Synthesis of the Bridgehead Ketol, 3,3-Dimethyl-1-hydroxynorbornan-2-one

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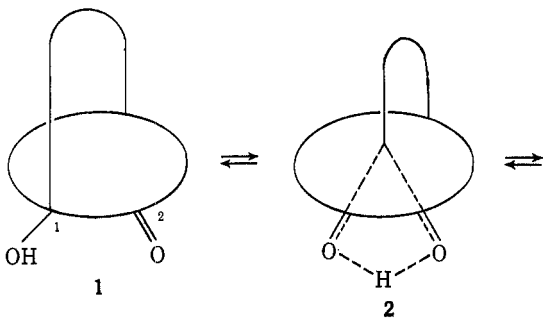
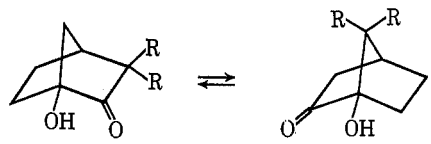
The objective was to synthesize and characterize 3,3-dimethyl-1-hydroxynorbornan-2-one (**5**) as an example of a bicyclo[2.2.1]heptyl bridgehead ketol potentially capable of interconversion with its 7,7-dimethyl analog (1-hydroxyapocamphor, **7**). Three different routes to **5** are described. The first involves the sequence 1-chlorocamphene (**9**) → 1-carboxycamphene (**12**) → 1-carboxycamphenilone (**13**) → 1-aminocamphenilone hydrochloride (**16**) → **5**. The second route involved Pd/C hydrogenation of 1-nitrocamphenilone (**20**) to 1-aminocamphenilone (**21**) followed by deamination to **5**. The third route consisted of 1-nitrocamphene (**19**) → 1-aminocamphene (**22**) → 1-acetoxycamphene (**23**) → 1-acetoxycamphenilone (**24**). Saponification of **24** provided a mixture, difficult to separate, of **5** and its rearranged isomer 1-hydroxyapocamphor (**7**). In alkali ketol **7** is favored over ketol **5** at equilibrium by a factor of 2 (at 31°).

α-Hydroxy carbonyl compounds (*e.g.*, ketols) are known for their ability to undergo rearrangements under cationic, anionic, and neutral conditions.[2] Recent publications have pointed out the potential usefulness of *bridgehead* ketols and their derivatives to probe skeletal rearrangements in bridged molecules, in which the stability and exact nature of the transition states and intermediates are perplexing problems.[3] Equation 1 illustrates in a schematic way neutral isomerization of ketol **1** to ketol **3** *via* a possible delocalized species **2**. The presence of the oxygens, their replacement by other heteroatoms, and replacement of the hydrogen by metals or other units could markedly alter the stability of bridged species and make them more amenable to study. Furthermore, ketols are convertible to their corresponding diols, amino alcohols, etc., whose specialized features makes them useful in mechanistic studies.[3b,c] Therefore, general and specific synthetic routes to bridgehead ketols are of current interest. The preparation of 1-hydroxynorbornan-2-one (**4**) has been achieved and its degenerate rearrangement (**4** ⇆ **6**) established.[3a] In this paper we describe the synthesis of 3,3-dimethyl-1-hydroxynorbornan-2-one (**5**, alternatively named 1-hydroxycamphenilone) by three routes. This substituted ketol is of interest because its rearrangement (to **7**, 1-hydroxyapocamphor) is not degenerate and the methyl groups can serve as markers for mechanistic studies of rates and equilibria.



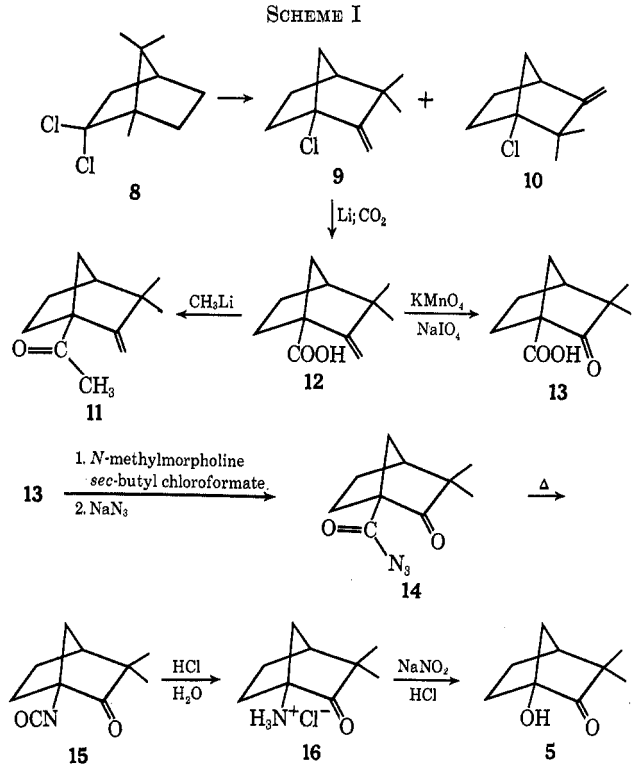
1 **2** **3** (1)



4, R = H
5, R = CH_3
6, R = H
7, R = CH_3

Our first route to the desired ketol **5** is summarized in Scheme I (absolute configurations are enantiomeric to

SCHEME I



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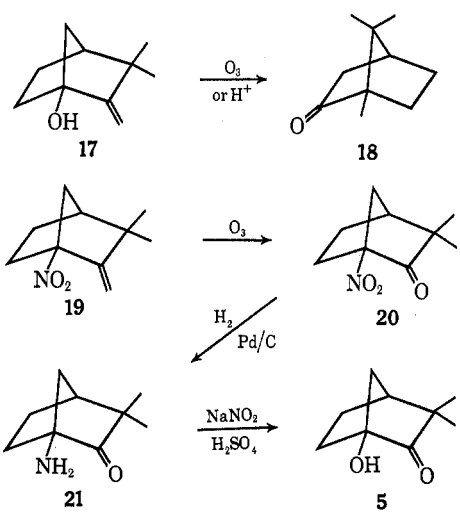
(2) (a) S. Selman and J. F. Eastham, *Quart. Rev., Chem. Soc.*, **14**, 221 (1960); (b) N. L. Wendler in "Molecular Rearrangements," P. de Mayo, Ed., Interscience, New York, N. Y., 1963, Chapter 16, p 1114.

(3) (a) A. Nickon, T. Nishida, and Y. Lin, *J. Amer. Chem. Soc.*, **91**, 6860 (1969); (b) A. Nickon and Y. Lin, *ibid.*, **91**, 6861 (1969); (c) Y. Lin and A. Nickon, *ibid.*, **92**, 3496 (1970).

those shown). The *gem*-dichlorocamphane **8** (obtained from camphor[4]) was converted to the known liquid chloro olefin **9** by treatment with potassium acetate in phenol. Although the product was in accord with the literature[4] and appeared homogeneous on gas chromatography, the nmr spectrum revealed the presence of *ca.* 16% of a by-product assigned structure **10** on the basis of its nmr characteristics. The formation of both olefins **9** and **10** are understandable in terms of ionization of a chlorine in **8** and conventional Wagner–Meerwein and Nametkin rearrangements prior to final proton loss.[5] Based on literature analogies,[6,7] the chloro olefin product was converted to the unsaturated acid **12** by means of lithium metal and carbonation. Acid **12** was further characterized by conversion to the methyl ketone **11** which is potentially useful for other transformations in this series, and which, along with **12**, showed expected ir and nmr spectral properties. Oxidation of **12** by the permanganate–periodate technique[8] gave keto acid **13**. The synthesis of **13** by another method has been described in the literature, but our melting point (106–107.5°) does not agree with the reported value (mp 135–136°).[9] The assigned structure (**13**) to our keto acid is supported by spectral and analytical data and was confirmed by subsequent transformations. A modified Curtius sequence[10] converted **13** to the crystalline amino ketone hydrochloride **16**, *via* the intermediate acyl azide **14** and isocyanate **15**, which were identified spectrally but were not separately characterized. Deamination of **16** was modeled on literature analogies[11] and gave the desired ketol 3,3-dimethyl-1-hydroxynorbornan-2-one (**5**), which was characterized by spectral and analytical data.

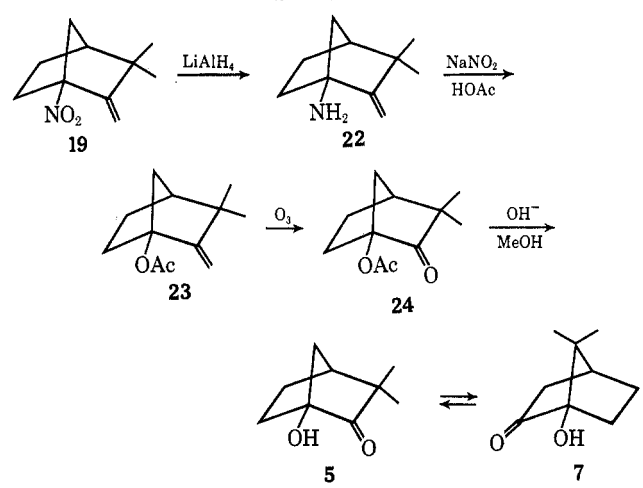
Our second and third routes to ketol **5** employed ozonolysis as a key step and had to take into account some specialized features of these bridged molecules.



Thus 30 years ago an attempt to ozonize hydroxy olefin **17** in cyclohexane gave the unexpected product, camphor (**18**).[12,13] This result seemed to be related to that observed earlier by Forster[14] in the rearrangement of **17** → **18** by acid. In contrast, ozonolysis of the nitro olefin **19** has been reported to proceed normally to **20**.[15] We prepared **20** by ozonolysis of **19** as reported[15] and the progress of this reaction was conveniently monitored by gas chromatography. Catalytic hydrogenation (Pd/C) converted **20** smoothly to the amino ketone **21**, which was characterized as its *p*-nitrobenzamide and which was deaminated to ketol **5**, identical (melting point, ir, nmr) with that prepared from our first route (Scheme I).

Since it seemed that an electron-attracting substituent at the bridgehead was advisable to preclude Wagner–Meerwein rearrangement on oxidation of a 2-methylene unit by ozone or by other electrophilic oxidants, our third route was designed as summarized in Scheme II. Reduction of nitro olefin **19** with $LiAlH_4$

SCHEME II



followed by deamination of the amino olefin **22** in acetic acid gave the acetoxy olefin **23** whose ir and nmr characteristics (*gem*-dimethyl, exocyclic C=CH_2) confirmed that no skeletal rearrangement had occurred during the deamination step. Ozonolysis of **23** proceeded without skeletal rearrangement to the keto acetate **24**. Alkaline hydrolysis of this keto acetate gave a mixture of the target compound **5** and its rearranged isomer **7** in a ratio *ca.* 1:2. These two ketols were separated by repeated preparative thin layer chromatography. The ir and nmr of ketol **5** obtained by this route were identical with those of **5** from the previous two routes. The structure of **7** was confirmed by direct comparison (ir, nmr) with an authentic sample separately synthesized by a reported method.[11a] The ease of the **5** ⇌ **7** ketol isomerization[16] and the difficulty in separating these isomers are decided drawbacks to this route.

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(11) (a) M. Ishidate and A. Kawada, *Chem. Pharm. Bull. (Tokyo)*, **4**, 483 (1956); (b) D. E. Applequist and J. P. Kliemen, *J. Org. Chem.*, **26**, 2178 (1961).

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(13) A somewhat different result has been reported recently in the ozonolysis of 1-hydroxycamphene in methanol: J. V. Paukstelis and B. W. Macharia, *Chem. Commun.*, 131 (1970).

(14) M. O. Forster, *J. Chem. Soc.*, **79**, 644 (1901).

(15) K. Ebisu, L. B. Batty, J. M. Higaki, and H. O. Larson, *J. Amer. Chem. Soc.*, **87**, 1399 (1965).

(16) Our kinetic studies showed that the apparent first-order rate constants in an aqueous solution buffered at pH 10 at 31° are 5.0×10^{-4} sec^{-1} for **5** → **7** and 2.5×10^{-4} sec^{-1} for **7** → **5**.

Experimental Section

General.—Melting points for compounds **8** to **16** were taken on a Thomas–Hoover apparatus and are corrected; those for compounds **19** to **24** were measured in a sulfuric acid bath and are uncorrected. Infrared spectra were recorded on Perkin–Elmer Model 337 grating and on Jasco Model IR-S spectrophotometers and band positions are expressed in cm^{-1}. Nuclear magnetic resonance spectra were recorded on a Varian Associates A-60 nmr spectrometer, with tetramethylsilane as an internal standard. Chemical shifts are expressed in ppm downfield from TMS (δ scale). Gas chromatograms were obtained with a Perkin–Elmer Model 226 instrument with a hydrogen flame ionization detector. Microanalyses were carried out by Mr. J. Walter of the Department of Chemistry at the Johns Hopkins University and by Miss N. Kameyama of the Shionogi Research Laboratory.

2,2-Dichlorocamphane (8).—A mixture of (+)-camphor (100 g, Eastman Organic Chemicals), phosphorus trichloride (85 g), and phosphorus pentachloride (147 g) was kept at 0° for 1.5 months. The reaction mixture was poured into 2 l. of crushed ice and vigorously stirred. An oily substance separated and solidified. The solid was collected, washed with cold water, and dried. Recrystallization of the gray product (120.4 g) from *n*-hexane gave pure 2,2-dichlorocamphane (**8**): 61.7 g, mp 148–150° dec (lit.[4] 146–148° dec); nmr (CCl_4) singlets at δ 1.05, 1.25, and 1.58, attributed to the three quaternary methyl groups.

1-Chloro-3,3-dimethyl-2-methylenenorbornane (9).—A mixture of 2,2-dichlorocamphane (15 g), anhydrous (fused) potassium acetate (13 g), and phenol (45 g) was heated at 170–180° for 20 min. The reaction mixture was made alkaline with concentrated sodium hydroxide solution and was distilled. The distillate was extracted with ether which was then washed with sodium hydroxide solution and water, dried over Na_2SO_4, and evaporated. Distillation of the residue gave 12.2 g (96%) of a colorless oil which partially solidified on standing: bp 88–89° (32 mm) [lit.[17] 74–75° (3.5 mm); lit.[4] 193–197° (760 mm); lit.[18] 72–73° (12 mm)]; nmr (CCl_4) δ 1.13 (s, 6, *gem*-dimethyl), 4.73 and 5.10 (both s, C=CH_2 of isomer **9**),[17] 4.59 and 4.76 (both s, C=CH_2 of isomer **10**). Integration of the olefinic protons indicated an 84:16 ratio of isomers **9** and **10**. The two isomers were not resolved on glpc (Golay MBMA; column 120°; block 170°; He pressure 20 psi), which showed only one peak, retention time 9.33 min.

1-Carboxy-3,3-dimethyl-2-methylenenorbornane (12).—The following procedure is modeled on a reported one.[7] Lithium (1.2 g, 0.16 g-atom) and Nujol (20 ml) were placed in a 125-ml, three-necked flask equipped with a stirrer, dropping funnel, and a reflux condenser protected with a drying tube. (The equipment was flamed, then purged with dry nitrogen for 0.5 hr before the lithium and Nujol were added.) The vigorously stirred oil was heated to a boil with a soft flame and the suspension of lithium sand so obtained was allowed to cool. The Nujol was removed by pipet under dry nitrogen and the lithium that remained was washed with three 20-ml portions of dry cyclohexane. A solution of 2.50 g (0.014 *m*) of the chloro olefin **9** (containing 16% of its isomer) in 10 ml of dry cyclohexane was added dropwise to a stirred suspension of the lithium sand in 20 ml of cyclohexane. The mixture was refluxed, vigorously stirred for 7 hr, and then allowed to cool. Carbon dioxide gas was dried by passage through concentrated H_2SO_4 and was then passed over the stirred mixture for 2.5 hr. The excess of lithium was decomposed by the addition of 20 ml of absolute ethanol, followed by 100 ml of water and 100 ml of ether. The mixture was acidified with hydrochloric acid and the layers were separated. The aqueous phase, after saturation with salt, was extracted with three 50-ml portions of ether. The combined ether layers were extracted with 10% aqueous sodium carbonate (three 50-ml portions), which was then acidified with hydrochloric acid, saturated with salt, and extracted with three 100-ml portions of ether. The ethereal extracts, dried over Na_2SO_4 and evaporated under reduced pressure, provided 2.5 g of an oil which solidified on standing. The crude carboxylic acid was purified by one sublimation (mp 58–76°) at 120° (8 mm) followed by one crystallization from *n*-hexane, mp 76–80.5°, some softening at 68°. Two recrystallizations gave 0.30 g of 1-carboxy 3,3-dimethyl-2-methylenenorbornane as plates: mp 81–82.5°; nmr ($CDCl_3$) δ 1.12 (s, 6, *gem*-dimethyl), 4.74 and 5.01 (both s, 1, C=CH_2), 11.65 (broad, s, 1, CO_2H); ir (CCl_4), 3300–2550 (OH), 1750 weak, 1700 strong (C=O), 1670, 895, and 898 (C=CH_2).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.40; H, 9.13.

1-Acetyl-3,3-dimethyl-2-methylenenorbornane (11).—A solution of the carboxylic acid **12** (0.11 g, 0.6 mmol) in dry ether (3 ml) was added dropwise at room temperature to a stirred solution made from commercial ethereal methyllithium (1 ml, 1.6 mmol, Foote Chemical Co.) and dry ether (2 ml). Methane was evolved immediately and after an additional 1 hr the mixture was poured onto crushed ice (50 g) and extracted with ether. The ether was washed with brine, dried with Na_2SO_4, and evaporated under vacuum, and left 0.075 g of oil comprised of 1-acetyl-3,3-dimethyl-2-methylenenorbornane (**11**) and a by-product, which is likely the tertiary alcohol corresponding to addition of methyllithium to the methyl ketone group: ir (neat) 3500 (OH), 1700 (C=O), 1650, 885 (C=CH_2); nmr (CCl_4) δ 1.12 (s, *gem*-dimethyl), 2.11 (s, $COCH_3$), 4.57 and 4.63 (both s, C=CH_2), as well as minor signals at δ 1.01, 1.06, 1.28, 4.67, and 4.95 attributed to the alcohol by-product. Glpc (Golay MBMA, column 150°, block 200°, He 20 psi) indicated a ratio of 79% of methyl ketone **11** (retention time 13.8 min) and 21% of the by-product (retention time 16.8 min). The pure 2,4-dinitrophenylhydrazone of the ketone was obtained by conventional procedures,[19a] mp 164–164.5° (ethanol).

Anal. Calcd for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.19. Found: C, 60.34; H, 6.25.

3,3-Dimethylnorbornan-2-one-1-carboxylic Acid (13).—Pure olefinic acid **12** (1.01 g, mp 81–83°, from pentane) in aqueous (50 ml) potassium carbonate (2.2 g) was treated with a solution of sodium metaperiodate (8.0 g) and potassium permanganate (0.6 g) in 100 ml of water. The mixture was stirred 1 day at room temperature and was acidified with dilute hydrochloric acid. Extraction with ether (two × 100-ml portions), drying with Na_2SO_4, and evaporation gave the crude keto acid which was purified by column chromatography on silica gel with ether eluent to give 0.71 g of solid. Crystallization from benzene–pentane yielded 0.46 g, mp 104–106° (sealed tube). The analytical sample was obtained after repeated recrystallization from benzene–pentane: mp 106–107.6° (lit.[9] mp 135–136°); ir ($CHCl_3$) 3500–2500 (broad, bonded COOH), 1760 (ketone), 1720 (CO_2H); nmr ($CDCl_3$) δ 1.12 (s, 3, CH_3), 1.17 (s, 3, CH_3), 9.08 (broad s, 1, CO_2H).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.90; H, 7.80.

1-Amino-3,3-dimethylnorbornan-2-one Hydrochloride (16) *via* Modified Curtius Reaction.[10]—A stirred solution of the keto acid (0.46 g) in dry tetrahydrofuran (10 ml) was cooled to −30° (Dry Ice–acetone bath) and this temperature was maintained throughout the reaction. To this solution was added dropwise a solution of *N*-methylmorpholine (0.26 g) in dry tetrahydrofuran (8 ml) followed by 0.35 g of *sec*-butyl chloroformate in 8 ml of the same solvent. The mixture was stirred an additional 1 hr and was treated with sodium azide (0.19 g) in 8 ml of water. After an additional 1 hr, the stirred mixture was brought to room temperature, poured into 100 ml of water, and extracted with ether (two 80-ml portions). The ethereal extract was washed with saturated $NaHCO_3$ to remove unchanged acid and then with brine and was dried over $CaCl_2$. The solvent was evaporated through a $CaCl_2$ drying tube under reduced pressure without heat to give the azido ketone **14** as a slightly yellow oil: ir (CCl_4) 2130, 1750, 1700.

The azide was converted to the isocyanate by 1-hr reflux in 60 ml of dry benzene. An aliquot was evaporated under reduced pressure and the residue in CCl_4 showed strong ir absorptions centered at 2235 and 1760, but very little at 2130 and 1700.

To the benzene solution of the isocyanate **15** was added 30 ml of 10% hydrochloric acid. The mixture was refluxed gently and stirred vigorously for 17 hr, and the benzene layer was separated and washed with 10 ml of water. The aqueous solutions were combined and evaporated to dryness *in vacuo* to give 0.40 g (85.5%) of solid, which was recrystallized from absolute methanol–absolute ether to give 0.34 g of 1-amino-3,3-dimethylnorbornan-2-one hydrochloride (**16**) as needles: mp 195.5–196.5° dec; ir (KBr) 3500–2400 (broad, N–H), 1730 (C=O).

(17) H. G. Richey, Jr., J. E. Grant, T. J. Garbacik, and D. L. Dull, *J. Org. Chem.*, **30**, 3909 (1965).

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Anal. Calcd for $C_9H_{16}ClNO$ (189.69): C, 56.98; H, 8.50; N, 7.39. Found: C, 57.23; H, 8.74; N, 7.15.

3,3-Dimethyl-1-hydroxynorbornan-2-one (5).—A solution of 0.7 g of sodium nitrite in 10 ml of water was added dropwise to a stirred solution of 0.33 g of the amino ketone hydrochloride (**16**) in 20 ml of 5% hydrochloric acid cooled in an ice bath. The cold mixture was stirred for 1 hr, allowed to come to room temperature, and stirred an additional 11 hr. The resultant mixture was neutralized with $NaHCO_3$ and extracted continuously with ether for 19 hr. The ethereal extract, dried over Na_2SO_4, was evaporated, and the crude oil was purified by column chromatography on silica gel with a mixture of pentane–ethyl ether (2:1) as eluent: 0.10 g of crystalline 3,3-dimethyl-1-hydroxynorbornan-2-one (**5**); mp 60–64°; ir (CCl_4) 3150 (OH), 1745 (C=O); nmr (CCl_4) δ 1.09 (s, 6, *gem*-dimethyl), 2.87 (broad s, 1, OH). Repeated recrystallization from pentane gave the analytically pure sample, mp 67.5–68°, as needles.

Anal. Calcd for $C_9H_{14}O_2$ (154.20): C, 70.10; H, 9.15. Found: C, 70.01; H, 9.17.

1-Nitro-3,3-dimethylnorbornan-2-one (20).[15]—Ozonolysis of **19** was carried out by a procedure modeled on one reported.[20] Oxygen gas containing ozone was bubbled into a stirred and ice-cooled solution of 2.70 g (0.0149 mol) of nitro olefin **19**, mp 53–53.5° (lit.[21] mp 54° and 56°[14]), in 100 ml of dichloromethane. The treatment was continued until the glpc peak of **19** (diethylene glycol succinate polyester column 15%; 100 × 0.3 cm; column temperature 150°; He pressure 1.0 kg/cm²; retention time 2.8 min for **19** and 23.6 min for **29**) completely disappeared (about 2 hr). The solution was washed with three 100-ml portions of 5% potassium iodide–acetic acid (9:1) solution. The resulting pink solution was washed successively with 1% aqueous sodium thiosulfate, aqueous sodium bicarbonate, and water, dried over Na_2SO_4, and evaporated under reduced pressure. Recrystallization of the crude crystals from *n*-hexane gave a first crop of 2.2 g (80.6%) of **20**, mp 98.5–100° (lit.[15] mp 96–97.2°), and a second crop of 0.25 g (9.1%), mp 91–94°, ir ($CHCl_3$) 1765 and shoulder at 1755 (C=O) 1540 and 1375 (NO_2).

1-Amino-3,3-dimethylnorbornan-2-one (21).—Hydrogen was absorbed rapidly by a solution of 1.29 g (7.1 mmol) of **20** and 1.30 g of 5% paladium on carbon in 60 ml of methanol and ended after 3 equiv mol of hydrogen was taken up. After separation of the catalyst, the methanol solution was evaporated under reduced pressure and left a partially solidified viscous oil, whose ir ($CHCl_3$) showed strong absorption at 1740 but no $-NO_2$ bands. The *p*-nitrobenzamide of **21** prepared as usual[19b] had mp 111–113°.

Anal. Calcd for $C_{16}H_{18}N_2O_4 \cdot H_2O$: C, 59.99; H, 6.29; N, 8.75; H_2O, 5.62. Found: C, 59.89; H, 6.27; N, 8.84; H_2O, 5.78.

1-Hydroxy-3,3-dimethylnorbornan-2-one (5).—The oily amino ketone obtained above was dissolved in 15 ml of cold 5% sulfuric acid and to this ice-cooled, stirred solution was added dropwise a solution of 2.92 g (42.4 mmol) of sodium nitrite in 5 ml of water.[22] After nitrogen evolution had subsided, the ice-cooled solution was stirred for 45 min and was extracted with two 100-ml portions of ether. The ether was washed successively with a solution of concentrated hydrochloric acid (5 ml) in saturated sodium chloride (20 ml), saturated sodium bicarbonate (5 ml), and saturated sodium chloride (30 ml). Evaporation of the dried (Na_2SO_4) ether left a yellow, viscous oil (1.01 g) which was taken up in *n*-pentane and the soluble portion was concentrated to 100 ml. A crystal seed was added and the solution was stored at −20° overnight. Ketol **5**, 0.34 g (31%), mp 66.5–67.5,° was obtained in the first crop, and a second crop (0.076 g, 6.9%) had mp 64–66°. The ir and nmr spectra were virtually identical with those exhibited by the ketol **5** prepared as described earlier.

1-Amino-3,3-dimethyl-2-methylenenorbornane (22).—To a stirred solution of 2.8 g of $LiAlH_4$ in 150 ml of ether was added dropwise a solution of 6.5 g (0.036 mol) of nitro olefin **19** in 50 ml of ether. Gentle reflux occurred throughout the addition, after which the reaction mixture was refluxed for 30 min and was then added in portions to ether saturated with water. The resulting mixture was poured into a solution of 50 ml of concentrated hydrochloric acid in 500 ml of ice–water. The water layer was poured into an ice-cooled solution of 150 g of potassium hydroxide in 110 g of water. The resulting cloudy solution was extracted twice with ether, dried over potassium hydroxide, and evaporated to give 3.0 g of a viscous oil used in the next step without further purification. A portion of this amino olefin was distilled at 20 mm (free flame) to give a translucent solid, mp 46.5–47.5° (lit. mp 46°[14]).

3,3-Dimethyl-1-acetoxy-2-methylenenorbornane (23).—Sodium nitrite (2.9 g, 0.042 mol) was added portionwise to a stirred ice-cooled solution of 2.9 g (0.019 mol) of the amino olefin in acetic acid (100 ml). After an additional 1 hr at room temperature, the reaction mixture was added in portions to a 10% aqueous potassium carbonate solution and extracted with ether. The ether was washed with a solution of 4 ml of concentrated hydrochloric acid in 40 ml of ice–water and then twice with water, dried over Na_2SO_4, and evaporated. Distillation yielded 1.2 g (32%) of a fraction, bp 115–118° (31 mm), $n^{24}D$ 1.4703, a 0.25-g fraction, bp 80° (2 mm), and 0.2 g of undistilled residue. The original amino olefin (*ca.* 0.5 g) was recovered from the acidic and aqueous wash layers: ir (neat) 1740 (C=O), 1665, 885 (C=CH_2); nmr ($CDCl_3$) δ 1.11 (s, 6, *gem*-dimethyl), 2.07 (s, 3, $OCOCH_3$), 4.66 and 4.76 (each s, 1, C=CH_2).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.25; H, 9.36.

3,3-Dimethyl-1-acetoxynorbornan-2-one (24).—An oxygen stream containing ozone was bubbled through a stirred ice-cooled solution of 3.35 g (0.0172 mol) of **23** in 200 ml of dichloromethane for 4 hr and the resulting stirred solution was decomposed by the successive addition of 20 ml of acetic acid, 4.0 g of zinc dust, and 1 ml of water. After a similar work-up as in the case of **20**, the reaction mixture gave a partially crystallized oil (2.6 g) which was purified by silica gel chromatography and elution with 4:1 petroleum ether–ether, 0.91 g (27%), mp 51–54°. The analytical sample had mp 54–55°: ir ($CHCl_3$) 1760 (shoulder), 1740; nmr (CCl_4) δ 1.04 and 1.13 (each s, 3, *gem*-dimethyl), 2.04 (s, 3, $OCOCH_3$).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.42; H, 8.28.

Hydrolysis of Ketol Acetate 24.—A solution of 0.67 g of **24** and 0.5 g of potassium hydroxide in 30 ml of methanol and 3 ml of water was refluxed for 30 min. The resulting solution was poured into saturated aqueous sodium chloride and extracted with two 100-ml portions of ether. The ether was dried over Na_2SO_4 and evaporated to yield a translucent solid which was subjected to preparative thin layer chromatography (20 × 100 cm plate) on Kieselgel G nach Stahl, with ether as solvent. The positions of **5** and **7** on the glass plate could be detected by the difference in the speed of getting wet (slower) and getting dry (faster) when sprayed with water, compared with the regions where **5** and **7** were not concentrated. The regions in which the two ketols were concentrated were divided into six parts, and from the lowest part 15 mg of **5**, mp 64–65°, was obtained by extraction with MeOH–ether (4:1) followed by evaporation under reduced pressure. This ketol contained less than 5% of the isomer **7** by comparison of the nmr (CCl_4) peak area ratio of the corresponding *gem*-dimethyl protons at δ 1.06 (s, 6) for **5** and a pair of singlets at 0.83 (3, anti CH_3) and at 1.08 (3, syn CH_3) for **7**. The ir and nmr spectra were virtually identical with those exhibited by ketol **5** prepared as described above. Ketol **7** (80 mg) extracted from the highest part by the same procedure was dissolved in ether, dried with Na_2SO_4, and concentrated under reduced pressure to give crystals: mp 164–166° (lit.[11a] mp 153°); ir ($CHCl_3$) 3500 (OH), 1745 (C=O); nmr (CCl_4) δ 1.08 (s, 3, syn CH_3), 0.83 (s, 3, anti CH_3), 2.95 (broad s, 1, OH). These spectral data were identical with those of an authentic sample obtained by a reported method.[11a]

Registry No.—**5**, 27694-11-7; **11**, 27694-12-8; **11** 2,4-DNP, 27694-13-9; **12**, 10309-20-3; **13**, 469-74-9; **16**, 27694-16-2; **21** *p*-nitrobenzamide, 27694-17-3; **23**, 26417-60-7; **24**, 27694-19-5.

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