5-Phenyl-2,4-hexanedione (**11**, R = CH_3) was prepared by the condensation of 2-phenylpropionyl chloride[16] and *t*-butyl acetoacetate effected by sodium.[17] The product was refluxed with *p*-toluenesulfonic acid in toluene. The mixture was neutralized with sodium bicarbonate and filtered. The toluene was evaporated and the residue was distilled to afford 54% of product, bp 129–139° (13 mm). The copper chelate was recrystallized from ethanol, mp 153–154°.

Anal. Calcd for $C_{24}H_{26}CuO_4$: C, 65.21; H, 5.93; Cu, 14.38. Found: C, 65.48; H, 6.03; Cu, 14.34.

The diketones **3–8** and **10** (R = CH_3) were made by condensing the respective monoketones and esters by means of sodium amide[18] in ether as described previously.[19] There were two new β-diketones formed by this method. Ethyl propionate was condensed with 3-methyl-2-butanone to afford 2-methyl-3,5-heptanedione (**5**) in 29% yield. After the usual isolation procedure,[19] **5** was further purified by extraction into aqueous base and acidification of the aqueous solution; the product was redistilled, bp 75–78° (20 mm). The copper chelate melted at 148–149° after recrystallization from methanol.

Anal. Calcd for $C_{16}H_{26}CuO_4$: C, 55.55; H, 7.52; Cu, 18.38. Found: C, 55.53; H, 7.28; Cu, 18.15.

Ethyl propionate was condensed with pinacolone to afford 2,2-dimethyl-3,5-heptanedione (**8**) in 31% yield, bp 86–88° (25 mm). The copper chelate melted at 119.5–121° after recrystallization from methanol.

Anal. Calcd for $C_{18}H_{30}CuO_4$: C, 57.81; H, 8.08; Cu, 16.99. Found: C, 58.03; H, 7.88; Cu, 17.16.

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[16] S. P. Bakshi and E. E. Turner, *J. Chem. Soc.*, 171 (1961).

[17] See R. L. Shriner, A. G. Schmidt, and L. J. Roe, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p 266.

[18] Lithium amide was used in the preparation of 2,6-dimethyl-3,5-heptanedione (**7**) as described by H. D. Murdock and D. C. Nonhebel, *J. Chem. Soc.*, 2153 (1962).

[19] J. T. Adams and C. R. Hauser, *J. Am. Chem. Soc.*, **66**, 1220 (1944); R. Levine, J. A. Conroy, J. T. Adams, and C. R. Hauser, *ibid.*, **67**, 1510 (1945). Compounds **6** and **10** (R = CH_3) were prepared by Dr. J. T. Adams

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Synthesis of 4-Substituted 1,1-Dimethyl-*trans*-2-decalones *via* Conjugate Addition of Grignard Reagents

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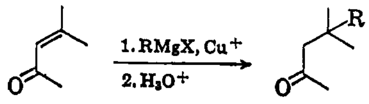
1,1-Dimethyl-*trans*-3-octal-2-one (**7a**) was prepared and used to study the stereochemistry of the cuprous ion catalyzed 1,4 addition of Grignard reagents to α,β-unsaturated ketones as a function of the bulk of the organomagnesium compound. The synthesis involved methylation of 1(9)-octal-2-one (**1**) followed by reduction of the resulting 1,1-dimethyl-8-octal-2-one (**2**) first with lithium aluminum hydride and then with hydrogen over a platinum catalyst. The alcohol obtained from this sequence gave 1,1-dimethyl-*trans*-2-decalone (**5a**) upon oxidation and this ketone afforded the required octalone **7a** *via* bromination and dehydrobromination. Methylmagnesium iodide afforded principally the 1,4 adduct, 1,1,4α-trimethyl-*trans*(10β-H)-2-decalone (**10**), in which the newly introduced methyl group is axially oriented. With isopropylmagnesium bromide a nearly 1:1 mixture of the isomeric, 1,4 adducts was obtained from octalone **7a**. Phenylmagnesium bromide afforded 1,1-dimethyl-4β-phenyl-*trans*(10β-H)-2-decalone (**19**) in which the newly introduced phenyl group possesses the equatorial conformation.

The cuprous ion catalyzed addition of Grignard reagents to α,β-unsaturated ketones constitutes a useful method for introducing an alkyl group to the β-position of a ketone (*e.g.*, I → II).[2] Information concerning the stereochemistry of this reaction is available from recent reports which deal with the addition of methylmagnesium iodide to Δ^1-3-keto steroids.[3] The major product can be related to the starting unsaturated ketone in each instance[4] by assuming the Grignard reagent attacks the least hindered face of the double bond to give a 1,4 adduct in which the new carbon–carbon bond possesses an axial conformation. Other studies not related to steroids support this picture of the reaction.[5]



I

II

Stereoelectronic factors may also play a part in the mechanism of conjugate addition to unsaturated ketones by Grignard reagents.[6] The results cited above could be explained satisfactorily according to this postulate, although a simple kinetic argument based upon steric hindrance of the double bond would serve equally well.

Because of our interest in its possible application to natural products synthesis we undertook a study of the alkylation reaction exemplified by I → II. We were particularly concerned with three points: (1) the relative importance of stereoelectronic factors; (2) the relationship between the size of the Grignard reagent and the stereochemistry of 1,4 addition; and (3) the effect of the cuprous ion catalyst on the stereochemistry of 1,4 addition.

We chose 1,1-dimethyl-*trans*-3-octal-2-one (**7a**, Chart I) as the substrate for these studies. This octalone seemed particularly appropriate for the following reasons. (a) The *trans*-fused rings offer a rigid, conformationally unambiguous system. (b) Yields of 1,4 adducts should be high because the conjugated double bond is relatively exposed and the *gem*-dimethyl group should hinder 1,2 addition. (c) The pathway leading to axial introduction of the alkyl group at the β carbon appears (from inspection of Dreiding models) more hindered than the alternative pathway leading to

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[1] National Science Foundation Predoctoral Fellow, 1964–1965.

[2] *Cf.* M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, pp 196–238; H. O. House, D. D. Traficante, and R. A. Evans, *J. Org. Chem.*, **28**, 348 (1963).

[3] (a) R. Wiechert, U. Kerb, and K. Kieslish, *Chem. Ber.*, **96**, 2765 (1963); (b) W. J. Wechter, *J. Org. Chem.*, **29**, 163 (1964); (c) H. Mori, *Chem. Pharm. Bull.* (Tokyo), **10**, 386 (1962).

[4] For a recent structure revision, see W. J. Wechter, G. Slomp, F. A. MacKellar, R. Weichert, and U. Kerb, *Tetrahedron*, **21**, 1625 (1965).

[5] H. O. House and H. W. Thompson, *J. Org. Chem.*, **28**, 360 (1963).

[6] A. J. Birch and M. Smith, *Proc. Chem. Soc.*, 356 (1962); E. Toromanoff, *Bull. Soc. Chim. France*, 708 (1962).

an equatorial β-alkyl group. Thus, the outcome of steric and stereoelectronic control should be different. (d) The products should be amenable to accurate analysis by gas chromatography. (e) The stereochemistry of the 1,4 adducts should be easy to prove by chemical and spectroscopic methods.

The synthesis of our requisite starting material is outlined in Chart I.

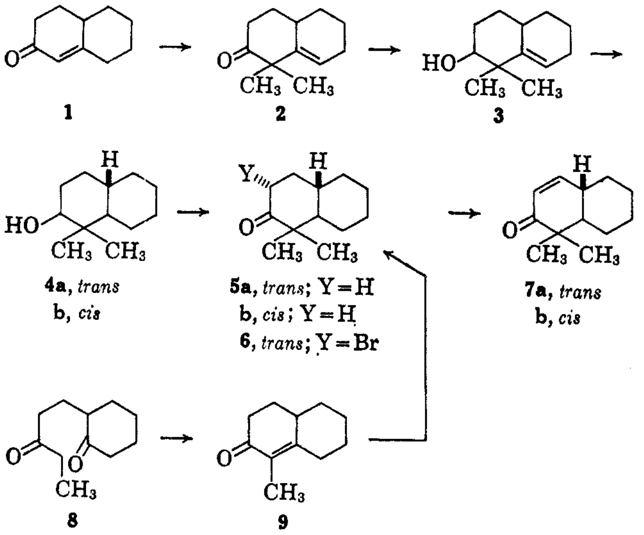

CHART I

Methylation of 1(9)-octal-2-one (**1**) under carefully controlled conditions afforded 1,1-dimethyl-8-octal-2-one (**2**). The nmr spectrum of this material confirmed the structural assignment, including placement of the double bond at the 8-position. Octalone **2**, upon hydrogenation over platinum in acetic acid, gave a mixture of stereoisomeric decalols **4a** and **4b** which was oxidized without purification to a mixture containing *trans*- and *cis*-1,1-dimethyl-2-decalone (**5a** and **5b**) in a 2:1 ratio. A more favorable ratio of **5a** to **5b** (7:1) resulted from hydrogenation of octalol **3** (obtained by reducing octalone **2** with lithium aluminum hydride) followed by oxidation of the resulting decalols.

Dreiding models show that the axial methyl group at C-1 in octalol **3** more effectively blocks the double bond than the corresponding methyl group of octalone **2**. The axial methyl group of the latter actually adopts a pseudo-axial conformation owing to the adjacent trigonal carbon atoms, and thereby offers less interference with the catalyst surface. By making the reasonable assumption that olefin reduction preceeds carbonyl reduction we can explain the greater stereoselectivity observed in the hydrogenation of **3** *vs.* **2** and assign a *trans* ring fusion to the predominant decalone stereoisomer.

An unequivocal synthesis of an authentic sample of 1,1-dimethyl-*trans*-2-decalone (**5a**) was achieved using the reduction–methylation method of Stork and coworkers.[7] The octalone **9** required for this synthesis was prepared by base-catalyzed aldol cyclization of dione **8** which, in turn, was obtained using the Stork enamine alkylation of cyclohexanone with ethyl vinyl ketone.[8] We secured this dione as a crystalline substance, mp 33–35°, which exhibited a single peak at 5.86 μ (ketone CO) in the infrared spectrum rather than a split carbonyl absorption at 5.94 μ as reported for a noncrystalline sample of the supposed same material.[8] (See Experimental Section.)

The synthesis of 1,1-dimethyl-*trans*-3-octal-2-one (**7a**) was completed by brominating decalone **5a** and dehydrobrominating the crystalline bromo ketone **6** using calcium carbonate in N,N-dimethylacetamide.[9] Hydrogenation of this compound gave, in 94% yield, decalone **5** containing 95% of the *trans* isomer **5a** and 5% of the *cis* isomer **5b**. Therefore, the conditions employed for dehydrobromination of bromo ketone **6** do not cause appreciable isomerization of the octalone product **7a**. Having thus established the stereochemical integrity of our *trans*-octalone **7a**, we investigated its behavior toward various Grignard reagents.

1,4 addition was nearly the exclusive reaction pathway with methylmagnesium iodide in the presence of cupric acetate,[6,10] using tetrahydrofuran as the solvent at −50°. The trimethyldecalones **10** and **16**, obtained in about 90% yield, were formed in the ratio 5:1. A nearly 1:1 ratio of the same isomers resulted when the cupric acetate was omitted. However, the yield of 1,4 adduct in this case was less than 10%. The stereochemistry of the isomeric 1,4 adducts was determined as follows.

The major isomer (**10**) from the cuprous ion catalyzed reaction, after purification through the semicarbazone derivative, afforded a crystalline bromodecalone (**11**) which showed a carbonyl band at 5.78 μ in its infrared spectrum. Therefore, the bromine occupies the equatorial conformation.[11] The nmr spectrum displayed a doublet (J = 4.7 cps) at 5.16 ppm, clearly resulting from the C-3 hydrogen of **11** which is split by the adjacent C-4 hydrogen. Since the coupling constant has the value expected for adjacent hydrogens with a dihedral angle of 60°,[12] and since the infrared evidence requires an axial C-3 hydrogen, bromodecalone **11** and likewise its precursor **10** must both possess axial C-4 methyl groups.

Reduction of octalone **13**, prepared by dehydrobromination of bromodecalone **11**, gave an authentic sample of the minor 1,4 adduct **16**. Both lithium in ammonia and hydrogen over palladium proved to be highly selective reducing agents, and decalone **16** of high purity resulted. The material prepared in this manner was identified by vpc peak enhancement as the minor component from the cuprous ion catalyzed conjugate methylation of octalone **7a**. The crystalline equatorial bromo ketone **17** (λ_{max} 5.81 μ)[11] prepared from this decalone showed a doublet in the nmr spectrum at 4.75 ppm due to the C-3 hydrogen. The coupling constant (J = 11.0 cps) was that expected for adjacent diaxial protons[13] of the type found in decalone **17**.

Isopropylmagnesium bromide afforded mainly 1,4-addition products with octalone **7a** in the initial pres-

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[7] G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Am. Chem. Soc.*, **87**, 275 (1965).

[8] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963).

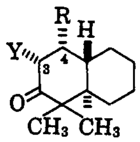
[9] G. Green and A. Long, *J. Chem. Soc.*, 2532 (1961).

[10] Cupric acetate should be readily reduced to cuprous ion by the excess Grignard reagent employed with these reactions. *Cf.* G. E. Coates and F. Glockling, "Organometallic Chemistry," H. Zeiss, Ed., Reinhold Publishing Corp., New York, N. Y., 1960, p 446.

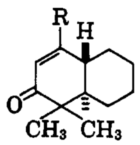
[11] *Cf.* R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Am. Chem. Soc.*, **74**, 2828 (1952).

[12] 4β-Acetoxy-3-cholestanone gives the value $J_{a,e}$ = 4.7 cps for H-4: W. S. Johnson and K. L. Williamson, *ibid.*, **83**, 4623 (1961).

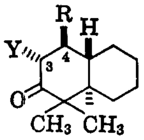
[13] 4α-Acetoxy-3-cholestanone gives the value $J_{a,a}$ = 11.6 cps for H-4.[12]



10, Y = H; R = CH_3
11, Y = Br; R = CH_3
12, Y = H; R = $(CH_3)_2CH$



13, R = CH_3
14, R = $(CH_3)_2CH$
15, R = C_6H_5



16, Y = H; R = CH_3
17, Y = Br; R = CH_3
18, Y = H; R = $(CH_3)_2CH$
19, Y = H; R = C_6H_5
20, Y = Br; R = C_6H_5

ence of cupric acetate. However, this reaction, unlike that involving octalone **7a** and methylmagnesium iodide, was not stereoselective; isopropyldecalones **12** and **18** were formed in nearly equal amount (52% **12** and 44% **18**). An authentic sample of the β isomer **18** was secured *via* bromination and dehydrobromination of the decalone mixture followed by hydrogenation of the resulting octalone **14**.

Octalone **7a** gave a single 1,4 adduct in high yield with phenylmagnesium bromide in the initial presence of cupric acetate. This material was shown to be 1,1-dimethyl-4β-phenyl-*trans*(10β-H)-2-decalone (**19**) by independent synthesis along the lines described above for the methyl- and isopropyl-substituted decalones **16** and **18**. Thus, dehydrobromination of the crystalline bromo ketone derivative **20** followed by hydrogenation of the resulting octalone **15** afforded, in high yield, material which proved identical with the 1,4 adduct **19**. The spectral characteristics of bromo ketone **20** provided confirmatory structural evidence. The infrared spectrum exhibited a peak at 5.80 μ owing to the carbonyl grouping of an equatorial α-bromocyclohexanone.[11] Therefore, H-3 possesses an axial orientation. This proton appeared as a doublet at 5.28 ppm in the nmr spectrum of bromo ketone **20**. The observed coupling constant (J = 12.6 cps) is fully consistent with the interaction expected for adjacent diaxial hydrogens.[13] H-4 of bromodecalone **20** appeared as a pair of doublets at 2.78 ppm with coupling constants ($J_{4,3}$ = 12.6 cps, $J_{4,10}$ = 11.0 cps) which confirm the axial orientation of this proton.

Table I summarizes our studies with octalone **7a** and various Grignard reagents. Apparently at least two factors should be considered in accounting for the stereochemistry of 1,4 addition. The extreme possibilities are depicted in Chart II.

With methylmagnesium iodide the favored pathway involves approach to the β-carbon atom of octalone **7a**, giving a product in which the newly introduced methyl group possesses the axial orientation. In this manner overlap can be maintained between the p orbitals of the developing enolate and the orbital involved in bond formation[5,6] (Chart II, **7a** → A) and the cyclohexene ring maintains the favored chair conformation throughout.[14] These considerations are associated with stereoelectronic control.

TABLE I

ADDITION OF RMgX TO 1,1-DIMETHYL-*trans*-3-OCTAL-2-ONE

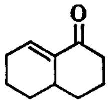
R	Catalyst	% 1,2	% axial 1,4	% equatorial 1,4
CH_3	$Cu(OAc)_2$	<1	82 (**10**)	17 (**16**)
CH_3	. . .	90	5	5
$(CH_3)_2CH$	$Cu(OAc)_2$	4	52 (**12**)	44 (**18**)
C_6H_5	$Cu(OAc)_2$	4	<1	95+ (**19**)

Phenylmagnesium bromide, on the other hand, approaches the β carbon of octalone **7a** from the less hindered side of the double bond to give a product in which the newly introduced phenyl group adopts the equatorial conformation. Assuming overlap of adjacent orbitals is highly favored,[6] this reaction would proceed through a boat cyclohexene conformation (Chart II, **7a** → B). Although this process might be considered unfavorable because of the higher energy associated with boat conformations, in this case it probably represents the lower energy pathway because of steric interactions which develop in the alternative reaction (Chart II, **7a** → A; R = C_6H_5). Thus, steric factors can exert decisive control in conjugate additions involving relatively bulky Grignard reagents.

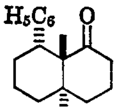
Isopropylmagnesium bromide seems nearly equally influenced by steric and stereoelectronic factors in its 1,4 addition to octalone **7a**.

Steroidal analogs of octalone **7a** give, with methylmagnesium iodide, 1,4 adducts in which the methyl group is axial. Thus, the formation of trimethyldecalone **10** as the major 1,4 addition product from this octalone is fully consistent with the results of these previous studies.[3]

At first sight, our finding that phenylmagnesium bromide affords the 1,4 adduct **19**, in which the phenyl group is equatorial, might seem to contradict House and Thompson, who found that 8-octal-1-one (III) gave decalone IV in which the phenyl group is axial.[5] Chart II depicts the conformational changes which octalone III would undergo following a pathway (III → D) analogous to that observed for octalone **7a** (**7a** → B). The most notable difference between B and D arises because the ring which adopts a boat conformation to preserve stereoelectronic stabilization contains two trigonal centers in the former and only one trigonal center in the latter. Therefore, the boat conformation of D should be less favorable than that of B,[15] whereas the pathways involving chair transition states for the two reactions should be of comparable energy (**7a** → A *vs.* III → C).



III



IV

In summary, steric factors seem to play an important part in the conjugate addition of Grignard reagents to α,β-unsaturated ketones. With methylmagnesium iodide, stereoelectronic factors favor the introduction of an axial methyl group at the relatively unhindered

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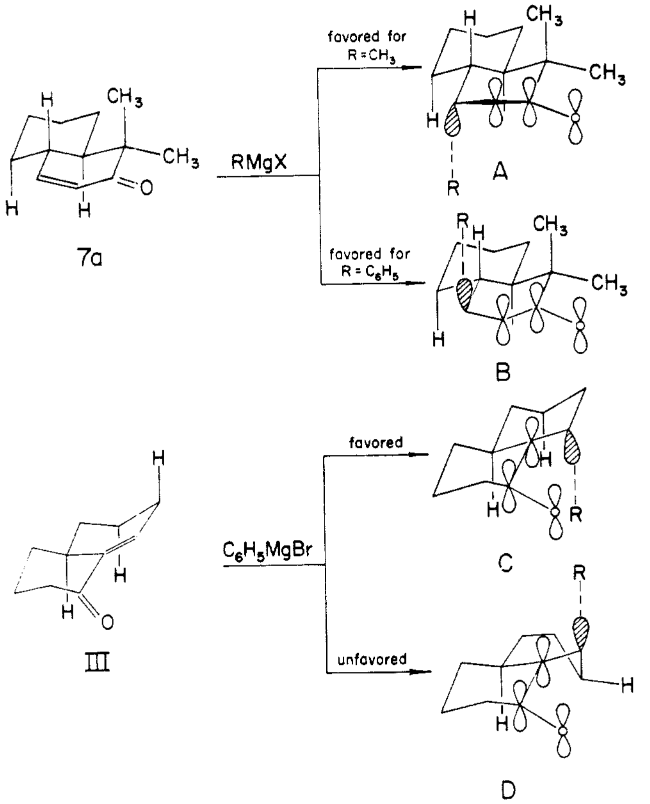
[14] For an analogous representation involving protonation, see G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).

[15] *Cf.* F. R. Jensen and C. H. Bushweller, *ibid.*, **87**, 3285 (1965), and E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 245, for a comparison between chair and boat forms of cyclohexene and cyclohexanone.

CHART II

PATHWAYS FOR 1,4-ADDITION REACTIONS



β-position of octalone **7a**, but steric factors render this pathway less favorable as the bulk of the Grignard reagent is increased. In such cases more of the equatorially substituted product forms. Although its role is not yet apparent, cuprous ion is clearly required in these reactions for effective 1,4 addition to octalone **7a**.[16] Furthermore, the stereochemistry of the addition reaction seems altered by the presence of this ion.[17] Since the yield of 1,4 adducts is very low with octalone **7a** in the absence of cuprous ion, additional work is needed to establish this point.

Experimental Section[18]

Melting points were determined on a Fisher-Johns hot stage. Nmr spectra were obtained with a Varian A-60 spectrometer. A Beckman IR-5 spectrophotometer was used for infrared spectra.

Vpc analyses were performed on an F & M Model 720 instrument employing helium as the carrier gas. Retention times are reported in minutes from the air peak and are designated t_R'. The retention time of air is designated as t_g. Column A refers to a 10 ft × 0.25 in. column of 10% Ucon 75H 90,000 Polar on 60–80 mesh Gas Pack-W employed at 185 ± 2° with a flow rate of 66 ± 2 cc/min (t_g = 0.8 min). Column B refers to a 8 ft × 0.25 in. column of 15% Carbowax 20M on 60–80 mesh Chromosorb-P employed at 192 ± 2° with a flow rate of 100 ± 2 cc/min (t_g 0.4 min). Column C refers to a 13 ft × 0.25 in. column of 16% Carbowax 20M on 60–80 mesh Diatoport-S employed at 191 ± 2° with a flow rate of 87 ± 2 cc/min. (t_g 1.06 min). Vpc traces were analyzed by the method of Bartlett and Smith.[19]

1(9)-Octal-2-one (**1**) was prepared and purified according to the procedure of Stork and co-workers.[8] Several recrystallizations from hexane at −70° gave the pure octalone.

1,1-Dimethyl-8-octal-2-one (**2**).—A mixture of 60.0 g (0.40 mole) of 1(9)-octal-2-one and 25 ml of *t*-butyl alcohol was added over a 1-min period to a solution of potassium *t*-butoxide in *t*-butyl alcohol (prepared from 47.7 g of potassium and 1.4 l. of *t*-butyl alcohol) under an atmosphere of nitrogen.[18b] The reaction mixture was cooled in an ice bath for 7 min, and methyl iodide (120 ml) was added to the stirred solution over 2 min with continued cooling. After 10 min the cooling bath was removed and the resulting slurry was stirred for 3 hr. The bulk of the solvent was removed on a rotary evaporator at reduced pressure, and the product was isolated with ether[18c] after the addition of 400 ml of water. Distillation through a 6-in. Vigreux column afforded the following fractions.

(a) 48.8 g (72.5%); bp 72–72.5° (0.5 mm); vpc analysis (column A), 91% dimethyloctalone **2**, 4% methyloctalone **9**, 1% octalone **1**, and 4% of two unidentified components.

(b) 13.1 g (19.0%); bp 73–75° (0.5 mm); vpc analysis, 88% **2**, 11% **9**, and 1% **1**.

(c) 3.1 g (4.4%); bp 75–76° (0.5 mm); vpc analysis, 49% **2**, 43% **9**, and 8% **1**.

The **semicarbazone**, mp 187–188° from methanol, was prepared by the method of Fieser[20] using material derived from fraction a.

Anal. Calcd for $C_{13}H_{21}N_3O$: C, 86.63; H, 9.00; N, 17.86. Found: C, 86.6; H, 9.0; N, 17.9.

A sample of octalone **2** was regenerated from the semicarbazone by steam distillation in the presence of phthallic anhydride.[21a] This material displayed bp 62–64° (0.25 mm); $n^{28}\text{D}$ 1.5023; $\lambda_{\max}^{\text{film}}$ 5.84 (C=O), 6.07 (C=C), 7.96, 8.75, 8.98, 9.18, 10.23, and 11.74 μ; $\delta_{\text{TMS}}^{\text{neat}} = 5.52$ (H-8, six lines, $J_{7,8} = 3.9$ cps, $J_{8,10} = 1.5$ cps), 1.13, and 1.22 ppm (*gem*-dimethyl, two singlets); lit.[21b] bp 116–121° (10 mm).

The **oxime**, mp 128–129° from ethanol–water, was prepared according to the method of Shriner and Fuson.[22]

Anal. Calcd for $C_{12}H_{19}NO$: C, 74.56; H, 9.91; N, 7.25. Found: C, 74.5; H, 9.9; N, 7.4.

We found it unnecessary to purify the ketone through the semicarbazone derivative. Careful fractionation gave material which was sufficiently pure for use in subsequent steps.

When the alkylation was carried out using a smaller excess of base (2.6–2.8 rather than 3.0 equiv) more starting material was recovered, but the nonconjugated ketone fraction was purer. The experiments described below employed samples of octalone **2** obtained in this manner.

1,1-Dimethyl-8-octal-2-ol (**3**).—Octalone **2** (8.46 g) was added to a stirred, cooled solution of 0.88 g of lithium aluminum hydride in 150 ml of ether. The mixture was stirred for 2 hr, and 1.76 ml of water and 1.41 ml of 10% aqueous sodium hydroxide were carefully added. The solvent was removed from the filtrate under reduced pressure, affording 7.88 g (93%) of a viscous oil which crystallized on standing. Several recrystallizations from hexane gave the alcohol, mp 79–85° (lit[21b] mp 86–88°), which was characterized as the phenylurethan, mp 148–149° from hexane (lit.[21b] mp 149–151°).

1,1-Dimethyl-2-decalone (**5**). **A. Hydrogenation of 1,1-Dimethyl-8-octal-2-ol** (**3**).—The unpurified octalol mixture obtained from 34.1 g of octalone **2** by lithium aluminum hydride reduction as described above was dissolved in 120 ml of acetic acid and shaken with 0.8 g of platinum oxide in a Parr bomb under an initial 45 psi of hydrogen for 16 hr. A solution of 14.1 g of chromium trioxide in 12 ml of water was added to the filtered acetic acid solution over 3 hr with rapid stirring. The solvent was removed on a rotary evaporator at reduced pressure after the addition of 10 ml of isopropyl alcohol. The resulting residue was treated with 200 ml of saturated aqueous sodium bicarbonate,

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[16] For some speculation regarding this requirement, see ref 2, p 220.

[17] Y. Inouyl and H. M. Walborsky, *J. Org. Chem.*, **27**, 2706 (1962). For a conflicting result, see ref 5.

[18] (a) The prefix *dl* is omitted from the names of racemic substances. (b) The apparatus described by W. S. Johnson and W. P. Schneider [*Org. Syn.*, **30**, 18 (1950)] was used to maintain a nitrogen atmosphere. (c) The isolation procedure consisted of thorough extraction and back-extraction with the specified solvent, washing the extracts with saturated brine, and drying over either anhydrous sodium sulfate or magnesium sulfate. The solvent was removed from the filtered extracts at 50° on a rotary evaporator under reduced pressure. (d) Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich., or Micro-Tech Laboratories, Inc , Skokie, Ill.

[19] J. C. Bartlett and D. M. Smith, *Can. J. Chem.*, **38**, 2057 (1960).

[20] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 339.

[21] (a) A. St. Pfau and Pl. A. Plattner, *Helv. Chim. Acta*, **22**, 649 (1939); (b) W. J. A. Vanden Heuvel and E. S. Wallis. *J. Org. Chem.*, **27**, 1233 (1962).

[22] R. Shriner and R. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p 202.

and the decalone (31.9 g, 92%) was isolated with hexane[18c]: bp 72.5° (0.55 mm), n^{20}_{D} 1.4873.

Vpc analysis (column B) revealed three components, t_R' 6.7 (2%, methyldecalone), 8.0 (86%, **5a**), and 9.2 min (12%, **5b**). The identity of the major component was established by peak enhancement with authentic *trans*-decalone **5a**.

The **oxime derivative** of decalone **5a** had mp 129–131°, after several recrystallizations from methanol.

Anal. Calcd for $C_{12}H_{21}NO$: C, 73.79; H, 10.84. Found: C, 73.8; H, 10.9.

The pure (vpc) decalone **5a** was obtained by hydrolysis of the oxime and has the following properties: bp 75° (0.6 mm); n^{20}_{D} 1.4883; λ_{max}^{film} 5.85 (C═O), 8.61, 8.79, 9.00, 9.51, 9.85, 10.11, 10.38, and 11.83 μ; $\delta_{TMS}^{CCl_4}$ = 0.98 and 1.01 ppm (C-1 *gem*-dimethyl, two singlets); lit.[7] bp 72–77° (0.2 mm).

B. Hydrogenation of 1,1-Dimethyl-8-octal-2-one (**2**). **Characterization of 1,1-Dimethyl-*cis*-2-decalone** (**5b**).—A Parr bomb was charged with 7.294 g of octalone **2**, 90 ml of acetic acid, and 0.55 g of platinum oxide and shaken for 7 hr under an initial 65 psi of hydrogen. The solvent was removed (toluene azeotrope) from the filtered reaction mixture and the residue was distilled to give 7.135 g (96%) of a mixture of decalols **4**, bp 65° (bath temperature) at 0.06 mm.

A 5.612-g sample of this decalol mixture dissolved in 10 ml of acetone was placed in a separatory funnel, and a 40-ml portion of acetone cooled to −70° was added. To this solution, 7.97 ml of 2.67 *M* chromium trioxide reagent[23] was added rapidly in one portion, and the reaction mixture was shaken until it had warmed to room temperature. Excess chromium trioxide was destroyed by adding several drops of isopropyl alcohol and shaking the mixture for several minutes. The mixture was filtered and the solvent was removed from the clear colorless filtrate affording 5.237 g (94%) of a mixture of decalones **5a** and **5b**, bp 40° (bath temperature) at 0.09 mm. Vpc analysis (column B) revealed peaks at t_R' 6.7 (3% methyldecalone), 8.0 (67%, **5a**), and 9.2 min (30%, **5b**). The nmr spectrum showed a broad resonance at 0.99 ppm and a sharp one at 0.92 ppm owing to the *gem*-dimethyl groupings in **5a** and **5b**, respectively. Integration of these peaks indicated a 70:30 ratio of **5a** to **5b** in agreement with the conclusions based on vpc analysis.

An oxime derivative, mp 125–156°, was prepared from this mixture in 40% yield according to the method of Shriner and Fuson.[22] Repeated recrystallization from methanol afforded **1,1-dimethyl-*cis*-2-decalone oxime**, mp 172–173.5°.

Anal. Calcd for $C_{12}H_{21}NO$: C, 73.79; H, 10.84; N, 7.17. Found: C, 74.0; H, 10.8; N, 7.4.

C. Reduction–Methylation of 1-Methyl-1(9)-octal-2-one (**9**).—The procedure outlined below gives results which are comparable with those reported recently by Stork and co-workers.[7]

To a mixture of 4.414 g (27.1 mmoles) of octalone **9**, 260 ml of ether, and 350 ml of ammonia (distilled through a potassium hydroxide tower) was added 310 mg (44.8 mg-atoms) of lithium wire. A permanent blue coloration developed, and after 20 min, 5.0 ml of methyl iodide (80.3 mmoles) was added in 0.5-ml portions. The blue color was discharged on addition of the first portion. The slurry remaining after the ammonia had evaporated was taken up in saturated aqueous ammonium chloride, and the product (4.429 g) was isolated with ether.[18c] The gas chromatogram (column B) displayed peaks at t_R' 7.1 [4%, 1α-methyl-*trans*(10β-H)-2-decalone], 8.0 (64%, **5a**), 12.8 (8%), and 14.6 min (24%, octalone **9**).

Two fractional evaporative distillations, in each of which only the first three quarters of the material was collected, afforded nearly pure (89% by vpc) decalone **5a**. The nmr spectrum displayed *gem*-dimethyl resonances at 0.98 and 1.01 ppm. The oxime derivative, mp 120–128°, was prepared in 84% yield from this material. One recrystallization from methanol gave platelets, mp 130–131.5°, which did not depress the melting point of the oxime prepared in part A.

D. Hydrogenation of 1,1-Dimethyl-*trans*-3-octal-2-one (**7a**).—A mixture of 204 mg of octalone **7a** (contaminated by a small amount of this *cis* isomer **7b**), 90 mg of 5% palladium on carbon, and 20 ml of absolute ethanol was stirred in an atmosphere of hydrogen for 10 min whereupon the calculated volume of hydrogen was consumed. The solvent was removed from the filtered reaction mixture, affording 193 mg (94%) of a decalone mixture. Vpc analysis revealed only *trans*- and *cis*-1,1-dimethyl-2-decalone in the ratio 95:5.

The **oxime derivative**, mp 131–132°, undepressed on admixture with the authentic *trans*-decalone oxime, was obtained in 74% yield.

1-(2-Oxocyclohexyl)-3-pentanone (**8**).—The procedure employed is essentially that of Stork and co-workers.[8] Ethyl vinyl ketone (10.7 g) was added to a stirred solution of 19.2 g of cyclohexanone pyrrolidine enamine in 150 ml of dioxane over 0.5 hr. The reaction mixture was stirred an additional 3.5 hr at room temperature under an atmosphere of nitrogen,[18b] and 30 ml of water, 16 ml of acetic acid, and 8.0 g of sodium acetate were added. The resulting mixture was heated on a steam bath for 20 min and stirred for 16 hr at room temperature. The product was isolated with ether[18c] after the addition of brine. Distillation afforded 18.0 g (78%) of the diketone: bp 106–107° (0.2 mm), mp 33–35°, $\lambda_{max}^{CCl_4}$ 5.86 μ (C═O); lit.[8] bp 125–128° (1 mm), λ_{max} 5.94 μ (C═O, split). The split carbonyl absorption reported by Stork, *et al.*,[8] suggests that their material had, in part, cyclized to octalone **9**.

One recrystallization from hexane gave the analytical sample, mp 34.5–35.5°.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.5; H, 10.0.

1-Methyl-1(9)-octal-2-one (**9**).—A 15.01-g sample of diketone **8** was added to a stirred solution containing 45 g of potassium hydroxide, 80 ml of water, and 800 ml of methanol. The resulting solution was stirred for 1 hr at *ca.* 40–45°,[18b] the reaction mixture was poured into 1.6 l. of brine, and the product was isolated with ether.[18c] Distillation afforded 12.10 g (90.4%) of octalone: bp 136–137° (14 mm); n^{29}_{D} 1.5250; λ_{max}^{film} 6.00 (C═O), 6.17 (C═C), 6.90, 7.02, 7.25, 7.34, 7.36, 7.46, 7.55, 7.68, and 8.33 μ; $\delta_{TMS}^{CCl_4}$ 1.70 ppm (C-1 methyl, doublet, J = 1 cps) [lit.[8] bp 150–155° (18 mm)]. This material was judged homogeneous by vpc (column B, t_R' 14.6 min).

3α-Bromo-1,1-dimethyl-*trans*(10β-H)-2-decalone (**6**).—To a stirred solution containing 18.9 g of decalone **5a** and 130 ml of acetic acid was added 52 ml of 2.00 *M* bromine in acetic acid over 40 min. After an additional 10 min, the reaction mixture was poured into 500 ml of water, whereupon a solid mass precipitated. The supernatant liquid was decanted and replaced with saturated aqueous sodium bicarbonate. The resulting slurry was stirred rapidly for 1 hr at 50° and cooled in ice. The crystalline bromo ketone (24.6 g, 91%), mp 95–99°, was collected by filtration and washed with water. One recrystallization from hexane afforded 18.0 g of colorless prisms: mp 98–99°; $\lambda_{max}^{CCl_4}$ 5.79 (C═O), 7.20, 7.30, 9.69, 10.25, and 11.39 μ; $\delta_{TMS}^{CCl_4}$ = 4.96 (H-3, four lines, $J_{3a,4a}$ = 13.3 cps, $J_{3a,4e}$ = 6.4 cps),[24] and 1.11 ppm (C-1 *gem*-dimethyl, singlet).

One additional recrystallization gave an analytical sample, mp 98.5–99°.

Anal. Calcd for $C_{12}H_{19}BrO$: C, 55.60; H, 7.39; Br, 30.83. Found: C, 55.6; H, 7.5; Br, 30.7.

The crystalline bromo ketone **6** could be obtained in 70–80% yield, using decalone **5a** which had been purified by distillation only.

1,1-Dimethyl-*trans*-3-octal-2-one (**7a**).—A mixture containing 18.0 g of bromo ketone **6**, 15 g of calcium carbonate, and 300 ml of N,N-dimethylacetamide was heated to reflux for 25 min.[9] The reaction mixture was cooled in ice–water and filtered, and the filtrate was extracted thoroughly with heptane. The combined extracts were washed with saturated aqueous sodium bicarbonate, water, and brine. The solvent was removed from the dried solution and the product was distilled, affording 10.75 g (87%) of the octalone: bp 49–51° (0.03 mm); n^{28}_{D} 1.5024; λ_{max}^{film} 5.98 (C═O), 6.08 (C═C), 7.21, 7.88, 8.69, 11.46, 11.74, 12.18, and 14.89 μ; $\delta_{TMS}^{CCl_4}$ = 5.72 (H-3, two doublets, $J_{3,4}$ = 10.1 cps, $J_{3,10}$ = 2.8 cps), 6.47 (H-4, two doublets, $J_{4,3}$ = 10.1 cps, $J_{4,10}$ = 1.6 cps), 0.88, and 1.00 ppm (C-1 *gem*-dimethyl, two singlets). Vpc analysis (column C) revealed two components: t_R' 10.2 (1.5%, 1,1-dimethyl-4-octal-2-one) and 12.3 min (98.5%, **7a**). Close examination of the later peak suggested the presence of about 5% of another conjugated ketone (**7b**) at t_R' ~13.0 min.

Material from the center cut of the distillation, bp 50° (0.03 mm), n^{28}_{D} = 1.5027, was submitted for combustion analysis.

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

(24) 2α-Bromo- and 2α-acetoxycholestanone are reported[12] to have $J_{a,a}$ = 13.1 cps and $J_{a,e}$ = 6.6 cps.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.6; H, 10.1.

Attempts to purify octalone **7a** through the oxime, mp 150–151° (from methanol), were only partially successful. The component at 10.2 min was completely removed (<0.3% vpc), but the component responsible for the shoulder at ~13.0 min was not. Hydrogenation of the distilled octalone indicated that *cis*-octalone **7b** was indeed the minor contaminant, since the previously characterized decalones **5a** and **5b** were obtained in a 95:5 ratio according to vpc analysis.

1,1,4α-Trimethyl-*trans*(10β-H)-2-decalone (**10**).—To a stirred solution containing 2.59 g (14.5 mmoles) of octalone **7a**, 260 mg of cupric acetate monohydrate, and 60 ml of tetrahydrofuran, maintained at −50° in a Dry Ice–acetone bath, was added 35 ml of 1.2 *M* ethereal methylmagnesium iodide. The addition required 30 min and was done under an atmosphere of nitrogen.[18b] The stirred mixture was allowed to reach room temperature over a 1-hr period and was heated to reflux for 30 min. The product (2.70 g, 96%) was isolated with ether[18c] after the addition of 50 ml of saturated aqueous ammonium chloride and 100 ml of water. The infrared spectrum indicated less than 5% of alcoholic products.

The decalone was characterized as the **oxime derivative**, mp 192–192.5° from ethanol.

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.6; H, 11.1; N, 6.8.

The decalone was further characterized as the **semicarbazone derivative,** mp 223° dec from methanol.

Anal. Calcd for $C_{14}H_{25}N_3O$: C, 66.89; H, 10.03; N, 16.72. Found: C, 66.9; H, 10.0; N, 16.7.

An analytical sample of decalone **10** was obtained on treating the semicarbazone with hot aqueous oxalic acid. This material has the following properties: bp 60° (bath temperature) at 0.3 mm; $n^{22.2}_{\mathrm{D}}$ 1.4893; $\lambda_{\max}^{\text{film}}$ 5.87 (C=O), 7.21, 7.30, 8.72, 9.49, 10.08, 11.68, and 12.4 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 0.77 (C-4 methyl, doublet, J = 7.0 cps), 0.96, and 0.98 ppm (C-1 *gem*-dimethyl, two singlets); vpc analysis (column C), t_{R}' 12.5 min (99⁺%).

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.0; H, 11.4.

The reaction was repeated employing 398 mg of octalone **7a** (containing 5.4% of the *cis*-octalone **7b**) and afforded 403 mg (93%) of a trimethyldecalone mixture. Vpc analysis (column C) revealed four components, t_{R}' 10.2 (1.2%), 11.2 (16.4%, **16**), ~11.8 (4.2%), and 12.5 min (78.2%, **10**). The two minor components correspond to isomeric trimethyl-*cis*-decalones derived from **7b**. Neither alcohols nor the corresponding olefins from 1,2 addition products were present (<0.2%).

When the reaction was performed exactly as described above but without the cupric acetate, the infrared spectrum of the product showed only about 10% of a saturated ketone carbonyl peak. Vpc analysis (column C) indicated that 90 ± 0.5% of the material (eluted as a mixture of dienes, t_{R}' 3–4 min) arose from 1,2 addition. Decalones **10** and **16** were present in a 1:1 ratio but accounted for less than 10% of the material.

3α-Bromo-1,1,4α-trimethyl-*trans*(10β-H)-2-decalone (**11**).—A stirred solution of 871 mg of decalone **10** in 10 ml of acetic acid was treated with 1.91 ml of 2.00 *M* bromine in acetic acid over a 10-min period. After an additional 5 min, 50 ml of water was added. The mixture was cooled in ice and, after 1 hr, the precipitated product (1.081 g, 88.5%) was collected by filtration: mp 110–114°; $\lambda_{\max}^{\text{CCl}_4}$ 5.78 (C=O), 7.20, 9.63, 9.72, 10.09, 10.49, and 11.38 μ; $\delta_{\text{TMS}}^{\text{CCl}}$ = 5.16 (H-3, doublet, $J_{3a,4e}$ = 4.7 cps),[12] 0.83 (C-4 methyl, doublet, J = 7.2 cps), and 1.08 ppm (C-1 *gem*-dimethyl, singlet).

Recrystallization from hexane gave colorless platelets, mp 116–116.5°.

Anal. Calcd for $C_{13}H_{21}BrO$: C, 56.67; H, 7.83; Br, 29.57. Found: C, 57.0; H, 7.8; Br, 29.6.

Crystalline bromo ketone **11**, mp 114.5–116°, could be obtained in 60% yield using the unpurified trimethyldecalone mixture obtained from octalone **7a**.

1,1,4-Trimethyl-*trans*-3-octal-2-one (**13**).—A mixture of 1.62 g of bromo ketone **11**, 1.10 g of calcium carbonate, and 40 ml of N,N-dimethylacetamide was heated at reflux for 30 min.[9] The product was obtained by extraction with heptane, as described for octalone **7a**, and distilled, affording 1.10 g (96%) of the octalone: bp 85° (bath temperature) at 0.5 mm; n^{23}_{D} 1.5136; $\lambda_{\max}^{\text{film}}$ 3.32 (vinyl H), 6.00 (C=O), 6.12 (C=C), 7.23, 7.71, 7.84, 8.48, 8.80, 11.18, 11.40, and 11.59 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 5.64 (H-3, unresolved multiplet), 1.88 (C-4 methyl, doublet, J = 1.2 cps), 0.88, and 1.02 ppm (C-1 *gem*-dimethyl, two singlets). This material was judged homogeneous by vpc (column C, t_{R}' 22.8 min).

The **oxime derivative** has mp 146–148° from hexane or methanol.

Anal. Calcd for $C_{13}H_{21}NO$: C, 75.31; H, 10.21; N, 6.76. Found: C, 75.1; H, 10.2, N, 6.7.

1,1,4β-Trimethyl-*trans*(10β-H)-2-decalone (**16**). **A. Lithium–Ammonia Reduction of Octalone 13.**—To a stirred solution of 330 mg of octalone **13**, 4 ml of ether, and 30 ml of ammonia, was added 90 mg of lithium wire in small pieces over 30 min. After an additional 40 min, a solution of 5.2 ml of absolute ethanol in 8 ml of ether was added over a 2-hr period. The residue remaining after the ammonia had evaporated was taken up in 30 ml of saturated aqueous ammonia chloride, and the alcohol product was isolated with ether[18c] after the addition of 30 ml of water. The crude alcohol was oxidized with 0.46 ml of 2.67 *M* chromium trioxide reagent[23] as described previously, affording 314 mg (94%) of decalone **16**: bp 50° (bath temperature) at 0.2 mm; n^{20}_{D} 1.4868; $\lambda_{\max}^{\text{film}}$ 5.86 (C=O), 7.22, 7.31, 7.83, 8.77, 9.00, 9.54, and 11.58 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 2.15 (C-3 methylene, broad singlet) and 0.98 ppm (three methyl resonances superimposed, a broad singlet); vpc analysis (column C), t_{R}' 11.2 min (99.7 +%).

On dilution with an equal volume of pyridine the methyl resonance in the nmr spectrum was resolved into two equal peaks (4.5 hydrogens each by the integration trace) at 0.95 and 1.07 ppm.

The decalone was characterized as the **oxime derivative**, mp 126.5–128° from methanol.

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.6; H, 11.0; N, 6.6.

B. Hydrogenation of Octalone 13.—A mixture of 168 mg of octalone **13**, 60 mg of 5% palladium on carbon, and 12 ml of ethanol was stirred for 10 min in an atmosphere of hydrogen. The solvent was removed from the filtered reaction mixture, affording 162 mg (95%) of decalone **16** which was identical with the sample prepared above. Vpc analysis (column C) indicated less than 0.5% of the epimeric decalone **10**.

3α-Bromo-1,1,4β-trimethyl-*trans*(10β-H)-2-decalone (**17**).—A stirred solution of 443 mg of decalone **16** in 8 ml of acetic acid was treated with 1.23 ml of 2.00 *M* bromine in acetic acid over 5 min. After the addition of 25 ml of water, the product was isolated with hexane[18c] in quantitative yield as an oil which crystallized on cooling and scratching. Recrystallization from pentane afforded 232 mg of bromo ketone: mp 76–79°; $\lambda_{\max}^{\text{KBr}}$ 5.81 (C=O), 7.24, 7.29, 8.67, 11.47, and 13.75 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 4.75 (doublet, $J_{3a,4a}$ = 11.0 cps),[12] 1.32 (C-4 methyl, doublet, J = 5.1 cps), 1.13, and 1.12 ppm (*gem*-dimethyl, two singlets).

The noncrystalline residues (414 mg) were chromatographed on 80 cc of acid-washed silica. Elution with 55–70% benzene in pentane gave 227 mg of bromo ketone **17**, mp 78–79.5°.

An analytical specimen, mp 79.5°, was secured by recrystallizing the later chromatographic fractions from hexane (88% recovery).

Anal. Calcd for $C_{13}H_{21}BrO$: C, 56.67; H, 7.83; Br, 29.57. Found: C, 56.9; H, 7.8; Br, 29.6.

1,1-Dimethyl-4-isopropyl-*trans*-3-octal-2-one (**14**).—To a stirred solution of 802 mg (4.50 mmoles) of octalone **7a** and 220 mg of cupric acetate monohydrate in 18 ml of tetrahydrofuran maintained at −50° was added 41.9 ml of 0.43 *M* isopropylmagnesium bromide in tetrahydrofuran. The addition required 0.5 hr and was performed in an atmosphere of nitrogen.[18b] The solution was allowed to warm to 35° over a 0.5-hr period. After an additional 2.0 hr of stirring at 35–40°, 30 ml of saturated aqueous ammonium chloride was carefully added and the resulting two-phase system was poured into 60 ml of water. The product (842 mg, 84.2%) was isolated with ether[18c] and distilled: bp 110° (bath temperature) at 0.3 mm. The infrared spectrum of the material indicated that 1,4 addition was the major pathway (~90%). Vpc analysis (column C, 220°, 102 cc/min) revealed six components: t_{R}' 1.0–5.0 (4%), 6.8 (4%), 8.3 (42%), and 9.3 min (50%). The retention time of the starting material under these conditions is 5.8 min.

A 730-mg sample of this mixture was chromatographed on 70 g of alumina (Merck). Elution with 270 ml of benzene afforded 638 mg of an alcohol-free mixture of epimeric decalones **12** and **18**: $\lambda_{\max}^{\text{film}}$ 5.86 μ (C=O); vpc analysis (column C, 220°, 102 cc/min), t_{R}' 4.0–6.0 (~1%), 8.3 (45%, **18**), and 9.3 min (54%, **12**). The β epimer was identified by peak enhancement with authentic 1,1-dimethyl-4β-isopropyl-*trans*(10β-H)-2-decalone prepared as described below.

A stirred solution of 604 mg of the decalone mixture **12** and **18** in 15 ml of acetic acid was treated with 0.70 ml of 3.88 *M* bromine in acetic acid over 4 min. After stirring an additional 2 min, 70 ml of water was added. The product (795 mg, 97%), a colorless oil, was isolated with ether and hexane.

A mixture of 788 mg of this bromo ketone mixture, 0.80 g of calcium carbonate, and 30 ml of N,N-dimethylacetamide was heated at reflux for 0.5 hr, and the octalone **14** (538 mg, 93%) was isolated as previously described: bp 115° (bath temperature) at 0.3 mm; $\lambda_{\max}^{\text{film}}$ 5.99 (C═O), 6.14 (C═C), 7.11, 7.20, 8.54, and 11.26 μ; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ = 5.76 (H-3), 1.19 (1.5 H), 1.14 (1.5 H), 1.05 (6 H), and 0.90 ppm (3 H). These latter peaks must be due to the C-1 *gem*-dimethyl and the nonequivalent methyl groups of the C-4 isopropyl group. Vpc analysis (column C, 220°, 102 cc/min) indicated that the octalone was homogeneous (t_R' 12.3 min).

The **oxime derivative**, mp 131–132.5°, was prepared according to the method of Shriner and Fuson[22] and sublimed (85°, 0.1 mm) after recrystallization from methanol.

Anal. Calcd for $C_{15}H_{25}NO$: C, 76.54; H, 10.71; N, 5.95. Found: C, 76.5; H, 10.7; N, 6.1.

1,1-Dimethyl-4β-isopropyl-*trans*(10β-H)-2-decalone (18).—A 360-mg sample of octalone **14** was stirred with palladium on carbon in 10 ml of absolute ethanol under an atmosphere of hydrogen until the theoretical uptake was complete (1 hr). The product (354 mg) was obtained after the solvent was removed from the filtered reaction mixture. Vpc analysis (column C, 220°, 102 cc/min) revealed peaks at t_R' 7.0 (1%), 8.3 (92%, **18**), 10.2 (2%), and 12.3 min (5% starting octalone **14**). Evaporative distillation removed some of the impurities, affording a sample judged to be 96% decalone **18**: $\lambda_{\max}^{\text{film}}$ 5.85 (C═O), 7.11, 7.20, 8.82, 11.48, 12.8, and 13.8 μ.

The **oxime derivative** displayed mp 156.5–157° upon recrystallization from methanol.

Anal. Calcd for $C_{15}H_{27}NO$: C, 75.89; H, 11.47; N, 5.90. Found: C, 75.8; H, 11.6; N, 5.9.

1,1-Dimethyl-4β-phenyl-*trans*(10β-H)-2-decalone (19). A. Addition to 7a.—This reaction was performed using 0.80 g of octalone **7a**, 0.22 g of cupric acetate, and 26.5 ml of 0.68 *M* phenylmagnesium bromide in tetrahydrofuran in the manner described above to give, after evaporative distillation, 1.35 g of partially crystalline material. A small portion of this material was dissolved in benzene for vpc analysis (column C, 220°, 102 cc/min): t_R' 5.2 (3%), 6.0 (14%, biphenyl), and 52 min (83%).

The semicrystalline mass was triturated with heptane and the resulting crystals were dried on adsorbent filter paper. This afforded 537 mg (47%) of decalone **19**: mp 90–98°; $\lambda_{\max}^{\mathrm{CCl_4}}$ 5.84 (C═O), 6.23 (C═C), 7.20, 7.29, 8.84, and 14.3 μ. Vpc analysis of this material indicated a purity of 99.2%. A 791-mg portion of the mother liquor was chromatographed on 100 g of alumina (Merck). The later benzene fractions afforded an additional 475 mg (41%) of decalone **19**: mp 96–99°; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ = 7.3 (phenyl group), 2.2–2.9 (a complex pattern owing to three hydrogens), 1.08, and 1.15 ppm (C-1 *gem*-dimethyl, two singlets).

The alcoholic material obtained on elution with ether–benzene was not investigated.

An analytical sample, mp 100.5–102°, was obtained by recrystallization from ethyl acetate: $\lambda_{\max}^{\mathrm{KBr}}$ 5.90 (CO), 6.23 (C═C), 7.29, 8.83, 9.33, 12.66, 13.16, and 14.21 μ.

Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.2; H, 9.55.

B. Hydrogenation of 1,1-Dimethyl-4-phenyl-*trans*-3-octal-2-one (15).—A mixture of 110 mg of bromo ketone **20**, 6.0 ml of N,N-dimethylacetamide, and 150 mg of calcium carbonate was heated at reflux for 0.6 hr.[9] The octalone **15** [$\lambda_{\max}^{\text{film}}$ 6.00 (C═O), 6.19, 6.34 (C═C), 8.59, 11.25, 12.98, and 14.29 μ] was obtained by extraction with heptane. Hydrogenation over palladium on carbon in ethanol afforded the crude ketone **19** which was treated with chromium trioxide reagent in acetone[23] to oxidize a small amount of alcoholic impurity. Sublimation of the material thus obtained gave 54 mg (64%) of the decalone **19**, mp 93–97°. Vpc analysis (column C, 220°, 102 cc/min) revealed only one peak (t_R' 52.0 min). The infrared spectrum was identical with that of the material prepared according to part A.

3α-Bromo-1,1-dimethyl-4β-phenyl-*trans*(10β-H)-2-decalone (20).—A stirred solution of 212 mg of decalone **19** (mp 90–98°) in 5 ml of acetic acid was treated with 0.22 ml of 3.88 *M* bromine in acetic acid over 4 min. After 1 min, 20 ml of water was added. The bromo ketone was isolated with ether[18c] and 251 mg (91%) of a white solid, mp 129–136°, was obtained after trituration with a small amount of hexane. This material was recrystallized from heptane–ethyl acetate, affording 204 mg (74%) of bromo ketone: mp 134–137.5°; $\delta_{\mathrm{TMS}}^{\mathrm{CDCl_3}}$ = 7.3–7.5 (phenyl group), 5.28 (H-3, doublet, $J_{3a,4a}$ = 12.6 cps), 2.78 (H-4, four lines, $J_{4a,3a}$ = 12.6 cps, $J_{4a,10a}$ = 11.0 cps), 1.27, and 1.24 ppm (C-1 *gem*-dimethyl, two singlets); $\lambda_{\max}^{\mathrm{KBr}}$ 5.80 (C═O), 6.23 (C═C), 6.69, 6.90, 7.20, 8.52, 9.37, 9.56, 9.76, 11.30, 12.45 13.29, 13.75, 13.95, and 14.21 μ.

Recrystallization from heptane–ethyl acetate gave colorless flat needles, mp 140–141°.

Anal. Calcd for $C_{18}H_{23}BrO$: C, 64.48; H, 6.91; Br, 23.83. Found: C, 64.4; H, 6.8; Br, 24.0.

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Structure of Hysterin, a New Sesquiterpene Lactone[1,2]

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Hysterin, a new sesquiterpene lactone, has been isolated from *Parthenium hysterophorus* L. together with some ambrosin. The structure of hysterin is shown to be Ia.

In continuation of our search for *Compositae* whose sesquiterpene lactone composition varies with the geographical location[3] we have investigated *Parthenium hysterophorus* L.,[4] a common weed growing in the West Indies and the sourthern part of North America. The material growing in Florida has previously been studied by Herz, *et al.*,[5] who isolated parthenin, a member of the class of pseudoguaianolides. The plant growing in the Valley of Mexico has now yielded a different pseudoguaianolide, which we have named hysterin, as well as some ambrosin.

Hysterin, $C_{17}H_{24}O_5$, mp 168°, $[\alpha]_D$ −80° (*c* 1.0, chloroform), has a free hydroxyl group as shown by the infrared absorption at 3620 cm⁻¹ and by the formation

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[2] Taken in part from a D.Sc. thesis to be submitted by E. A. Bratoeff to the Universidad Nacional Autónoma de México.

[3] A. Romo de Vivar and H. Jiménez, *Tetrahedron*, **21**, 1741 (1965).

[4] Identified by the late Dr. Faustino Miranda from the botanical department of the Universidad Nacional Autónoma de México with a herbarium number 9138.

[5] W. Herz, H. Watanabe, M. Miyazaki, and Y. Kishida, *J. Am. Chem. Soc.*, **84**, 2601 (1962).