The Synthesis of 9-Substituted Pinanes[1]

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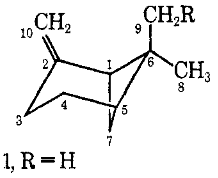
The nitrite and hypobromite photolysis techniques for functionalization of unactivated carbon atoms have been demonstrated to be suitable methods for the introduction of substituents at C-9 in the pinane series.

The nitrite and hypohalite photolysis techniques (Barton reactions) for effecting substitution at unactivated carbon atoms have been of considerable value in synthesis[2] and structure determination.[3]



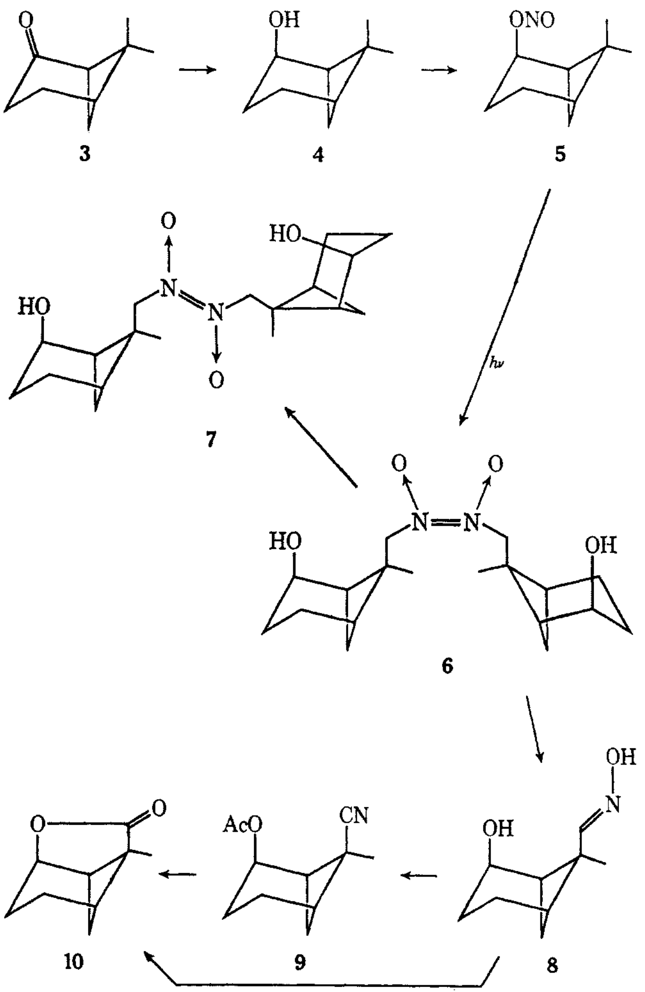
1, R = H
2, R = $CH_2CH{=}C(CH_3)_2$

The present report describes some of our attempts to utilize these methods for substitution at C-9 in the pinane series. This study was originally undertaken with two objectives in mind. The first of these was the development of a degradative sequence which would make possible the determination of the specific activity of each of the substituent methyl groups in ^{14}C-labeled β-pinene (**1**) biosynthesized from mevalonate-2-^{14}C; specifically, this would enable the determination of whether the C-8 and C-9 methyls retain a distinct identity during the biosynthesis of β-pinene,[4] or whether they become randomized[5] at some point during this process. Our second objective was the synthesis, starting from β-pinene (**1**), of the structure **1** assigned to β-bergamotene, a sesquiterpene isolated from Indian valerian oil (*Valeriana wallichi*);[6] however, during the course of this work, Gibson and Erman[7] reported a synthesis of **2** (which established its nonidentity with naturally occurring β-bergamotene) *via* a route similar to that anticipated in this study.

The transformations described in this paper complement those reported by Gibson and Erman;[7] several of the reactions described are presently being adapted on a smaller scale for use in the biosynthetic studies mentioned above.[8]

A. Nitrite Photolysis Route.—Ozonolysis of β-pinene (**1**)[9] in methanol–methylene chloride at −70° yielded nopinone (**3**) which was reduced to α-nopinol (**4**)[10] on treatment with lithium aluminum hydride.[11] Conversion of the alcohol **4** into its nitrite ester **5** was effected in 87% yield by adding sulfuric acid to a rapidly stirred water–diethyl ether mixture containing dissolved **4** and sodium nitrite at 0–5°.[12] Irradiation[13] of the nitrite ester **5** in cyclohexane using a high-pressure mercury arc lamp in a Pyrex lamp-well resulted in precipitation of a solid nitroso dimer in 50% yield. The nitroso dimer had the *cis*-azodioxy structure **6** (see below) as evidenced by its uv spectrum [λ_{max} 275 mμ

SCHEME I



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[1] This work was supported by Grant 5-R01-GM-13441-01 to -03 from the U. S. Public Health Services, National Institutes of Health.

[2] M. Akhtar in "Advances in Photochemistry," Vol. 2, W. A. Noyes, Jr., G. S. Hammond, and J. N. Pitts, Jr., Ed., Interscience Publishers, New York, N. Y., 1964, p 263.

[3] A. Nickon, F. J. McGuire, J. R. Mahajan, B. Umezawa, and S. A. Narang, *J. Amer. Chem. Soc.*, **86**, 1437 (1964).

[4] See J. H. Richards and J. B. Hendrickson, "The Biosynthesis of Steroids, Terpenes, and Acetogenins," W. A. Benjamin, Inc., New York, N. Y., 1964, pp 254, 255, and 286, for a review of similar studies in the diterpene and triterpene series in which the terminal methyl groups of acyclic isoprenoid precursors are found to retain their identity throughout the biosynthesis. A similar result was ingeniously obtained for an acyclic monoterpene: A. J. Birch, M. Kocor, N. Sheppard, and J. Winter, *J. Chem. Soc.*, 1502 (1962).

[5] Such randomization is a frequent occurrence in the biosynthesis of methylcyclopentane monoterpenoids, and in the isoprenoid portion of certain indole alkaloids: H. Auda, H. R. Juneja, E. J. Eisenbraun, G. R. Waller, W. R. Kays, and H. H. Appel, *J. Amer. Chem. Soc.*, **89**, 2476 (1967), and references cited therein.

[6] K. S. Kulkarni, S. K. Paknikar, and S. C. Bhattacharyya, *Tetrahedron*, **22**, 1917 (1966).

[7] T. W. Gibson and W. F. Erman, *Tetrahedron Lett.*, 905 (1967).

[8] These studies are being done in collaboration with Professor C. J. Coscia, Biochemistry Department, St. Louis University School of Medicine.

[9] J. Meinwald and P. G. Gassman, *J. Amer. Chem. Soc.*, **82**, 5445 (1960).

[10] O. Wallach, *Ann.*, **356**, 227 (1907).

[11] (a) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, **77**, 3054 (1955); (b) E. C. Friedrich and S. Winstein, *ibid.*, **86**, 2721 (1964) [*cf.* P. von R. Schleyer, W. E. Watts, and C. Cupas, *ibid.*, **86**, 2722 (1964)].

[12] L. Hunter and J. A. Marriott, *J. Chem. Soc.*, 285 (1936). Treatment of **5** with methanolic sodium carbonate solution led to recovery of **4** in high yield.

[13] D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Amer. Chem. Soc.*, **83**, 4076 (1961).

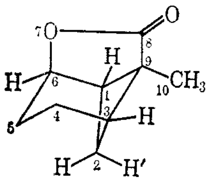
(ϵ 9200)][14] and by its tendency to isomerize in chloroform solution to yield the thermodynamically more stable *trans*-azodioxy structure 7 [λ_{max} 293 (ϵ 9600)], a transformation considered to be typical of such compounds.[14]

Upon refluxing a solution of the *cis*-nitroso dimer **6** in 2-propanol,[13] an oily oximino alcohol, which was satisfactory for further transformations, was obtained in essentially quantitative yield. An analytically pure sample of the oximino alcohol in crystalline form exhibited only one 3 H singlet (δ 1.37) in the methyl region, a 1 H singlet at δ 7.41 (C–H of an aldoxime), and no olefinic protons in its nmr spectrum. The oximino alcohol could also be converted[13] to an acetoxynitrile, which, upon hydrolysis under basic conditions followed by neutralization of the reaction mixture, afforded a γ-lactone (ir ν_{max} 1770), as evidenced by reduction of the latter compound to a diol on treatment with lithium aluminum hydride.

The possible occurrences of isomerization of the pinane nucleus[11,12] during formation of **5**, as well as epimerization at the carbinol carbon[3,15] and/or ring cleavage[2] during photolysis of **5**, are eliminated by these data, which thereby serve to establish the structure **8** for the oximino alcohol, and structures **9**, **10**, and **11** for the derived acetoxynitrile, lactone, and diol, respectively.

Further confirmation of the structure of lactone **10** came from a detailed analysis of its nmr spectrum (Table I) which exhibited parameters characteristically associated with protons located on a bicyclo[3.1.1]-heptane carbon skeleton; *i.e.*, $J_{1,3}$ = 5.4 Hz (long-range coupling),[16] $J_{2,2'}$ = 9.8 Hz (geminal coupling),[16] and a marked anisotropic shift[16,17] of H_2 relative to $H_{2'}$.

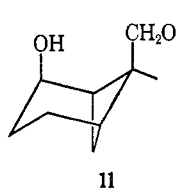
TABLE I
NUCLEAR MAGNETIC RESONANCE DATA FOR LACTONE 10[a]



Proton(s)	Chemical shift, δ	Multiplicity	Observed coupling constants[b,c]
H-1	2.75	d, d, d (six lines)[d]	$J_{1,6} = 7.0$, $J_{1,3} = 5.4$, $J_{1,2'} = 5.4$, $J_{1,2} = 0$
H-2	1.74	d	$J_{2,2'} = 9.8$
H-2'	~2.38	m	
H-3	~2.28	m	$J_{2,3} = 0$
H-4,4' H-5,5'	1.96	m[e]	
H-6	5.01	d (br)	$J_{1,6} = 7.0$
H-10	1.36	s	

[a] Measured in CCl_4 solution with a Varian HA-100 spectrometer. [b] All coupling constants are in hertz and were confirmed by spin-decoupling experiments; $J_{2',3}$, $J_{5,6}$, and $J_{5',6}$ were not determinable. [c] Estimated accuracies are 0.2 Hz. [d] Intensity ratio: 1:2:1:1:2:1 (theoretical); 1:2:1:2:2:1 (observed). [e] This pattern appeared as a *ca.* 3 H singlet (br) at 1.96 superimposed on a very broad multiplet.

Oxidation of the oximino alcohol **8** with Jones–Weedon reagent[18] resulted in a complex mixture of products containing varying amounts of lactone **10**, presumably formed *via* acidic hydrolysis of the oximino function followed by oxidation of the resulting cyclic hemiacetal.[13] Although the course of the reaction was markedly influenced by temperature, a procedure could be developed which afforded essentially pure lactone **10** in 57% yield starting from crude **8** (or 25–30% from nopinol).



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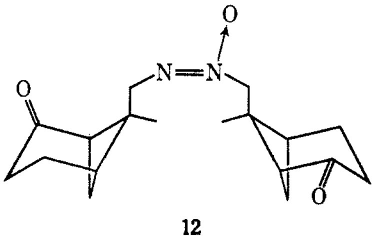
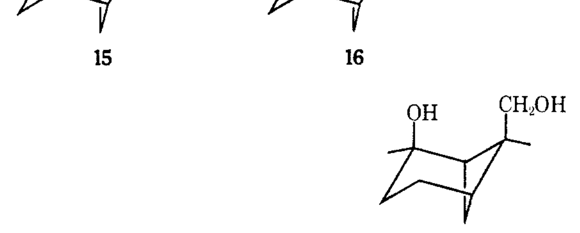


12

Attempts to form a keto oxime *via* oxidation of *cis*-hydroxynitroso dimer **6** with Jones oxidant at 5° led to the formation of a mixture of products, one of which was assigned the azoxy structure **12** on the basis of analytical and spectral data (see Experimental Section).

Hypobromite Photolysis Route.—Methylnopinol (**13**)[10] was treated in the dark with mercuric oxide and bromine in carbon tetrachloride at 0–5° to yield a solution of the hypobromite **14**;[19] brief irradiation of a filtered solution of **14** with a G. E. sunlamp led to rapid formation of the cyclic ether (**15**).[7] The ether was not isolated, but oxidized[20] directly to the lactone **16**, which was generally obtained in 25–35% overall yield from **13**. Reduction of lactone **16** gave diol **17** in high yield.



13 14 15 16 17

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[14] *Cf.* A. Mackor, Th. A. J. W. Wajer, and Th. J. de Boer, *Tetrahedron Lett.*, 2757 (1967), and references cited therein.

[15] H. Suginome, N. Sato, and T. Masamune, *ibid.*, 1557 (1967).

[16] *Cf.* F. Kaplan, C. O. Schulz, D. Weisleder, and C. Klopfenstein, *J. Org. Chem.*, **33**, 1728 (1968); R. B. Bates and V. P. Thalacker, *ibid.*, **33**, 1730 (1968).

[17] N. Nakagawa, S. Saito, A. Suzuki, and M. Itoh, *Tetrahedron Lett.*, 1003 (1967).

[18] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[19] *Cf.* R. A. Sneen and N. P. Matheny, *J. Amer. Chem. Soc.*, **86**, 5503 (1964). Ir and nmr spectral data indicated that the most of the oxide **15** was formed from **14** during the irradiation step which was run at 4–8°.

[20] G. Cainelli, B. Kamber, J. Keller, M. Lj. Mihailović, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **44**, 518 (1961).

The reactions reported here, and those described earlier,[7] make possible the facile production of novel 9-oxygenated pinanes. The only other known compound of this type is the naturally occurring glucoside, paeoniflorin.[21]

Experimental Section[22]

(+)-Nopinone (3).—(+)-Nopinone (**3**) was prepared from (−)-β-pinene (**1**) (Fritzsche Bros., Inc; $[\alpha]^{25}\mathrm{D}$ −17.5°; d^{26} 0.866) essentially by the ozonolytic method of Meinwald and Gassman;[9] bp 81–82° (10.5 mm); $[\alpha]^{24}\mathrm{D}$ +17.2° (neat) [lit.[9] bp 83–86° (12 mm); $[\alpha]^{25}\mathrm{D}$ +18.4° (neat)].

(−)-*cis*-Nopinol (4).—(−)-*cis*-Nopinol was prepared by lithium aluminum hydride reduction of (+)-nopinone (**3**) as described by Winstein and Holness:[11] mp 101–102°; $[\alpha]^{24}\mathrm{D}$ −10.7° (*c* 5, $CHCl_3$) [lit.[10] mp 101.5–102°; $[\alpha]^{18}\mathrm{D}$ −5.32° (*c* 6.5, Et_2O)].

(−)-*cis*-Nopinyl Nitrite (5).—A two-phase mixture containing 16.20 g (0.115 mol) of (−)-*cis*-nopinol (**4**) and 31.70 g (0.460 mol) of $NaNO_2$ in 40 ml of H_2O and 400 ml of Et_2O was protected from light, cooled to −8°, and maintained at this temperature during the addition, with vigorous stirring, of 22.5 g (0.230 mol) of concentrated H_2SO_4 in 25 ml of H_2O. The cooling bath was removed and stirring was continued at ambient temperature for 3.5 hr. After flushing the flask with N_2 to remove oxides of nitrogen, and addition of H_2O (200 ml), the aqueous layer was separated, extracted once with Et_2O (80 ml), and discarded. The combined ether solutions were washed with saturated $NaHCO_3$ solution and brine and dried over $CaSO_4$. Concentration at reduced pressure gave a light yellow liquid (18.9 g) which on distillation yielded 16.9 g of **5** (87%): bp 46–48° (1.8 mm); $[\alpha]^{28.5}\mathrm{D}$ −24.4° (*c* 22.6, cyclohexane), $[\alpha]^{28.5}\mathrm{D}$ −24.8° (*c* 55.2, $CHCl_3$); ir (neat) 1635 (s), 1598 (m), and 828 cm^{-1} (s); uv λ_{max} (cyclohexane) 327 (ϵ 28), 337 (ϵ 38), 347 (ϵ 54), 358 (ϵ 69), and 371 mμ (ϵ 67); nmr δ 0.98 (s, 3.5), 1.09 [s, 0.5 (low-field portion of d at δ *ca.* 1.04, J = 6–8 Hz)], 1.22 (s, 3), 1.4–2.8 (m, 7), and 5.86 [d (br), J = 11 Hz].

Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.28. Found: C, 64.16; H, 8.88; N, 8.06.

The distilled nitrite ester **5** is stable for prolonged periods when stored at −10° with an added trace of pyridine.

***cis* Dimer of 9-Nitroso-*cis*-nopinol (6).**—A solution of freshly distilled (−)-*cis*-nopinyl nitrite (**5**) (4.98 g, 0.0294 mol) in 550 ml of cyclohexane (Fischer, reagent grade) was purged with N_2 for 15 min and irradiated[13] for 60 min at *ca.* 10–20° using a Hanovia 450-W high-pressure mercury lamp mounted in a water-cooled Pyrex lamp-well. A white solid precipitated during the photolysis and was filtered, washed with cyclohexane, and dried in a vacuum dessicator at room temperature to yield 2.49 g of **6** (50%): mp 96.2–97.7°;[23] ir (Nujol) 3400 (s), 1203 (s), 1150 (s), 1025 (s), 1015 (s), and 978 cm^{-1} (s); uv λ_{max} 275 mμ (ϵ 9200);[14] nmr[24] δ 1.43 (s, 6), 4.35 (m, 2), 4.47 (d, 2, J = 13.5 Hz), and 5.03 (d, 2, J = 13.5 Hz).

Photolysis of crude undistilled nitrite **5** gave similar yields of **6**; optimum yields of *ca.* 60% from alcohol **4** were occasionally obtained.

(−)-*trans* Dimer of 9-Nitroso-*cis*-nopinol (7).—The *cis* dimer **6** (0.525 g) was dissolved in a minimal amount of $CHCl_3$ at room temperature, and petroleum ether (bp 89–94°) was added until the solution became faintly turbid. About one-third of the solvent was allowed to evaporate slowly at room temperature, yielding 0.237 g of crystalline *trans* dimer **7** (45%) having mp 136–138°. Several recrystallizations gave an analytically pure sample of **7**: mp 143–145°; $[\alpha]^{25}\mathrm{D}$ −173.5° (*c* 4.2, $CHCl_3$); ir ($CHCl_3$) 3350 (s), 1355 (s), 1180 (s), 1155 (s), 1010 (m), 985 (m), and 948 cm^{-1} (m); uv λ_{max} 293 mμ (ϵ 9600);[14] nmr δ 1.07 [d, 2, J = 8 Hz (upfield portion of an AB pattern with $\Delta\nu^{25}$ *ca.* 73 Hz)], 1.24 (s, 6), 4.35 (m, 2), and 4.84 and 4.46 (AB pattern, 4, J = 13.5 Hz).

Anal. Calcd for $C_{18}H_{30}N_2O_4$: C, 63.88; H, 8.93; N, 8.28. Found: C, 63.75; H, 9.00; N, 8.12.

(−)-(2*R*,6*S*)-6-Carboxaldehydo-6-methylbicyclo[3.1.1]heptan-2-ol Oxime (8).—The *cis* dimer **6** (9.00 g) was added in small portions to 600 ml of 2-propanol at 71°, allowing each portion to dissolve completely between additions; an intense blue color was noted to appear and fade rapidly after each addition. The solution was refluxed for 1.5 hr, cooled, and concentrated *in vacuo*. Trituration of the resulting oil with petroleum ether (bp 67–70°)–ethyl acetate (19:1) afforded 5.48 g of **8** (61%) as cream-colored crystals exhibiting mp 113–123°. An analytical sample was obtained after several recrystallizations from 2-propanol–petroleum ether (bp 66–70°): mp 129–131.5°; $[\alpha]^{25}\mathrm{D}$ −24.9° (*c* 2.0, $CHCl_3$); ir ($CHCl_3$) 3225 (s), 1065 (m), 1015 (m), and 965 cm^{-1} (s); nmr δ 1.37 (s, 3), 4.09 (m, 1), and 7.41 (s, 1).

Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.28. Found: C, 64.02; H, 9.08; N, 8.43.

(+)-(2*R*,6*S*)-2-Acetoxy-6-cyano-6-methylbicyclo[3.1.1]heptane (9).—The crude oily oxime **8** (8.52 g, 0.0504 mol) obtained by refluxing *cis*-nitroso dimer **6** in 2-propanol for 1 hr under nitrogen, was treated with 25 ml of pyridine and 20 ml of acetic anhydride at 60° for *ca.* 20 min. The reaction mixture was cooled to room temperature, allowed to stand for 5 hr, and heated again at 60° for 30 min. Water was added and the reaction mixture was cooled and extracted with several portions of diethyl ether. The combined extracts were washed successively with water, saturated $NaHCO_3$ solution, and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to yield an orange oil which appeared to contain about 80–90% of the diacetate of **8** (ir and nmr analysis). The oil was dissolved in 40 ml of acetic anhydride containing 2 g of sodium acetate, and the flask containing the resulting mixture was immersed in an oil bath kept at 95–100°. After heating for 1.25 hr with continual stirring, H_2O (200 ml) and pyridine (30 ml) were added and the reaction mixture was brought to room temperature and extracted with five small portions of $CHCl_3$. The extracts were washed successively with H_2O, 10% HCl (five times), H_2O, 5% Na_2CO_3 solution, and brine, dried, concentrated, and distilled at reduced pressure (0.07 mm) using a 6-in. Vigreux column. Four fractions and 0.84 g of pot residue were obtained: (1) 0.62 g, bp 48–68°; (2) 0.87 g, bp 69.5–79.5°; (3) 4.57 g, bp 81.5–118°; (4) 2.18 g, bp 114–165°. Fractions 2 and 3 each contained about 70% of acetoxy nitrile **9** (ir, nmr analysis); fraction 4 contained at least five components by tlc analysis. Upon cooling to 5°, fraction 3 yielded 1.38 g of **9** (14%) as heavy prisms having mp 40–43° (uncorrected). Four recrystallizations from *n*-hexane gave an analytical sample: mp 43–44° (uncorrected); $[\alpha]^{24}\mathrm{D}$ +83.3°; ir (CCl_4) 2240 (w), 1742 (s), and 1240 cm^{-1} (vs); nmr (CCl_4) δ 1.64 (s, 3), 2.04 (s, 3), and 5.08 (m, 1).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.19; H, 7.82; N, 7.46.

Treatment of 0.242 g of fraction 3 with 3 ml of 1.25 *N* KOH at reflux temperature for 13 hr under N_2 gave, after extraction with Et_2O (discarded) followed by acidification and extraction with CH_2Cl_2, 0.091 g of an oil which was nearly pure lactone **10** by ir, nmr, and glpc analysis.

9-Methyl-8-oxo-7-oxatricyclo[4.3.0.0^{3,9}]nonane (10).—A solution of crude oily oxime **8** (8.45 g, 0.050 mol) in 250 ml of reagent-grade acetone was cooled to 17° under N_2. Jones–Weedon reagent[18] was slowly added to the stirred solution during about 10 min until an excess of oxidant persisted in the solution for 3 min; the temperature of the reaction mixture was carefully maintained between 19 and 24° during the addition, which required 16.5 ml (132 mequiv) (corrected for blank titer) of oxidizing solution. Excess oxidant was destroyed by addition of 3 ml of 2-propanol, and the resulting mixture was diluted with H_2O (250 ml) and extracted with four portions of CCl_4. The combined extracts were washed with H_2O, saturated $NaHCO_3$ solution, and brine, dried ($MgSO_4$), and concentrated *in vacuo* to yield

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[21] S. Shibata, N. Aimi, and M. Watanabe, *Tetrahedron Lett.*, 1991 (1964); N. Aimi, M. Inaba, M. Watanabe, and S. Shibata, *Tetrahedron*, **25**, 1825 (1969).

[22] All boiling points are uncorrected. All melting points were taken on an Hoover capillary melting point apparatus and are corrected unless stated otherwise. Infrared spectra were obtained using a Perkin-Elmer Model 21 or Model 457 spectrophotometer. Nmr spectra were determined on *ca.* 20% solutions in $CDCl_3$ (unless indicated otherwise) using a Varian A-60A instrument; peak positions are reported in δ (parts per million) using tetramethylsilane at δ 0.00 as an internal standard. Ultraviolet spectra were determined on ethanol solutions using Cary Model 11 and Model 14 recording spectrophotometers. Specific rotations were determined using a Rudolph polarimeter. Microanalyses were performed by the Microanalytical Laboratory at the Institute of Physical Chemistry, Vienna, Austria, and by Galbraith Laboratories, Inc., Knoxville, Tenn. 37921.

[23] The melting point of **6** is not a good criterion of purity due to the tendency of **6** to undergo thermally induced isomerization. Attempts to recrystallize **6** yielded mixtures of **6**, **7**, and **8**.

[24] Run at 20°; the *cis* dimer **6** was converted into **7** to the extent of about 20% in 30 min under these conditions.

[25] Determined by spin-decoupling experiments.

6.19 g of crude lactone **10**. Distillation gave 4.32 g of pure **10** (57%) as a colorless oil: bp 57–60° (0.10 mm); $[\alpha]^{27.5}$D +92.3° (*c* 5.3, $CHCl_3$); ir (CCl_4) 1770 (vs), 1342 (s), 1220 (s), 1200 (s), 1144 (s), 1095 (s), 1065 (s), 1034 (s), 1005 (s), and 962 cm^{-1} (vs); nmr, see Table I. The analytical sample was obtained by glpc.[26]

Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.19; H, 8.10.

The yield of **10** in this preparation has been optimized; complex mixtures of products are obtained at temperatures 10–15° higher and lower than those stated.

(−)-9-Hydroxy-*cis*-nopinol (11).—Lactone **10** (4.32 g, 0.028 mol) in 20 ml of Et_2O was added to a suspension of lithium aluminum hydride (0.806 g, 0.021 mol) in 30 ml of Et_2O. The usual work-up yielded 3.2 g (73%) of nearly pure diol. An analytical sample was obtained by sublimation at 85° (bath) (0.1 mm): mp 100–116° (wax); $[\alpha]^{27.5}$D −31.3° (*c* 2.3, $CHCl_3$); ir ($CHCl_3$) 3620 (m), 3400 (s, br), 1070 (m), 1022 (s), and 985 cm^{-1} (m); nmr δ 0.92 (d, 1, J = 8.8 Hz), 1.30 (s, 3), 4.31 (br, d, 1, J = 9 Hz), and an AB pattern (J = 11.5 Hz) centered at δ 3.25 and 3.98.

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.38; H, 10.52.

Azoxy Compound 12.—The *cis* dimer **6** (1.68 g, 0.00493 mol) was dissolved in 300 ml of chloroform–acetone (1:4) and the solution was maintained at 0–5° while 3.95 ml (0.0316 equiv) of Jones–Weedon reagent[18] was slowly added. The solution was stirred for an additional 5 min, during which the orange color of the oxidant persisted, diluted with H_2O (160 ml), and extracted twice with $CHCl_3$. The organic layer was washed with saturated $NaHCO_3$ solution and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*, yielding 0.844 g (52%) of crude product having mp 160–165°. An analytical sample of **12** prepared by repeated recrystallization from chloroform–petroleum ether (bp 63–69°) exhibited mp 201–202°; ir ($CHCl_3$) 1705 (vs), 1495 (vs), and 1197 cm^{-1} (m); uv[27] λ_{max} 237 mμ (ϵ 7900); nmr[27] δ 1.37 (s, 3), 1.43 (s, 3), 3.20 (s, 2), and 3.86 (AB pattern, 2, J = 13 Hz and $\Delta\nu$ = 19.5 Hz).

Anal. Calcd for $C_{18}H_{26}N_2O_3$: C, 67.90; H, 8.23; N, 8.80. Found: C, 68.11; H, 8.51; N, 8.98.

(−)-2-Hydroxy-*trans*-pinane (13).[10]—(+)-Nopinone (**3**) (88.0 g, 0.64 mol) in 250 ml of diethyl ether was added during 2.75 hr to 250 ml of a stirred solution of 3 *N* methylmagnesium bromide in ether (Arapahoe) at 0–5°. The usual work-up followed by crystallization of the product from diethyl ether–petroleum ether (bp 63–69°) at −70° gave two crops of nearly pure alcohol **13** melting from 51.5–53.5° (uncorrected) [lit.[10] mp 58–59°]; yield 70.0 g (71%); nmr (CCl_4) δ 1.07 (s, 3) and 1.20 (s, 6).

(+)-6,9-Dimethyl-8-oxo-7-oxatricyclo$[4.3.0.0^{3,9}]$nonane (16).—A solution of alcohol **13** (52.6 g, 0.346 mol) in 750 ml of CCl_4 was stirred in the dark at 0–5° with 217 g of mercuric oxide while a solution of 19 ml of bromine (59.1 g, 0.37 mol) in 250 ml of CCl_4 was added over 1.3 hr. After stirring for 2.75 hr at 0–2°, an nmr spectrum of a portion of the solution exhibited signals at δ 1.02 (s, *ca.* 3) and 1.24 (s, *ca.* 6) believed to be due to the presence of hypobromite **14**.[19] The reaction mixture was rapidly filtered and maintained at 4–8° while being irradiated for 1.25 hr with a G. E. 200-W sunlamp placed 30 cm from the reaction flask; nitrogen gas was bubbled through the solution during irradiation to remove hydrogen bromide gas as it was formed. The solution was then refluxed for 1 hr and the final reaction mixture was cooled, washed with brine, dried (Na_2SO_4), and concentrated to yield a straw-brown oil which contained 60–70% of 2,8-epoxypinane (**15**),[7] as indicated by a comparison of the integrated area under the AB pattern (J = 8.8 Hz) centered at δ 3.25 and 3.74 with that of the remaining peaks in the nmr spectrum (CCl_4). Distillation at reduced pressure gave 30.4 g of oxide **15** (*ca.* 75% pure) as a yellow oil, bp 69–79° (40 mm); *ca.* 20 g of tarry residue remained in the pot. The crude oxide was dissolved in 200 ml of glacial acetic acid at 100° and a hot solution of CrO_3 (50.0 g, 0.50 mol) in water (60 ml) and glacial acetic acid (400 ml) was added[20] over 12 min, during which time the reaction temperature was allowed to drop gradually to 80°. After the temperature was raised to 100° during 15 min and the solution was stirred at 100–102° for 25 min, 50 ml of 2-propanol was added over *ca.* 10 min. The usual work-up procedure gave an orange oil which was fractionally distilled at reduced pressure to yield 5.04 g of **15**, bp 32–34.5° (0.1 mm), and 15.1 g of lactone **16** (26% from **13**), bp 51–54° (0.1 mm). The lactone **16** crystallized during the distillation yielding prisms: mp 38–40° 1 (uncorrected); $[\alpha]^{24}$D +40° (*c* 5.3, $CHCl_3$); ir (CCl_4) 1772 (s), 1077 (m), 1038 (m), and 932 cm^{-1} (m); nmr δ 1.37 (s, 3), 1.46 (s, 3), 1.68 (d, 1, J = 9.6 Hz), and 1.90 ("s," 4).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.45; H, 8.33.

2,9-Dihydroxy-*trans*-pinane (17).—A solution of lactone **16** (12.82 g, 0.0774 mol) in 50 ml of dry diethyl ether was added to a suspension of 2.2 g (0.058 mol) of lithium aluminum hydride in 250 ml of ether. The usual work-up procedure yielded 10.27 g of diol **17** (78%) as heavy bars, mp 83.5–85.0°. Two recrystallizations from petroleum ether (bp 37–39°) afforded an analytically pure sample of **17**: mp 84–85°; ir (CCl_4) 3340 (s), 1122 (s), and 1030 cm^{-1} (s); nmr (CCl_4) δ 1.00 (d, 1, J = 9.5 Hz), 1.26 (s, 3), 1.29 (s, 3), 4.10 (m, 1), and an AB pattern (J = 10.8 Hz) centered at δ 3.08 and 3.92.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.36; H, 10.58.

Registry No.—**5**, 21321-49-3; **6** (*cis*), 21339-83-3; **7** (*trans*), 21321-50-6; **8**, 21321-51-7; **9**, 21321-52-8; **10**, 21321-53-9; **11**, 21321-54-0; **12**, 21321-55-1; **13**, 21321-56-2; **16**, 271321-57-3; **17**, 21321-58-4.

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(26) A 10.5 ft × 0.25 in. aluminum column containing 5% G. E. cyanosilicone rubber (XE-60) on Anakrom ABS (60/70) was used.

(27) *Cf.* J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963); S. S. Hecht and F. D. Greene, *J. Amer. Chem. Soc.*, **89**, 6761 (1967).