reaction product. The reaction product was chromatographed on a silica-gel column with a mixture of ethyl acetate and *n*-hexane (5 : 95 by volume) in order to separate five eluates.

The first eluate (0.4 g) was composed of complex minor components; it was further subjected to preparative gas chromatography. This resulted in the isolation of (−)-carvone (**3**): $[\alpha]_D^{25}$ −46° (*c* 0.45, MeOH); IR (liq.) 1677 (α,β-unsaturated C=O) and 1651 cm^{-1} (C=C). It was identified by a comparison of the IR spectrum with that of an authentic sample. The second eluate (3.2 g) was proved to be 2α-acetoxy-10β-pinan-3-one (**2**). The third eluate (13.5 g) consisted of two components in the ratio of 2 : 1; it was evaluated from the peak ratio of the C-4 proton signals on the NMR spectrum. A portion (5.0 g) was chromatographed twice on a silica-gel column with a mixture of ethyl acetate and *n*-hexane (1 : 99), but the complete separation was difficult. This procedure resulted in the separation of 4α-acetoxy-10α-pinan-3-one (**4**) (0.66 g) and 4β-acetoxy-10α-pinan-3-one (**6**) (0.11 g), and a mixture of **4** and **6** (4.05 g). The fourth eluate (3.9 g) gave a crystalline mass, which was then recrystallized from *n*-hexane to obtain (+)-4β-acetoxy-10β-pinan-3-one (**5**) (3.5 g). The fifth eluate (1.1 g) consisted of several compounds. One of the compounds was unchanged hydroxyketone (**1**) (0.8 g), but the others failed to separate.

*a) 2α-Acetoxy-10β-pinan-3-one (**2**)*: mp 38—40°C (from *n*-hexane), $[\alpha]_D^{25}$ +23.1° (*c* 0.26, MeOH); UV (MeOH) 300 nm (ε 29.5); IR (KBr) 1745 ($OCOCH_3$) and 1724 cm^{-1} (C=O); NMR (CCl_4) δ 0.86 (s, C_9-3H), 1.37 (s, C_8-3H), 1.49 (s, C_{10}-3H), and 1.92 ppm (s, $OCOCH_3$); mass *m/e* (rel. intensity) 210 (5, M^+), 192 (10), 168 (35) 153 (67), 150 (70), and 43 (100).

*b) 4α-Acetoxy-10α-pipan-3-one (**4**)*: $[\alpha]_D^{25}$ −78.1° (*c* 0.49, MeOH); UV (MeOH) 298 nm (ε 30.2); IR (liq.) 1744 ($OCOCH_3$) and 1728 cm^{-1} (C=O); NMR (CCl_4) δ 1.06 (s, C_9-3H), 1.07 (d, J=7,0 Hz, C_{10}-3H), 1.39 (s, C_8-3H), 2.02 (s, $OCOCH_3$), and 5.28 ppm (b.s, C_4-H); mass *m/e* (rel. intensity) 210 (1, M^+), 168 (2), 150 (7), 127 (16), 85 (56), 83 (25), 55 (30), 43 (82), and 28 (100).

*c) 4β-Acetoxy-10β-pinan-3-one (**5**)*: mp 100.5—101.0°C (from *n*-hexane - ethyl acetate), $[\alpha]_D^{25}$ +66.1° (*c* 6.0, EtOH); UV (MeOH) 292 nm (ε 27.7); IR (KBr) 1747 ($OCOCH_3$) and 1717 cm^{-1} (C=O); NMR (CCl_4) δ 0.93 (s, C_9-3H), 1.21 (d, J=7.0 Hz, C_{10}-3H), 1.33 (s, C_8-3H), 2.06 (s, $OCOCH_3$), and 5.26 ppm (b.s, C_4-H); mass *m/e* (rel. intensity) 210 (1, M^+), 168 (2), 150 (4), 127 (39), 85 (95), 83 (41), 55 (39), and 43 (100).

*d) 4β-Acetoxy-10α-pinan-3-one (**6**)*: $[\alpha]_D^{25}$ −8.5° (*c* 0.37, MeOH); UV (MeOH) 302 nm (ε 27.1); IR (liq.) 1745 ($OCOCH_3$) and 1727 cm^{-1} (C=O); NMR (CCl_4) 0.95 (s, C_9-3H), 1.14 (d, J=7.5 Hz, C_{10}-3H), 1.34 (s, C_8-3H), 2.04 (s, $OCOCH_3$), and 5.09 ppm (b.s, C_4-H); mass *m/e* (rel. intensity) 210 (4, M^+), 168 (2), 150 (7), 127 (20), 85 (25), 83 (20), 55 (11), 43 (25), and 28 (100).

*Hydrolysis of the Acetate (**4**).* To a stirred solution of 10 m*l* of 3 N methanolic potassium hydroxide, we added 2.00 g of **4**; the mixture was kept at room temperature overnight. The mixture was then diluted with 100 m*l* of water and extracted with ether. The removal of the solvent from the ether solution gave 1.40 g of an oily product, which was then chromatographed on a silica-gel column with a mixture of *n*-hexane and an increasing amount of ethyl acetate; we thus separated two components. The first eluate gave 419 mg of **7** and the second eluate, 208 mg of **8**.

*a) 4α-Hydroxy-10α-pinan-3-one (**7**)*: $[\alpha]_D^{25}$ −52.8° (*c* 0.55, MeOH); UV (MeOH) 285 nm (ε 29.7); IR (liq.) 1715 (C=O), and 1371 and 1387 cm^{-1} (*gem*-dimethyl);

10) D. D. Van Slyke and J. Folch, *J. Biol. Chem.*, **136**, 509 (1940).

NMR (CCl_4) δ 1.00 (s, C_9-3H), 1.06 (d, J=7.0 Hz, C_{10}-3H), 1.37 (s, C_8-3H), and 4.07 ppm (b.s. C_4-H). The acetylation of **7** with acetic anhydrade in pyridine gave the acetate (**4**); $[\alpha]_D^{25}$ −75.6° (*c* 0.37, MeOH). The acetate was identified by direct comparisons of its spectral data.

*b) 3β-Hydroxy-10α-pinan-4-one (**8**)*: mp 44—45°C (from *n*-hexane), $[\alpha]_D^{25}$ −147.7° (*c* 0.27, MeOH); UV (MeOH) 282 nm (ε 36.9); IR (CCl_4) 1716 (C=O), and 1378 and 1391 cm^{-1} (*gem*-dimethyl); NMR (CCl_4) δ 0.74 (s, C_9-3H), 1.23 (d, J=7.0 Hz, C_{10}-3H), 1.37 (s, C_8-3H), and 3.70 ppm (d, J=6.5 Hz, C_3-H). The acetylation of **8** with acetic anhydride in pyridine gave the acetate (**9**); mp 38—39°C (from *n*-hexane), $[\alpha]_D^{25}$ −135.2° (*c* 0.49, MeOH); UV (MeOH) 284 nm (ε 54.9); IR (KBr) 1743 ($OCOCH_3$) and 1723 cm^{-1} (C=O); NMR (CCl_4) δ 0.81 (s, C_9-3H), 1.15 (d, J=7.0 Hz, C_{10}-3H), 1.38 (s, C_8-3H), 2.12 (s, $OCOCH_3$), and 5.12 ppm (d, J=6.5 Hz, C_3-H); mass *m/e* (rel. intensity) 210 (1, M^+), 168 (15), 150 (4), 135 (15) 95 (26), 83 (65), 55 (43), and 43 (100).

*4α-Tosyloxy-10α-pinan-3-one (**10**).* The tosylation of 350 mg of **7** with 500 mg of *p*-toluenesulfonyl chloride in 5 m*l* of pyridine at room temperaure for 5 days gave 545 mg of a crude product, which was then subjected to chromatography on a silica-gel column to give 453 mg of the tosylate (**10**); mp 68—69°C (from *n*-hexane - ethyl acetate); IR (KBr) 1722 (C=O) and 1595 cm^{-1} (C=C); NMR (CCl_4) δ 0.98 (s, C_9-3H), 1.05 (d, J=7.0 Hz, C_{10}-3H), 1.39 (s, C_8-3H), 2.44 (phenyl methyl), 4.80 (b.s, C_4-H), and 7.25—7.88 ppm (q, phenyl proton, 4H).

*3β-Tosyloxy-10α-pinan-4-one (**13**).* The treatment of 100 mg of **8** with 150 mg of *p*-toluenesulfonyl chloride in 3 m*l* of pyridine gave 137 mg of the tosylate (**13**); mp 118.0—118.5°C (from *n*-hexane - ethyl acetate); IR (KBr) 1740 (C=O) and 1598 cm^{-1} (C=C); NMR (CCl_4) δ 0.78 (s, C_9-3H), 1.26 (d, J=7.0 Hz, C_{10}-3H), 1.34 (s, C_8-3H), 2.44 (s, phenyl methyl), 4.73 (d, J=6.5 Hz, C_3-H), and 7.20—7.90 ppm (q, phenyl proton, 4H).

*Reduction of the Hydroxyketone (**7**),* To a stirred solution of 127 mg of **7** in 15 m*l* of ether, we added 100 mg of lithium aluminum hydride under ice-cooling, and then the mixture was refluxed for 2 hr. The mixture, after cooling, was treated with water and then dilute hydrochloric acid. The ether extract gave 120 mg of an oily product, which was separated by preparative thin-layer chromatography on silica-gel with a 3 : 7 mixture of ethyl acetate and *n*-hexane to give 60 mg of the *cis*-glycol, **20**, and 55 mg of *trans*-glycol, **21**.

*a) 10α-Pinan-3α,4α-diol (**20**)*: mp 52—53°C (from *n*-hexane), $[\alpha]_D^{25}$ −1.0° (*c* 0.59, MeOH); IR (0.002 M CCl_4) 3627 (OH, free) and 3537 cm^{-1} (OH, intramol. bonded); NMR (CCl_4) δ 0.81 (s, C_9-3H), 0.97 (d, J=7.0 Hz, C_{10}-3H), 1.23 (s, C_8-3H), and 4.00 ppm (b.s, C_3- and C_4-H); mass *m/e* (rel. intensity) 170 (0.5, M^+). 152 (2), 137 (3), 85 (100), 43 (73), and 41 (54).

*b) 10α-Pinan-3β,4α-diol (**21**)*: mp 146.0—146.5°C (from ethyl acetate), $[\alpha]_D^{25}$ −2.9° (*c* 0.14, MeOH); IR (0.002 M CCl_4) 3616 cm^{-1} (OH, free); NMR (pyridine) δ 0.98 (s, C_9-3H), 1.20 (d, J=7.0 Hz, C_{10}-3H), 1.22 (s, C_8-3H), 3.89 (d.d, J=7.0 and 6.0 Hz, C_3-H), and 4.42 ppm (b.d, J=6.0 Hz, C_4-H); mass *m/e* (rel. intensity) 170 (0.5, M^+), 152 (6), 137 (6), 85 (100), 43 (85), 41 (72), and 28 (87).

*Reduction of the Hydroxyketone (**8**).* A solution of 113 mg of **8** in 10 m*l* of ether was added to a strired suspension of 100 mg of lithium aluminum hydride in 10 m*l* of ether, and then the mixture was refluxed for 2 hr. After the degradation of the excess reagent, the mixture was extracted with ether to yield 110 mg of a crude product, which was subjected to preparative thin-layer chromatography on silica-gel with a mixture of ethyl acetate and *n*-hexane (3 : 7) to separate 91 mg of 10α-pinan-3β,4β-diol (**23**): mp 95.5—96.0°C (from a mixture of ethyl acetate and *n*-hexane), $[\alpha]_D^{25}$ −24.7° (*c* 0.11, MeOH); IR (0.002 M CCl_4) 3626 (OH, free) and 3547 cm^{-1} (OH, intramol. bonded); NMR (CCl_4) δ 1.00 (s, C_9-3H), 1.02 (d, J=7.0 Hz, C_{10}-3H), 1.19 (s, C_8-3H), 3.48 (m, C_3-H), and 4.10 ppm (b.s, C_4-H); mass *m/e* (rel. intensity) 137 (6), 85 (92), 43 (100), and 41 (77).

*Reduction of the Tosylate (**10**).* To a stirred suspension of 300 mg of lithium aluminum hydride in 15 m*l* of ether, we added a solution of 300 mg of **10** in 5 m*l* of ether at room temperature over a 30-min period, after which the mixture was further refluxed for 4 hr. The ether extract gave 139 mg of a reaction product, which was separated into two components by thin-layer chromatography on silica-gel with a mixture of ethyl acetate and *n*-hexane (3 : 7). The more eluted component (89 mg) was confirmed to be (−)-pinocampheol (**11**); mp 66—67°C (from *n*-hexane) (lit,[11] mp 67°C), $[\alpha]_D^{25}$ −57.2° (*c* 0.33, MeOH); IR (KBr) 3350 (OH), and 1370 and 1388 cm^{-1} (*gem*-dimethyl); NMR δ 0.92 (s, C_9-3H), 1.00 (d, J=7.0 Hz, C_{10}-3H), 1.21 (s, C_8-3H), and 3.56 ppm (d.t, J=9.0 and 7.0 Hz, C_3-H); the 3,5-dinitrobenzoate, mp 118—119°C (lit,[12] mp 118—119°C). The other component (21 mg) was found to be (+)-neopinocampheol (**12**); mp 26—27°C (from *n*-hexane) (lit,[11] mp 27°C), $[\alpha]_D^{25}$ +14.0° (*c* 0.15, MeOH); IR (Nujol) 3440 (OH), and 1370 and 1391 cm^{-1} (*gem*-dimethyl); NMR (CCl_4) δ 0.77 (s, C_9-3H), 0.93 (d, J=7.0 Hz, C_{10}-3H), 1.21 (s, C_8-3H), and 3.99 ppm (b.t, J=6.5 Hz, C_3-H). These physical properties and spectral data coincided with those of authentic samples.[5]

*Reduction of the Tosylate (**13**).* To a stirred suspension of 140 mg of lithium aluminum hydride in 5 m*l* of ether, we added a solution of 130 mg of **13** in 5 m*l* of ether at room temperature over a 10-min period. After refluxing for 3 hr, the treatment of the mixture in the usual manner gave 61 mg of a reaction product, which was chromarographed on a silica-gel column to separate 13 mg of the pinan-diol (**23**) (mp 95.5—96.0°C) and 42 mg of (+)-neovervanol (**14**); mp 78—79°C (from *n*-hexane), $[\alpha]_D^{25}$ +11.6° (*c* 0.17, MeOH); IR (KBr) 3340 (OH), and 1370 and 1389 cm^{-1} (*gem*-dimethyl); NMR (CCl_4) δ 0.88 (d, J=7.0 Hz, C_{10}-3H), 1.06 (s, C_9-3H), 1.21 (s, C_8-3H), and 4.14 ppm (m, C_4-H). The spectral data coincided with those of an authentic sample.[5]

*Hydrolysis of the Acetate (**5**).* To a stirred solution of 420 mg of **5** in 20 m*l* of methanol, we added 10 m*l* of 0.1 N methanolic sodium hydroxide at 15°C over a 10-min period. The mixture was further stirred for 20 min and then extracted with ether to give 292 mg of hydroxyketone, **19**; mp 67—68°C (from *n*-hexane), $[\alpha]_D^{25}$ +33.5° (*c* 0.25, MeOH); UV (MeOH) 288 nm (ε 29.8); IR (KBr) 1710 (C=C), and 1376 and 1390 cm^{-1} (*gem*-dimethyl); NMR (CCl_4) δ 0.86 (s, C_9-3H), 1.20 (d, J=7.0 Hz, C_{10}-3H), 1.32 (s, C_8-3H), and 3.98 ppm (b.s, C_4-H). This hydroxyketone was derived to the acetate (**6**) by acetylation.

*4β-Tosyloxy-10β-pinan-3-one (**18**).* The treatment of 200 mg of **19** with 300 mg of *p*-toluenesulfonyl chloride in 4 m*l* of pyridine at room temperature for 5 days gave 370 mg of the tosylate, **19**; mp 97—98°C (from *n*-hexane - ethyl acetate); IR (KBr) 1734 (C=O) and 1597 cm^{-1} (C=C); NMR (CCl_4) δ 0.92 (s, C_9-3H), 1.16 (d, J=7.5 Hz, C_{10}-3H), 1.35 (s, C_8-3H), 2.45 (s, phenyl methyl), 4.78 (b.s,

11) H. Schmidt, *Chem. Ber.*, **77**, 544 (1944).

12) T. Takemoto, G. Kusano, and H. Hikino, *Yakugaku Zasshi*, **86**, 1162 (1966).

C_4-H), and 7.20—7.90 ppm (q, phenyl proton, 4H).

*Reduction of the Acetate (**5**).* A suspension of 110 mg of **5** and 120 mg of lithium aluminum hydride in 50 m*l* of ether was refluxed for 7 hr under agitation, and then it was treated in the usual manner to give 80 mg of glycol, **22**; mp 79—80°C (from *n*-hexane); IR (0.0024 M CCl_4) 3634 (OH, free) and 3533 cm^{-1} (OH, intramol. bonded); NMR ($CDCl_3$) δ 1.10 (d, J=7.5 Hz, C_{10}-3H), 1.16 (s, C_9-3H), 1.20 (s, C_8-3H), and 4.35 ppm (m, C_3- and C_4-H); mass *m/e* (rel. intensity) 170 (1, M^+), 152 (1), 137 (7), 86 (92), 85 (100), 43 (54), and 41 (36).

*Reduction of the Tosylate (**18**).* To a stirred suspension of 300 mg of lithium aluminum hydride in 10 m*l* of ether, we added a solution of 290 mg of **18** in 15 m*l* of ether at room temperature over a 30-min period; this was followed by further refluxing for 3 hr. The mixture, after the usual treatment, gave 185 mg of a reaction product, which was subjected to column-chromatography on silica-gel with a mixture of *n*-hexane and an increasing amount of ethyl acetate to give 90 mg of (−)-neoisopinocampheol (**16**) [mp 50.5—51.0°C (from *n*-hexane) (lit,[11] mp 48°C), $[\alpha]_D^{25}$ −34.5° (*c* 0.75, C_6H_6); IR (KBr) 3340 (OH), and 1369 and 1388 cm^{-1} (*gem*-dimethyl); NMR (CCl_4) δ 1.05 (d, J=7.0 Hz, C_{10}-3H), 1.06 (s, C_9-3H), 1.18 (s, C_8-3H), and 4.35 ppm (d.t, J=5.0 and 10.0 Hz, C_3-H)], 20 mg of (+)-isopinocampheol (**17**) [mp 56—57°C (from *n*-hexane) (lit,[11] mp 57°C), $[\alpha]_D^{25}$ +29.0° (*c* 0.15, C_6H_6); IR (KBr) 3280 (OH), and 1372 and 1388 cm^{-1} (*gem*-dimethyl); NMR (CCl_4) δ 0.91 (s, C_9-3H), 1.08 (d, J=7.0 Hz, C_{10}-3H), 1.20 (s, C_8-3H), and 3.94 ppm (d.t, J=9.0 and 5.0 Hz, C_3-H)], and 18 mg of 10β-pinan-3β,4β-diol (**22**) (mp 79—80°C).

*Reduction of the Acetate (**6**).* A solution of 50 mg of **6** in 15 m*l* of ether was treated with 50 mg of lithium aluminum hydride under reflux for 1 hr to give 39 mg of the pinanediol (**23**); mp and mixed mp 95—96°C, $[\alpha]_D^{25}$ −21.0° (*c* 0.20, MeOH).

Preparation of Radioactive Acetic Anhydride. To a stirred suspension of 1-^{14}C-sodium acetate (3.50 g; 8620±80 dpm/mmol) in ether, we added acetyl chloride (4 m*l*) over a 5-min period at room temperature. The mixture was then further stirred for 3 hr. The distillation of the reaction gave acetic-1-^{14}C anhydride (2.82 g; 4462±40 dpm/mmol).

Rearrangement of Radioactive Acetate. 2α-(1-^{14}C-Acetoxy)-10β-pinan-3-one (**2**) and 4β-(1-^{14}C-acetoxy)-10β-pinan-3-one (**5**) were prepared by treating 2α-hydroxy-10β-pinan-3-one (**1**). The radioactive acetic anhydride in the manner as above. The radioactive acetates, (**2**) and (**5**), were then each treated with acetic anhydride in the manner to be shown below. The reaction product was purified by column-chromatography, followed preparative thin-layer chromatography or recrystallization. The proportion of products was evaluated on the basis of the gas chromatography and the peak ratio of the C-4 proton signals on the NMR spectra.

*a) Rearrangement of the ^{14}C-Acetate (**2**):* A solution of 840 mg (0.004 mol) of the radioactive acetate (**2**) (187.3±2.0 dpm/mmol) in 1632 mg (0.016 mol) of acetic anhydride was refluxed for 5 hr. The usual treatment of the reaction mixture then gave 830 mg of an oily product, which was composed of 54 mg of the acetate (**4**) (119.2±2.0 dpm/mmol), 58 mg of the acetate (**5**) (97.3±2.0 dpm/mmol), 25 mg of the acetate (**6**) (104.6±2.0 dpm/mmol), and 257 mg of the unchanged acetate (**2**) (136.1±2.0 dpm/mmol).

*b) Rearrangement of the ^{14}C-Acetate (**5**):* A sample of 1680 mg (0.008 mol) of the radioactive acetate (**5**) (182.4±2.0 dpm/mmol) was refluxed with 3264 mg (0.032 mol) of acetic anhydride for 5 hr. The ether extract of the mixture gave 1632 mg of an oily product, which was composed of 15 mg of **2** (126.5±2.0 dpm/mmol), 91 mg of **4** (138.7±2.0 dpm/mmol), 32 mg of **6** (131.4±2.0 dpm/mmol), and 660 mg of the unchanged **5** (170.2±2.0 dpm/mmol).

The author wishes to express his hearty gratitude to Dr. Takayuki Suga of Hiroshima University for his guidance and encouragement and to Dr. E. von Rudoloff of National Research Council of Canada, Saskatchewan, Canada, for measuring the NMR spectra with a Varian Associates, HA-100, Spectrometer.