position of the rings is involved and compounds **1**, **2**, and **3** were identified by their relatively simple nmr spectra.

The direction of addition in **4**, **5**, **12**, and **13** was decided by the absence of terminal methyl group protons in their nmr spectra, which would have been present had the addition taken place in the opposite direction.

The monoaddition product of the reaction of butadiene with NM-2-Py showed the presence of both cis (675 cm^{-1}) and trans (966 cm^{-1}) double bonds. It was also identified by the nmr spectrum of its hydrogenated analog **6**. The diadduct of the reaction was also identified in the same fashion. The monoaddition products from the reaction of isoprene with NM-2-Py and NM-2-Pi were found by vpc and nmr to be a mixture of both head- and tail-addition products in an approximate ratio of 15:85. The assignment of the structures are based on an earlier report.[12] They were confirmed by hydrogenating the double bonds and studying the nmr of the saturated analogs.

Acknowledgment.—The authors wish to thank Dr. B. Stipanovič for active participation in the discovery of the described reactions.

Registry No.—**1**, 21053-47-4; **2**, 21053-48-5; **3**, 29883-83-8; **4**, 29883-84-9; **5**, 29883-85-0; **6**, 29883-86-1; **7**, 29883-87-2; **8**, 29883-88-3, **9**, 29883-89-4; **10**, 29969-85-5; **11**, 29883-90-7; **12**, 29883-91-8; **13**, 29969-86-6; **14**, 29883-92-9; **15**, 29883-93-0; NM-2-Py, 875-20-4; NM-2-Pi, 931-20-4.

Stereospecific Syntheses of the Seven Dimethylcycloheptanes[1a]

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Unequivocal stereospecific syntheses of the seven possible dimethylcycloheptanes are reported. Separate preparation of the two (inseparable) 1,4 isomers to assure isomer purity involved synthetic problems of special interest.

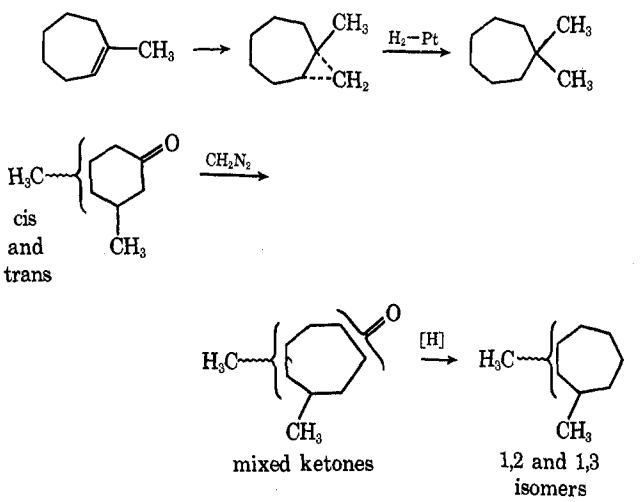
In order to apply experimental tests to the theoretical predictions about the conformational behavior of seven-membered rings,[2,3] we required stereochemically pure samples of the seven possible dimethylcycloheptanes. Inasmuch as the likelihood of reasonable separation of cis and trans isomers was remote, we were obliged to synthesize each one separately by an unambiguously stereospecific route. The four 1,2 and 1,3 isomers could be prepared by diazomethane ring expansion of the appropriate dimethylcyclohexanones, which were known. In order to eliminate the possibility of epimerization, none of the dimethylcyclohexanones were acceptable with methyl α to the ketone. For this reason the 1,4-dimethylcycloheptanes required other syntheses, and these presented an interesting problem in unequivocal stereospecificity. The *cis*-4,4-dimethylcycloheptane was created by cleaving a 1,4 bridge across a cycloheptane ring (Scheme II). The trans 1,4 isomer was created by initial synthesis of an authenticated 1,4-cis derivative followed by SN2 displacement of one substituent by a methyl anion (Scheme III).

While our work was in progress, a report appeared on the preparation of the dimethylcycloheptanes by diazomethane ring expansion.[4] We felt, however, that their preparations did not satisfy our needs for purity and unambiguous stereochemistry. The 1,2 isomers were separated chromatographically, but their relative stereochemistry was not independently assigned. The 1,4 isomers, inseparable chromatographically, may have involved epimerization in the ring expansion. Since their physical properties for the 1,4 isomers are completely identical,[4] only different chemical routes can guarantee their purity.

Our routes to the 1,1, 1,2, and 1,3 isomers are shown in Scheme I. The cyclopropane route to the *gem*-dimethyl compound is briefer than ring expansion.[5] The commercial *cis*- and *trans*-3,4-dimethylcyclohexanones were purified and confirmed first as to identity by Clemmensen reduction and vpc comparison with authentic samples of the two 1,2-dimethylcyclohexanes. The *cis*- and *trans*-1,2-dimethylcycloheptanes produced from them (Scheme I) were identical in vpc retention time with the two components (4:1 = cis:trans) of the mixture formed on hydrogenation of 1,2-dimethylcycloheptenes. The latter was a mixture of three isomeric olefins produced by the action of methyllithium on 2-

SCHEME I

PREPARATION OF THE FIVE 1,1-, 1,2-, AND 1,3-DIMETHYLCYCLOHEPTANES



(1) (a) Financial Assistance from the National Institutes of Health (Grant No. GM-10714) is gratefully acknowledged; (b) taken from the doctoral thesis of R. K. B., National Institutes of Health Predoctoral Fellow, 1969–1970.

(2) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **89**, 7036, 7043, 7047 (1967).

(3) The results of these experiments are being prepared for publication.

(4) G. Mann, M. Mühlstädt, R. Müller, E. Kesn, and W. Hadeball, *Tetrahedron*, **24**, 6941 (1968).

(5) C. W. Woodworth, V. Buss, and P. v. R. Schleyer, *Chem. Commun.*, 569 (1968).

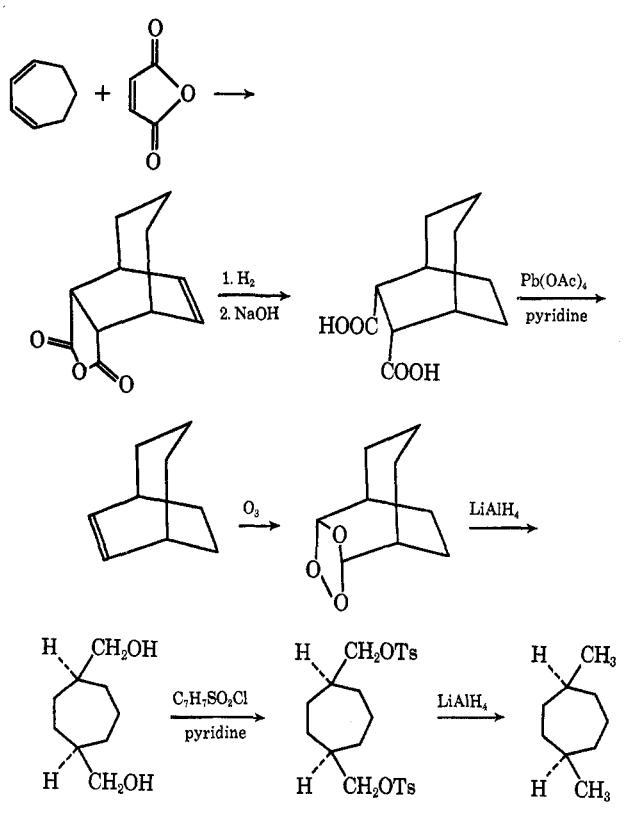
methylcycloheptanone followed by iodine dehydration.[6]

For the 1,3 isomers, the commercial mixture of 3,5-dimethylcyclohexanones served as a source of pure cis ketone *via* its crystalline oxime[7] and pyruvic acid regeneration. The trans ketone was prepared by conjugate addition of methylmagnesium iodide to 5-methyl-2-cyclohexenone,[8] a reaction previously shown to give essentially pure trans isomer by an independent synthesis.[9] These ketones were then separately ring enlarged and reduced (Scheme I).

The 1,4 isomers presented a much more serious synthetic challenge since hydrogenation of 1,4-dimethylcycloheptene produced a mixture inseparable by preparative vpc and hardly resolved in analytical vpc. The synthetic scheme elected for the stereospecific synthesis of the cis isomer depended on bridging cycloheptadiene with a two-carbon bridge *via* the Diels–Alder reaction and then cleaving this unequivocally cis bridge, as outlined in Scheme II. Cycloheptadiene[10] was allowed to react with maleic anhydride[11] and the adduct was hydrogenated and saponified. Treatment with lead tetraacetate and pyridine at 60° led to vigorous evolution of carbon dioxide and produced an olefin with a two-proton doublet at τ 3.83 (J_1 = 8.5, J_2 = 3 cps) in the nmr spectrum. This olefin was ozonized at −78° and the crude ozonide reduced directly to a diol with lithium aluminum hydride; the viscous diol exhibited a four-proton doublet at τ 6.69 (J = 5 cps). The corresponding ditosylate was crystalline and reduced to pure *cis*-1,4-dimethylcycloheptane.

SCHEME II

SYNTHESIS OF *cis*-1,4-DIMETHYLCYCLOHEPTANE



To obtain two functional groups across a seven-membered ring, we relied on cleavage of a bicyclic system. The two groups, hydroxymethylene and epoxide, were shown to be cis through their interaction, and the epoxide was displaced by methyl (Scheme III). Creation and cleavage of the bicyclooctanone to 4-cycloheptenecarboxylic acid was reported by Stork,[12] and reduction of the crystalline acid yielded the unsaturated alcohol exhibiting in the nmr spectrum a two-proton multiplet at τ 4.31 (olefin) and a two-proton doublet at τ 6.63 (hydroxymethylene).

Epoxidation yielded a mixture of hydroxy epoxides in a favorable ratio (72:28 = cis:trans) owing presumably to hydrogen-bonded assistance to cis approach of the peracid.[13] Assignment of relative configuration, as well as separation of the pure cis isomer, was achieved by treatment with toluenesulfonic acid in boiling benzene, which converted the trans isomer cleanly to a bicyclic ether without affecting the cis isomer. The cis isomer, separated by chromatography and refluxed with dimethylmagnesium[14] in dioxane,[15] was transformed into the diol, characterized in the nmr spectrum by a three-proton doublet at τ 8.97 (J = 5 cps), a three-proton multiplet at τ 5.87–7.15 (−CH_2OH + −CHOH), and a two-proton singlet at τ 7.37 (−COH). The subsequent tosylation and reduction was carried out without intermediate isolation and afforded pure *trans*-1,4-dimethylcycloheptane.

All seven hydrocarbons were shown to be >98% pure by vpc analysis and exhibited mass spectra or elemental analyses consistent with C_9H_{18}. Their detailed nmr spectra will be reported elsewhere.[3]

Experimental Section[16]

1-Methylbicyclo[5.1.0]octane.—Active Zn·Cu[17] dried/vac/-P_2O_5 overnight. 20 g (305 mmol) suspended/150 ml anhyd Et_2O; several crystals/I_2 added, stirred to color discharge. Mixture of CH_2I_2 (79 g, 295 mmol) and 1-methylcycloheptene (Aldrich Chemical Co.) (27.5 g, 250 mmol) added, heated, and stirred. Monitored/vpc (5 ft 3% SE-30/75°): 84% conversion after 72 hr reflux. Cooled, filtered, washed residues 2×/Et_2O and combined Et_2O with satd aq NH_4Cl (100 ml), then aq $NaHCO_3$ and H_2O. Dried, evap Et_2O/room temp and distilled oil/24-in. Teflon spinning band column. Major = 17 g (55%) 1-methylbicyclo[5.1.0]octane, bp 149–150°, $n^{21.5}D$ 1.4580, 98% pure vpc (3% SE-30/75°). Ir (λ_{max}) 3.21, 3.37, 7.24, 9.78, 11.43 μ; nmr (τ) 7.57–8.33 (m, 10), 8.95 (s, 3), 9.30–9.92 (m, 3).

(6) Rearrangement to 1-methyl-1-vinylcyclohexane has been reported[4] in this dehydration, but we observed none of this product.

(7) J. von Braun and W. Haensel, *Ber.*, **59**, 1999 (1926).

(8) J. P. Blanchard and H. L. Goering, *J. Amer. Chem. Soc.*, **73**, 5863 (1951).

(9) (a) N. L. Allinger and C. K. Riew, *Tetrahedron Lett.* 1269 (1966); (b) N. L. Allinger, *J. Amer. Chem. Soc.*, **81**, 5727 (1959).

(10) A. C. Cope and L. L. Estes, *ibid.*, **72**, 1128 (1950).

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(13) H. B. Henbest, *Proc. Chem. Soc., London* 159 (1963).

(14) P. D. Bartlett and C. M. Berry, *J. Amer. Chem. Soc.*, **56**, 2683 (1934).

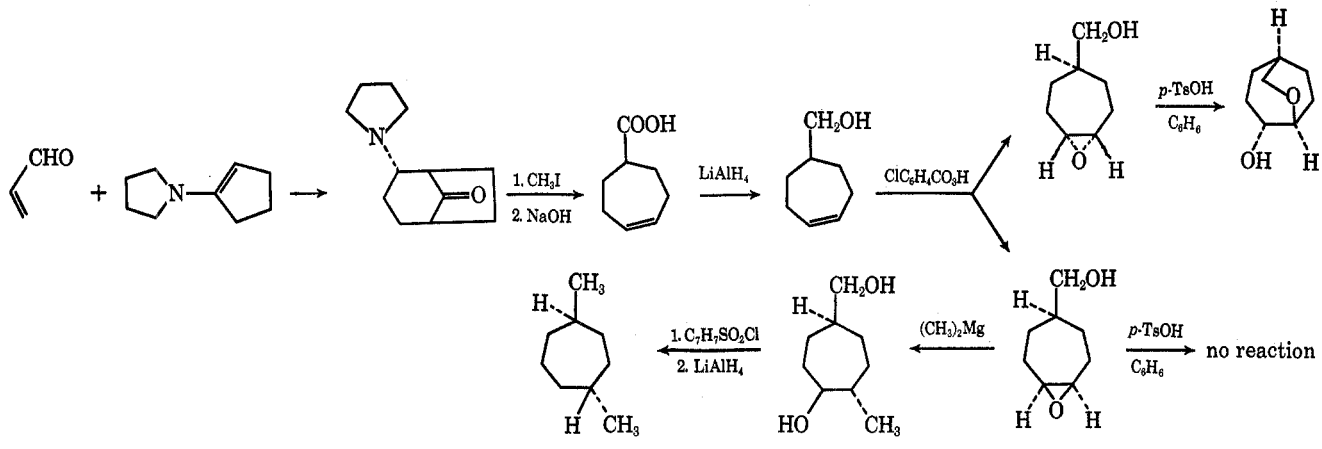
(15) B. G. Christiansen, R. G. Strackan, N. R. Trenner, B. H. Arison, R. Hirschmann, and J. M. Chemerda, *ibid.*, **82**, 3995 (1960).

(16) Melting points were determined on a Fisher-Johns apparatus and are accurate to within ±1.0°; boiling points are uncorrected. The ir spectra were determined on Perkin-Elmer 137 or DR-69 spectrophotometers, solid samples in KBr, liquids as neat films unless otherwise noted. All nmr spectra were determined on Varian A-60D instrument, in CCl_4 or $CDCl_3$ solution unless otherwise noted and reported in "τ (multiplet size, no. of hydrogens, coupling constant)." Mass spectra were determined on the AEJ MS-12 mass spectrometer, purchased under NSF research instrument Grant No. GP-3644. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(17) H. Simmons and R. Smith, *Org. Syn.*, **41**, 72 (1961).

SCHEME III

SYNTHESIS OF *trans*-1,4-DIMETHYLCYCLOHEPTANE



Anal. Calcd for C_9H_{16}: C, 87.02; H, 12.98. Found: C, 87.11; H, 12.88.

1,1-Dimethylcycloheptane.—1-Methylbicyclo[5.1.0]octane (1.24 g, 10 mmol) in 25 ml glac HOAc, added 224 mg PtO_2 and shook/H_2/60 psi 48 hr. Filtered, diluted/H_2O (200 ml), extracted 3×/hexane (25 ml). Hexane soln washed/aq $NaHCO_3$, dried and evap. Distillation of residue gave 900 mg (71%) 1,1-dimethylcycloheptane, bp 147–148°, $n^{24}D$ 1.4416 (lit.[4] bp 152°, $n^{20}D$ 1.4439), 98% pure (vpc as above). Ir (λ_{max}) 3.43, 6.93, 7.23, 7.35 μ; nmr (τ) 8.25–8.78 (m, 12), 9.07 (s, 6).

Anal. Calcd for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85.40; H, 14.37.

***cis*-3,4- (and 4,5-) Dimethylcycloheptanones.**—*cis*-3,4-Dimethylcyclohexanone (Chemical Samples Co.) (17.2 g, 136 mmol) in 70 ml of 95% EtOH + 5 ml H_2O. Added Diazald (Aldrich Chemical Co.) (32.1 g, 150 mmol), cooled to 0–5°/ice-salt. Slow mechanical stirring and dropwise addition of soln/KOH (5 g, 75 mmol) in 15 ml 1:1 H_2O–EtOH. Temp <10° (50 min). Stirred 30 min more, added concd HCl (10 ml), then added soln/KOH (15 g) in 40 ml H_2O and refluxed 1 hr. Diluted/300 ml H_2O, extracted 3×/hexane (75 ml). Combined extracts washed (H_2O, dil HCl, dried and evap to oil. Vpc (as above) showed 75% conversion to two products. Teflon spinning band distillation yielded 1.4 g starting ketone, bp 74–76° (12 mm), mixed fractions and 8.22 g of ~1:1 mixture of product dimethylcycloheptanones, bp 91–95° (12 mm) (47%). Ir (λ_{max}) 3.37, 5.83, 7.23 μ.

***cis*-1,2-Dimethylcycloheptane.**—Mixture/last preparation (8.2 g, 58 mmol) added to 42.5 g (650 mmol) mossy Zn amalgam.[18] Added soln: concd HCl (20 ml), H_2O (10 ml), glac HOAc (20 ml). Refluxed stirred 24 hr. Additional 10 ml portions/HCl every hour/1st 4 hr. Cooled, diluted/H_2O, extracted 2×/hexane (75 ml). Washed hexane/H_2O, 10% aq NaOH dried, and evap. Residual liquid distilled: major = 4.68 g (62%) *cis*-1,2-dimethylcycloheptane, bp 157–159°, containing 10% *trans*/vpc (above). Preparative vpc (20 ft 30% SE-30/125° at 150 ml flow): retention times = cis, 60 min; trans, 47 min. Pure *cis*-1,2-dimethylcycloheptane: bp 161°, $n^{24.5}D$ 1.4481 (lit.[4] bp 161°, $n^{20}D$ 1.4491). Ir (λ_{max}) 3.37 3.40, 6.86, 7.21 μ; nmr (τ) 8.0–9.0 (m, 12), 9.17 (d, 6, J = 6 cps).

Anal. Calcd for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85,41; H, 14.20.

***trans*-3,4- (and 4,5-) Dimethylcycloheptanones.**—*trans*-3,4-Dimethylcyclohexanone (Chemical Samples Co.) fractionated/Teflon spinning band column to 99% pure (vpc, above) ketone, $n^{24.5}D$ 1.4451; 2,4-DNP (rexld/EtOH), mp 132–134°. Ketone (33.2 g, 290 mmol) in EtOH (50 ml) + H_2O (10 ml) and added Diazald (Aldrich Chemical Co.) (63 g, 290 mmol), cooled to 0°/ice-salt. As above with KOH (12 g in 40 ml 1:1 EtOH–H_2O) and work-up. Distillation as above yielded 4.14 g recovered starting ketone and 14.51 g (45%) of product dimethylcycloheptanone mixture (~1:1), which was redistilled, bp 81–85° (6–8 mm), $n^{24.5}D$ 1.4594, >98% pure (vpc). Ir (λ_{max}) 3.40, 6.84, 7.25, 7.29, 11.57 μ.

***trans*-1,2-Dimethylcycloheptane.**—As with the *cis*-dimethylcycloheptanones above, the trans mixture (13.2 g, 95 mmol) was reduced with fresh mossy Zn amalgam[18] in 50 ml 75% aq HOAc + 70 ml concd HCl for 18 hr/reflux. Similar work-up afforded *trans*-1,2-dimethylcycloheptane (6.38 g, 53%), bp 154–155°, $n^{23}D$ 1.4461 (lit.[4] bp 157°, $n^{20}D$ 1.4439). Ir (λ_{max}) 3.45, 6.85, 7.27, 7.33 μ; nmr (τ) 7.67–9.00 (m, 12), 9.04 (d, 6, J = 6 cps). Purity >99% vpc.

Anal. Calcd for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85.42; H, 14.27.

***cis*-3,5-Dimethylcyclohexanone.**—3,5-Dimethylcyclohexanone (Aldrich Chemical Co.) (4:1 = cis:trans/vpc on 20% SE-30/75) converted to oxime with H_2NOH·HCl and 10% NaOH. Crystalline oxime[7] washed/H_2O, dried. Oxime (55 g, 390 mmol) in 800 ml 50% aq HOAc, pyruvic acid (320 g, 3.64 mol) added and refluxed 18 hr. Cooled, diluted/H_2O (950 ml), extracted 3×/hexane (350 ml). Hexane washed/aq $NaHCO_3$, aq NaCl, dried, and evap. Distillation of residue gave 37.4 g (77%) *cis*-3,5-dimethylcyclohexanone, bp 86° (33 mm), $n^{24}D$ 1.4407 (lit.[7] $n^{20}D$ 1.4407). Ir (λ_{max}) 3.36, 3.42, 5.80, 7.25, 7.33 μ. Purity >99%/vpc.

***cis*-3,5-Dimethylcycloheptanone.**—*cis*-3,5-Dimethylcyclohexanone (36.0 g, 280 mmol) in EtOH (100 ml) + H_2O (8 ml) and added Diazald as before (64.2 g, 300 mmol). Same procedure afforded 5.36 g recovered starting ketone and 19.71 g (58%) of *cis*-3,5-dimethylcycloheptanone, bp 94–96° (44 mm), $n^{23.5}D$ 1.4532 (lit.[19] $n^{23}D$ 1.4524), 98% pure/vpc (20% SE-30/70°). Ir (λ_{max}) 3.32, 5.79, 7.19, 7.26 μ; nmr (τ) 7.30–7.90 (m, 4), 7.90–8.78 (m, 6), 9.03 (d, 3, J = 5 cps), 9.03 (d, 3, J = 6 cps). Semicarbazone, mp 163–164° (aq MeOH) (lit.[19] mp 165.7–166.6°).

***cis*-1,3-Dimethylcycloheptane.**—*cis*-3,5-Dimethylcycloheptanone semicarbazone (1.0 g, 5.1 mmol) was fused with 5 g KOH in a short-path still and distillate collected at 120°. Distillate in Et_2O washed/10% HCl, 5% $NaHCO_3$, dried, and evap to clear oil (237 mg, 37%). Further purified by passing through silica gel in petrol (20–40°) and distillation to *cis*-1,3-dimethylcycloheptane, bp 151°, $n^{21}D$ 1.4410 (lit.[4] bp 153°, $n^{20}D$ 1.4408), >99% pure/vpc (3% SE-30/85°). Ir (λ_{max}) 3.42, 6.87, 7.29, 7.35 μ; nmr (τ) 9.13 (d, 6, J = 6.5 cps).

Anal. Calcd for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85.51; H, 14.21.

***trans*-3,5-Dimethylcyclohexanone.**—5-Methylcyclohex-2-en-1-one, prepared by ref 8, had bp 82° (30 mm), $n^{20}D$ 1.4745 (lit.[8] 1.4739), 2,4-DNP mp (MeOH) 148–150° (lit.[8] 152°). This ketone (8.8 g, 80 mmol) in Et_2O (100 ml) added dropwise/10–12° to metal-free Grignard from 2.46 g (100 mmol) Mg + 17.1 g (120 mmol) CH_3I + 100 mg Cu_2Cl_2. After addition, refluxed 1.5 hr and stirred overnight. Soln decomposed with ice + 12 g glac HOAc, extracted/Et_2O. Et_2O washed/5% $NaHCO_3$, aq NaCl, dried, and evap to yellow oil. Distillation gave 7.27 g (72%) *trans*-3,5-dimethylcyclohexanone, bp 78–80° (25 mm), $n^{25}D$ 1.4474 (lit.[9] 1.4467), contaminated with 9% cis isomer by vpc (3% SE-30/85°), 2,4-DNP mp (EtOH) 108–109° (lit.[9] 109–110°). The pure trans isomer was originally prepared by recovery from the ring enlargement (next procedure), but later

(18) Amalgamation/Zn: 2 short washings s/5% HCl, then shaken/$HgCl_2$ (10% by weight of Zn) in 10× (w/v) volume/H_2O.

(19) N. L. Allinger, *J. Amer. Chem. Soc.*, **81**, 232 (1959).

could be separated (>99% pure/vpc) by careful spinning band distillation.

trans-**3,5-Dimethylcycloheptanone.**—Ring enlargement procedure as with the other isomers: 22.2 g (176 mmol) pure *trans*-3,5-dimethylcyclohexanone, 40.8 g (190 mmol) Diazald, 5.3 g (94 mmol) KOH, and addition over 2 hr/10–15°. Final oil distilled to a fraction 60–100° (20 mm) which was redistilled/spinning band column to 5.25 g (28%) *trans*-3,5-dimethylcycloheptanone, bp 89–91° (10 mm), n^{23}D 1.4573 (lit.[19] 1.4572), >99% pure/vpc, and 5.43 g recovered *trans*-3,5-dimethylcyclohexanone. Product ir (λ_{max}) 3.38, 5.85, 6.85, 7.25, 7.39, 7.99, 8.48, 12.24 μ; nmr (τ) 7.17–8.60 (m, 10), 9.05 (d, 6, J = 6 cps); semicarbazone, mp (aq MeOH) 163.5–164° (lit.[19] mp 164.5–165.5°).

trans-**1,3-Dimethylcycloheptane.**—Clemmensen reduction on *trans*-3,5-dimethylcycloheptanone (4.8 g, 34 mmol) with 22 g (343 mmol) fresh Zn·Hg[18] as for 1,2-dimethylcycloheptanes above. Product oil passed through silica gel column in petrol (20–40°) and distilled to 2.17 g (50%) *trans*-1,3-dimethylcycloheptane, bp 147–148°, n^{23}D 1.4476, >98% pure/vpc (3% SE-30/85°). Ir (λ_{max}) 3.37, 6.81, 7.22, 7.25 μ; nmr (τ) 7.69–9.00 (m, 12), 9.14 (d, 6, J = 6 cps).

Anal. Calcd for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85.91; H, 14.30.

Bicyclo[3.2.2]nonane-2,2-dicarboxylic Acid.—Unsaturated analog (Scheme I), prepared by ref 11 (4.30, 22.4 mmol), in 50 ml 4:1 glac HOAc–Ac_2O. Added PtO_2 (430 mg) and stirred/H_2 (1 atm) until theoretical uptake. Filtered and evap/vac. Residue in $CHCl_3$ washed/H_2O, 5% $NaHCO_3$, dried, and evap to 4.36 g pale yellow solid, rexld 2×/petrol (60–110°) to saturated anhydride, mp 136–138°. Ir (λ_{max}) 3.37, 3.45, 5.35, 5.59, 8.08, 8.22, 9.28, 10.96, 10.53, 13.22 μ; nmr (τ) 6.70 (s, 2), 7.48 (m, 2), 7.83–8.55 (m, 10).

The anhydride (3.18 g, 16.4 mmol) suspended in 75 ml 10% aq NaOH and stirred/room temp until dissolved, cooled/ice and acidified to pH 1/concd HCl. Thick ppt filtered, washed/H_2O, and air-dried to 3.13 g (90%) of bicyclo[3.2.2]nonane-2,3-dicarboxylic acid. Although used without further purification, rexln/acetone gave mp 133–135° (hydrate) (lit.[11] 132–134°). Ir (KBr; λ_{max}) 2.9–4.0, 5.83, 8.14 μ; nmr (τ) 4.28 (s, broad, 2) due to hydrate, 6.99 (s, 2), 7.52 (m, 2), 8.00–8.77 (m, 10).

Bicyclo[3.2.2]non-2-ene.—Bicyclo[3.2.2]nonane-2,3-dicarboxylic acid (2.89 g, 13.6 mmol) suspended in 48 ml dry C_6H_6 under N_2. Dry pyridine (1.62 g, 20.6 mmol) added, then 688 mg (13.6 mmol) 90% $Pb(OAc)_4$ with stirring. Clear yellow soln heated/50°, gas evolved vigorously, and temp rose to 60–65°. Then refluxed 2 hr, cooled, filtered, washed/H_2O, 5% $NaHCO_3$, 10% HCl, and aq NaCl, and dried. Solvent carefully removed/room temp/vac to red oil. Chromatography/silica gel in petrol (20–40°); first 100 ml eluate evap at or below room temp to 550 mg (33%) bicyclo[3.2.2]non-2-ene, mp 67–69° (subl). Ir (λ_{max}) 6.05, 14.18 μ; nmr (τ) 3.83 (dd, z, J = 3, 8.5 cps), 7.58 (m, 2), 7.83–8.90 (m, 10); m/e 122 (parent ion).

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.40; H, 11.77.

cis-**1,4-Bis(hydroxymethylene)cycloheptane.**—Bicyclo[3.2.2]-non-2-ene (488 mg, 4.0 mmol), in 50 ml CH_2Cl_2 cooled to −78° and ozonized until excess O_3 showed in KI trap. Soln dried and evap to gum and placed in extraction thimble. $LiAlH_4$ (1.9 g, 50 mmol) suspended in 100 ml dry THF and refluxed in soxhlet overnight (no residue in thimble). Diluted/Et_2O and decomposed/H_2O (2 ml), 15% NaOH (2 ml), and H_2O (6 ml). White ppt filtered and washed/Et_2O. Soln evap to 609 mg (96%) *cis*-1,4-bis(hydroxymethylene)cycloheptane as pale yellow oil, pure by tlc (EtOAc). Distillation to clear, viscous liquid, bp 120–122°. Ir (λ_{max}) 2.98, 3.43, 9.40, 9.70, 9.93 μ; nmr (τ) 6.23 (s, 2), 6.27–6.95 (m, 4), 7.72–9.42 (m, 12). Bis-3,5-dinitrobenzoate prepared and xld 2×/EtOH to mp 158–160°.

Anal. Calcd for $C_{23}H_{22}N_4O_{12}$: C, 50.55; H, 4.06. Found: C, 50.68; H, 3.97.

cis-**1,4-Bis(tosyloxymethylene)cycloheptane.**—Diol/last preparation (600 mg, 3.8 mmol) in 5 ml dry pyridine. Cooled to 0° and added 3.2 g (16.8 mmol) freshly rexld TsCl in 20 ml pyridine, dropwise. Yellow soln stood 72 hr/6°, then poured onto ice–concd HCl (10 ml) and extracted 3×/Et_2O. Et_2O soln washed/50% HCl (2×), H_2O, dried ($MgSO_4$–K_2CO_3), and evap to pale yellow oil which xld from petrol (20–40°) at −78° to 828 mg (47%) of ditosylate. Ir (λ_{max}) 6.23, 8.40, 8.50, 9.12 μ. Rexld/Et_2O–petrol to mp 78.5–79.5°.

Anal. Calcd for $C_{23}H_{30}S_2O_6$: C, 59.22; H, 6.48. Found: C, 59.28; H, 6.55.

cis-**1,4-Dimethylcycloheptane.**—*cis*-Ditosylate (last preparation) (16.3 g, 35 mmol) in 75 ml dry THF and added dropwise to stirred suspension of $LiAlH_4$ (12.16 g, 320 mmol) in 100 ml THF. After addn, refluxed 6 hr, cooled, diluted/Et_2O, and decomposed/H_2O, NaOH, filtered, washed/Et_2O. Et_2O soln dried and evap to clear oil which was passed through silica gel in petrol (20–40°). First 100 ml of eluate evap to 313 mg *cis*-1,4-dimethylcycloheptane, bp 153°, n^{20}D 1.4395 (lit.[4] on mixed 1,4 isomers: bp 154°, n^{20}D 1.4398). Ir (λ_{max}) 3.39, 3.42, 6.90, 7.27, 7.35 μ; m/e 126 (parent ion); purity >99%/vpc.

5-Hydroxymethylcycloheptene.—Cyclohept-4-enecarboxylic acid[13] (280 mg, 2.0 mmol) in 19 ml Et_2O added dropwise rapidly to suspension of 152 mg (4.0 mmol) $LiAlH_4$/25 ml Et_2O and refluxed 1 hr. Excess decomposed/H_2O, NaOH and salts filtered, washed/Et_2O. Et_2O dried and evap to 212 mg (84%) 5-hydroxymethylcycloheptene as clear oil, bp 98–99° (20 mm). Ir (λ_{max}) 2.9–3.1, 3.29, 3.42, 6.01, 14.35 μ; nmr (τ) 4.31 (t, 2, J = 3 cps), 5.90 (s, 1), 6.63 (d, 2, J = 6 cps), 7.33–9.33 (m, 9).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.01; H, 11.35.

Epoxidation of 5-Hydroxymethylcycloheptene.—5-Hydroxymethylcycloheptene (1.015 g, 8.05 mmol) in 15 ml C_6H_6 cooled to 5°/ice and added 1.82 g (9.0 mmol) 85% *m*-chloroperbenzoic acid/30 ml C_6H_6 dropwise. To room temp, stirred overnight. Soln washed/10% NaOH, dried, and evap to mixed epoxides, oil, 709 mg (62%). Vpc (Carbowax 20M/156°) = 72:28 mixture/epoxides and 1.4% bicyclic ether-alcohol (below). On prep vpc (20 ft 30% SE-30/180°) minor component completely converted to bicyclic ether-alcohol.

Epoxide mixture (1.04 g, 7.04 mmol) in 20 ml C_6H_6 and 100 mg *p*-TsOH refluxed 2 hr to complete conversion vpc. Soln washed/10 NaOH, H_2O, dried, and evaporated to 987 mg, separated by silica gel chromatography/EtOAc. First eluate = *cis*-5-hydroxymethylcycloheptene oxide, bp 85–86° (0.5 mm). Ir (λ_{max}) 2.83, 3.44, 9.26, 9.59, 9.92, 10.84, 11.55, 12.44 μ; nmr 6.68 (d, 2, J = 5 cps), 6.87 (d, 2, J = 5 cps), 7.33–9.40 (m, 9); m/e 142 (parent ion).

Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.38; H, 9.94.

Second eluate, 2-hydroxy-7-oxabicyclo[3.2.2]nonane crystallized on evaporation. Sublimed/70° (20 mm) to mp 130° (subl); ir (λ_{max}) 2.92, 3.42, 9.54 μ; nmr (τ) 5.83–6.73 (m, 4), 6.93 (s, 1), 7.50–9.17 (m, 9).

Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.27; H, 10.17. 3,5-Dinitrobenzoate (EtOH) mp 136–137°.

trans-**2-Methyl-*cis*-5-hydroxymethylcycloheptanol.**—Soln/$(CH_3)_2Mg$ in Et_2O[15] and solvent exchanged for dry dioxane (same white ppt), approx 1 mmol/ml. To 30 ml soln added dropwise 1.42 g (10.0 mmol) *cis*-epoxy alcohol (above) in 10 ml dry dioxane and refluxed (101°) for 44 hr. Cooled, decomposed excess carefully with satd NH_4Cl solution, diluted/H_2O and extracted/Et_2O (8 × 50 ml). Et_2O dried and evap to pale yellow oil (1.49 g, 94%), one spot/tlc. Distillation yielded *trans*-2-methyl-*cis*-5-hydroxymethylcycloheptanol, bp 118° (0.5 mm). Ir (λ_{max}) 2.95, 3.41, 6.87, 9.51, 10.00 μ; nmr (τ) 5.87–7.15 (m, 3), 7.37 (s, 2), 7.58–9.48 (m, 10), 8.97 (d, 3, J = 5 cps); m/e 158 (parent ion).

trans-**1,4-Dimethylcycloheptane.**—Diol above (475 mg, 3.0 mmol) in 15 ml dry pyridine and added 2.30 g (12.0 mmol) freshly rexld tosyl chloride and left at 6°/44 hr. Diluted/H_2O and extracted/Et_2O. Et_2O washed/1:1 HCl, H_2O, and dried over K_2CO_3–Na_2SO_4, and evaporated to 1.306 g (93%) oil which could not be crystallized and decomposed on silica gel chromatography, but ir and nmr in accord with expectation. Oil dissolved in 5 ml dry DME, added to suspension of 550 mg (15 mmol) $LiAlH_4$ in 15 ml DME, and refluxed 24 hr. Excess decomposed/H_2O and sais dissolved/10% HCl. Extracted/Et_2O, dried, and evaporated carefully to oil and passed through silica gel in petrol (20–40°). First 100 ml/eluate evaporated and distilled to 61 mg *trans*-1,4-dimethylcycloheptane, bp 152°, n^{23}D 1.4381. Ir (λ_{max}) 3.39, 3.42, 6.87, 7.28, 7.35 μ; m/e 126 (parent ion); purity >99%/vpc.

Registry No.—1-Methylbicyclo[5.1.0]octane, 13388-61-9; 1,1-dimethylcycloheptane, 13151-49-0; *cis*-3,4-dimethylcycloheptanone, 29584-58-5; *cis*-4,5-dimethylcycloheptanone, 29584-59-6; *cis*-1,2-dimethylcycloheptane, 13151-51-4; *trans*-3,4-dimethylcycloheptanone, 29577-66-0; *trans*-4,5-dimethylcyclohep-

tanone, 29577-67-1; *trans*-1,2-dimethylcycloheptane, 13151-50-3; *cis*-1,3-dimethylcycloheptane, 13151-53-6; *trans*-1,3-dimethylcycloheptane, 13151-52-5; bicyclo[3.2.2]nonane-2,2-dicarboxylic anhydride, 29577-71-7; bicyclo[3.2.2]non-2-ene, 7124-86-9; *cis*-1,4-bis(hydroxymethylene)cycloheptane, 29577-72-8, 29577-73-9 (bis-3,5-dinitrobenzoate); *cis*-1,4-bis(tosyloxymethylene)-cycloheptane, 29577-74-0; *cis*-1,4-dimethylcycloheptane, 14190-15-9; 5-hydroxymethylcycloheptene, 17328-87-9; *cis*-5-hydroxymethylcycloheptene oxide, 29577-76-2; 2-hydroxy-7-oxabicyclo[3.2.2]nonane, 17328-88-0, 29577-78-4 (3,5-dinitrobenzoate); *trans*-2-methyl-*cis*-5-hydroxymethylcycloheptanol, 17328-91-5; *trans*-1,4-dimethylcycloheptane, 13151-54-7.

The Synthesis and Stereochemistry of the Four Isomeric Pinane-2,3-diols

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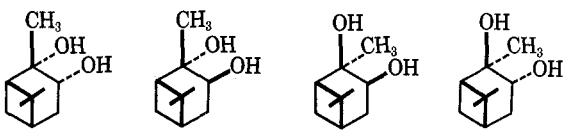
The synthesis of the four possible pinane-2,3-diols, **1–4**, is described and rigorous stereochemical assignments are made. Several anomalous reactions were observed in which an attacking species reacts preferentially on the pinane ring system from the same side as the *gem*-dimethyl bridge.

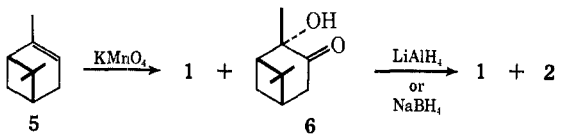
In connection with our study of the base-catalyzed rearrangement of 2,3-pinanediol monotosylates,[3] we required synthetic routes to the four possible pinane-2,3-diols **1–4**. At the time this study was initiated,



1 **2** **3** **4**

two of these diols (**1** and **2**) had been reported in the literature but there was confusion and disagreement as to the stereochemistry of these diols.[4–9] We have presented evidence which clarified the stereochemistry of these diols[10] and these assignments have been independently confirmed by other workers.[11–13]

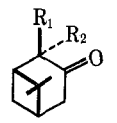
Diols 1 and 2.—Oxidation of α-pinene (**5**) with potassium permanganate under neutral conditions gives a modest yield of the ketol **6**, whereas oxidation



5 **6**

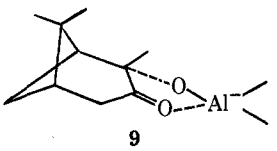
under basic conditions gives the diol **1** in low yield. None of the diol **3** can be detected by spectral methods or by thin layer chromatography (tlc) in the crude product from this reaction. Thus, the reaction of **5** with permanganate ion is highly stereoselective and the attack of the oxidant occurs from the side opposite the *gem*-dimethyl bridge. The expectation that attack of external reagents on the pinane skeleton should occur from this direction has been widely used in assigning stereochemistry to various pinane derivatives, but, as will be shown below, it is not an unfailing guide to stereochemical assignments in this system.

Because the metal hydride reduction of both isopinocamphone (**7**) and pinocamphone (**8**) have been



7, R_1 = Me; R_2 = H
8, R_1 = H; R_2 = Me

reported[14] to be highly stereoselective with attack of the reagent from the side opposite the *gem*-dimethyl bridge, it was expected that the reduction of ketol **6** with lithium aluminum hydride ($LiAlH_4$) would give mainly diol **2**. Surprisingly, this reduction produced the readily separable diols **1** and **2** in the ratio 54:46. Two previous reports of the reduction of ketol **6** with $LiAlH_4$ had claimed that only diol **2** was produced,[6,15] whereas Suga[8] reports that diols **1** and **2** are formed in the ratio 63:37 in reasonable agreement with our results. This seemingly anomalous stereochemical result might be rationalized by assuming that a complex of the type **9** is formed. In such a complex C-3 is pulled



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downward in order to obtain coplanarity in the five-membered complex ring and molecular models indicate that in such an arrangement attack of hydride from the top side would be favored. In order to determine

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