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Synthesis of a New Ketone and Alcohol with C2 Symmetry; (S,S,S,S) Tricyclo[6.3.0.0^{3,7}]undecan-2-one[1a] and (S,S,S,S) Tricyclo[6.3.0.0^{3,7}]undecan-2-ol[1b]

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Abstract: *Dissolving metal reduction of known enone* ***5*** *affords predominantly the racemic form of title ketone* (***3***) *whereas catalytic reduction gives the meso isomer* ***6***. *Neither ketone* ***3*** *nor alcohol* ***4*** *could be satisfactorily resolved. Asymmetric synthesis of (-)-****3*** *and (+)-****4*** *(ee=91%) was effected from ketone (+)-****13***.

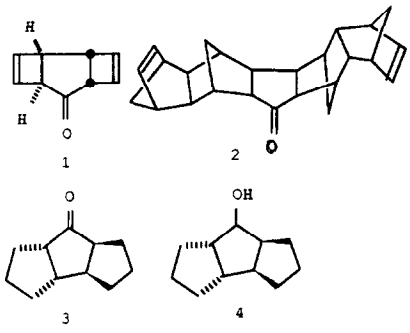
The design and synthesis of compounds which can supplement the materials supplied by nature and serve as stereochemical control units is an active research area. Among the most interesting of these are compounds with C2 symmetry. The advantage gained by the use of this class of stereoisomer has been the subject of a recent excellent review.[3]

Our continuing interest in the stereochemistry of alkylation of glycine derivatives led us to consider how chiral auxiliaries possessing C2 symmetry might be utilized to control the stereochemical aspects of this important process. In previous reports from our laboratories and others, the chiral influence has been present as an imine and our interest in this reaction has been focused on the use of camphor imines.[4] Other naturally occurring and readily available chiral ketones [e.g. menthone,[5] 2-hydroxypinanone,[6] ketopinic acid,[7] 10-hydroxymethylcamphor[4b]] have also been employed by various groups but the relationship between the structure of the chiral adjunct and the stereochemical results obtained have been unpredictable.[8] The advantages of using an adjunct with C2 symmetry led us to consider possible structures which would be either ketonic, and thus potentially useful in glycine imine reactions or alcoholic and therefore useful in formation of chiral esters of glycine and other important amino acids.[9]

At the outset of this work, we were aware of only two ketones (**1**,**2**)[10a,b] which possessed both the required C2 axis and, most importantly, which appeared to offer the possibility of significant diastereofacial selection in a postulated transition state for the alkylation reaction.[11] Ketone **1** is a relatively labile material which has not been resolved. Ketone **2**, although it has been resolved,[10b] is not an attractive candidate as a chiral adjunct either from a synthetic or spectroscopic point of view.

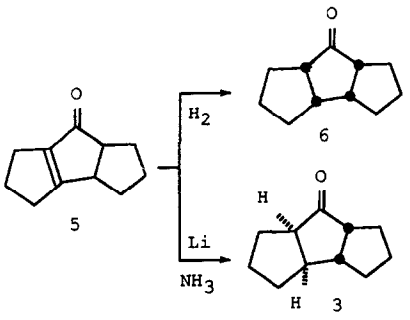
Examination of molecular models suggested that the tricyclic ketone **3** or its derived alcohol **4** might be effective in such a scenario and afford further insight into this important alkylation process. Relative to

its homologs which possess either a central, or two peripheral six membered rings, **3** has the advantage of avoiding ambiguous or undesirable ring fusions which would destroy the C2 symmetry. Parenthetically it should be noted that ketone **3** and the other materials structurally related to it that are mentioned here are simple examples of linear triquinanes.[12] However, the lack of substitution makes much of the excellent synthetic methodology which has been developed for triquinane synthesis inapplicable here. This paper documents both a short synthesis of racemic **3** and **4** and also an unambiguous asymmetric synthesis of one enantiomer of these compounds.



The preparation and catalytic hydrogenation of **5** to meso ketone **6** has been reported.[13] Ketone **6** is clearly the less stable of the two possible stereoisomers. In our hands, the ^{13}C NMR spectrum of the hydrogenation product indicated the presence of a 9:1 mixture of isomers which could not be separated, either by gas or thin layer chromatography. Using ^{13}C NMR data as an indicator, Eaton reported the formation of pure **6**. Reduction of **5** using lithium in ammonia afforded a 70% yield of the same two products in a 1:9 ratio as evidenced by the ^{13}C NMR data.

Although we also have been unable to separate the two materials, it is clear that the major product from the dissolving metal reduction of **5** is identical with the minor isomer obtained from the catalytic hydrogenation of the same material and the desired stereoisomer **3** satisfies all the spectroscopic information available and subsequently proved identical to those of **3** prepared by an unambiguous route. A comprehensive review of dissolving metal reductions of conjugated enones[14] indicates that these reactions usually lead to a preponderance of the more stable stereoisomer even though reversible protonation at the β-carbon of the enone is unlikely and it has been established[15] that steric hindrance to protonation in these reacts is negligible. Rationalization of this result has proven difficult, but the experimental evidence is clear. In the current case, neither steric nor stereoelectronic arguments adequately explain why protonation should occur from the face *syn* to the established cyclopentane ring. Nevertheless, the evidence for such a mode of attack is compelling.

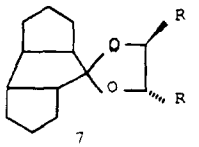


Scheme 1

The ^{13}C NMR spectrum of **5** is noteworthy. The olefinic sp^2-hybridized carbons resonate at 189 and 150 ppm. The former is a particularly low field, even for the β-carbon of a conjugated enone. However, the chemical shifts of the same carbons in the related molecule which lacks the saturated 5-membered ring are 187 and 148.[16] In each case the chemical shift values indicate the presence of significant strain in the system.

In order for **3** to be useful as a chiral auxiliary, it must be available in resolved form. To date we have been unable to achieve this resolution on a synthetically useful scale. Kinetic resolution by reduction with

Baker's yeast[17] and formation of chiral ketals (eg. 7, R=Me) were both unsuccessful. The carbamate **8** from reaction of **4** with R(-)-(1-naphthyl)ethyl isocyanate or the camphanic **9** or Mosher esters **10** could be prepared. In each case the NMR spectra indicated the presence of a mixture of diastereomers, but these could not be separated by chromatography. Three recrystallizations of **9** from 95% ethanol resulted in a 40:1 ratio of the two isomers. However, the large material losses encountered in this recrystallization did not encourage us to pursue this resolution further.



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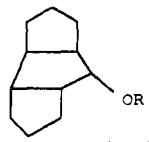
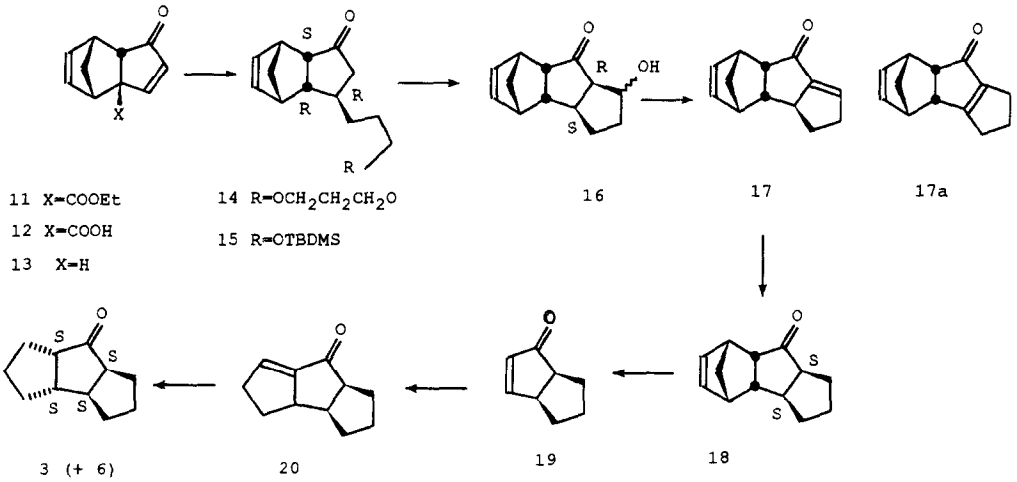


8 R=C(O)NHCH(CH$_3$)Napth

9 R=camphanoyl

10 R=C(O)CH(CF$_3$)C$_6$H$_4$OCH$_3$

This failure led us to proceed with an asymmetric synthesis of **3**. The preparation[18] and enzyme catalyzed kinetic resolution of **11**[19] and its decarboxylation to (+)-**13**[20] have been reported. The absolute configuration of (+)-**13** is given in Scheme 2. The enantiomer of (+)-**13** can be obtained from the neutral fraction of the enzyme-catalyzed hydrolysis. It should be noted that although the optical rotations reported for "enantiomerically pure" **11** and **12** are reasonably consistent, those for (+)-**13** vary considerably.[20] The optical rotation for (+)-**13** obtained directly from the decarboxylation reaction was $[\alpha]_D$= +128 whereas one recrystallization afforded higher melting material with $[\alpha]_D$= +139. It has been reported[19d] that the source of this discrepancy lies in the racemization of acid **12** during the decarboxylation step, presumably via a reversible Diels-Alder reaction.

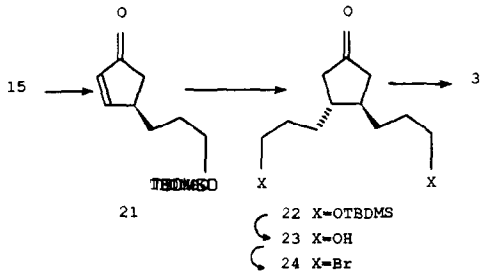


Scheme 2

Two routes (Schemes 2 and 3) from resolved **13** to resolved **3** and **4** have been successfully completed. Addition of the cuprate derived from the propylene ketal of 3-bromopropanal to ketone (+)-**13** afforded **14**. Hydrolysis with 1% HCl in 90% aqueous acetone afforded the aldol product **16** as a 5:1 mixture of epimers which could best be dehydrated to enone **17** by treatment of the mesylate of **16** with DBU. It was important to avoid isomerization to **17a** as the intervention of this material would effectively negate the resolution of

(+)-13. Reduction of 17 to ketone 18 was achieved using Li/NH_3. Thermal reversal of the Diels-Alder reaction has been reported[21] to proceed in the presence of $BF_3.Et_2O$. In our hands this was unsuccessful, but the use of $EtAlCl_2$[22] afforded 19 in excellent yield. A second five-membered ring was then annulated using the same set of reactions to give 20 (Scheme 2). Catalytic hydrogenation of 20 gave a 4:1 mixture of 3 and 6 which, as before, could not be separated. The overall yield of 3 using this route was 10% from (+)-13 . Although the NMR and chromatographic data for 20 indicated the presence of only one compound, the formation of two diastereomers in the hydrogenation reaction indicates a lack of stereoselectivity in the hydrogenation reaction or the intermediacy of the isomer of 20 with a fully substituted double bond.

In order to avoid this difficulty, an alternate route (Scheme 3) beginning from 15 was employed. Retro Diels-Alder reaction of 15 followed by cuprate addition afforded (-)-22. The retro Diels-Alder on



Scheme 3

14 or 15 was unsuccessful when either of $EtAlCl_2$ or BF_3 was employed, but the uncatalyzed thermal version of this reaction was successful. Deprotection and cyclization of both five-membered rings by an *alkylative* procedure afforded (+)-3 in 37% overall yield from (+)-13. Reduction to (+)-4 with LAH was routine. Analysis of the 300 MHz. ^1H NMR spectrum of the camphanate ester of 4 showed it to have an enantiomeric excess of 91%.

Assignment of the absolute configuration to (+)-3 and (+)-4 follows directly from the reactions used. The stereochemical designators change several times due to the changing priorities of the substituents on the chiral centers. However, the enzyme specificity for the 2S-isomer of 11 leads unambiguously to the assignment of the S,S,S,S configuration to (+)-3 and (+)-4. The enantiomeric all-R series could be prepared by conversion of (+)-13 to its enantiomer by the Wharton Reaction,[23] by the general route shown in Scheme 2 but utilizing catalytic hydrogenation of 17a in place of the Li/NH_3 reduction of 17, or by using the 2R-isomer of 11 obtained from the residue from the enzymatic hydrolysis reaction.

The carbonyl group in 3 is surprisingly hindered. The ethylene ketal (7 R=H) and the 2,4-DNP derivative could be formed relatively easily. However, LAH reduction to alcohol 4 did not proceed at a convenient rate below 60 °C and attempted preparations of 7 (R=Me or Ph) or imines from *tert*-butyl glycinate or benzyl amine failed. The latter appeared to react initially as evidenced by the disappearance (gc) of the starting materials, but the imines, if they were formed, were hydrolyzed by traces of moisture and only ketone 6 could be isolated by column chromatography. Thus our original intentions for 3 were negated. Other synthetic applications of this new chiral auxiliary will be reported in the future.

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Experimental

Infrared spectra were run as neat liquids unless otherwise noted. ^{1}H NMR were run at 300 MHz and ^{13}C NMR spectra were run at 75 MHz in $CDCl_3$ solution. Both NMR spectra are reported in ppm downfield from TMS as an internal standard. Absorptions listed in brackets [ ] are for the minor stereoisomer. Where DEPT editing of carbon spectra (DEPT-135 pulse sequence) was performed, the multiplicity of the ^{13}C signals which would have been seen in off-resonance experiments are indicated. Silica gel G60 was used for column chromatography, the drying agent used was anhydrous $MgSO_4$ and solvents were removed at reduced pressure.

The preparation of **5** was carried out as described in the literature.[13] Because the original description of **5** did not include the ^{13}C NMR spectrum, this is presented below without comment.

5: 207.20(s), 189.01(s), 150.11(s), 57.57(d), 42.98(d), 31.41(t), 29.38(t), 27.90(t), 27.68(t), 24.64(t), 24.35(t)

cis,syn,cis-tricyclo[6.3.0.0^{3,7}]undecan-2-one (**6**). This product was prepared by hydrogenation of **5** as indicated in the literature.[13] It was obtained as a 9:1 mixture of isomers as was indicated by the ^{13}C NMR data; IR (neat): 1732cm^{-1}; ^{1}H NMR: 2.82 (bs, 4H), 1.92-1.50 (m, 6H), 1.47 (pent, 4H, J = 7 Hz), 1.38-1.25 (m, 2H); ^{13}C NMR: 223.30, 54.60 [53.50], 41.69 [46.69], 29.37 [35.00], 27.32 [30.30], 27.26 [26.32].

The 2,4-DNP melted at 162-164 °C [lit[13] 169-170 °C] .

rac cis,anti,cis-tricyclo[6.3.0.0^{3,7}]undecan-2-one (**3**). To 150 mL of ammonia which had been condensed in a 250 mL flask equipped with a dropping funnel and a Dry Ice condenser was added 0.27 g (0.04 mol) of lithium metal. The solution was stirred for 20 min to allow for complete solution of the metal. Enone **5** (2.5 g, 0.015 mol) in 20 mL of dry THF was added dropwise with stirring over 1 h. The deep blue color of the solution persisted after stirring an additional 20 min. The reaction was quenched by the addition of 1.3 g of anhydrous NH_4Cl and allowing the mixture to stir at -78 °C for 10 min. The condenser was removed and the ammonia allowed to evaporate overnight. Water was added and the aqueous layer was extracted with 2x20 mL of ether. The organics were dried and concentrated to afford 2.4 g of a clear oil which was dissolved in 20 mL of methylene chloride containing 5.4 g of PDC. The mixture was stirred at ambient temperature overnight, 20 mL of ether were added and the solution was filtered through a pad of $MgSO_4$. Concentration and column chromatography (3:1 pet. ether:ether) afforded 1.8 g (70%) of **3** contaminated by 10% of **6** as a clear oil; IR (neat): 1731 cm^{-1}; ^{1}H NMR: 2.59 (dt, 2H, J = 4.2, 8.9 Hz), 2.34 (m, 2H), 1.95 (m, 6H), 1.51 (pent, 4H, J = 7 Hz), 1.32 (m, 2H); ^{13}C NMR: 226.93, 53.57 [54.60], 46.59 [41.69], 34.99 [29.36], 30.30 [27.34], 26.32 [27.28].

Anal. Calcd. ($C_{11}H_{16}O$): C, 80.44; H, 9.81. Found: C, 80.17; H, 9.66.

The 2,4-DNP derivative melted at 146-148 °C.

Ketal 7 (R=H) Ketal **7** was prepared using the literature procedure for reaction of ketone **6**.[13] Distillation (Kugelrohr, 100-120 °C, 0.01mm) afforded 86% of **7**, contaminated with a few percent of ketone

3 as a clear oil. ^{1}H NMR: 3.95-3.85 (m, 4H), 2.70-2.40 (m, 2H), 2.05 (m, 1H), 1.95-1.30 (m, 13H); ^{13}C NMR: 120.11(s), 64.60(t), 51.70(d), 49.10(d), 36.87(t), 26.00(t), 26.36(t).

rac cis,anti,cis-Tricyclo[6.3.0.0^{3,7}]undecan-2-ol (4) Ketone 3 (0.5 g, 3 mmol) was added via syringe to 0.25 g, (7 mmol) of LAH in 4 mL of dry THF over 10 min and the reaction was refluxed overnight. Work-up consisted of adding enough sat. NH_4Cl solution to form two phases, separation of the phases and extraction of the aqueous phase with ether. The combined organic phases were dried, concentrated and distilled (Kugelrohr, 75-85 °C, 0.2 mm) to afford 0.5 g (98%) of a clear oil, IR: 3360-3380cm^{-1} (broad); ^{1}H NMR: 3.88 (t, 1H, J = 6.8 Hz), 2.49 (m, 1H), 2.27 (m, 1H), 2.00 (m, 2H), 1.84-1.23 (m, 13H); ^{13}C NMR: 81.38(d), 52.23(d), 50.49(d), 49.90(d), 49.61(d), 34.38(t), 33.89(t), 30.31(t), 26.45(t), 25.67(t), 25.22(t).

The carbamate 8 was prepared by adding 0.21 g (1.3 mmol) of 4 and 0.25 g (1.3 mmol) of R(-)-(1-naphthylethyl)isocyanate to 2 mL of dry benzene. The reaction was refluxed for 24 h at which time, tlc (2:1 pet. ether:ether) showed no remaining starting material. The cooled reaction mixture was poured into 5 mL of water, extracted with ether and the extracts were dried and concentrated to afford 0.5g of a thick oil. Column chromatography using the same solvent mixture gave 0.34 g (72%) of a white solid, mp 93-97 °C; IR: 3348, 2943, 1684, 1539cm^{-1}; ^{1}H NMR: 8.1 (broad, 1H), 7.80 (m, 2H), 7.60-7.40 (m, 4H), 5.62 (br, 1H), 4.95 (bs, 1H), 4.78 (bt, 1H), 2.70 (m, 1H), 2.40 (m, 1H), 2.05 (m, 2H), 1.90-1.20 (m, 15H); ^{13}C NMR: 155.9, 134.1, 128.9, 128.2, 126.4, 125.8, 125.4, 123.5, 122.2, 83.9, 50.0, 49.6, 49.2, 48.4, 46.6, 34.3, 33.7, 30.1, 26.5, 26.0, 25.5, 21.8.

The camphanate 9 was prepared from 50 mg of 4, 70 mg of camphanic acid chloride and 1 eq. of AgCN in 2 mL of dry benzene according to the published procedure.[24] The reaction was refluxed for 24 h, cooled, filtered through Hyflow and chromatographed (2:1 pet. ether:ether) to give 84 mg (85%) of a white solid, mp 88-93 °C; IR: 2942, 1790, 1743cm^{-1}; ^{1}H NMR: 5.00 (dt, 1H, J = 6.5, 6.7 Hz), 2.80-2.30 (m, 3H), 2.21-1.35 (m, 20H), 1.09 (s, 3H), 0.95 (s, 3H). This material (25 mg) was recrystallized three times from 95% ethanol to give 3 mg of a ~40:1 mixture of diastereomers.

The MPTA ester 10 was prepared in 52% yield using the standard procedure.[25] Compound 10 was an oil which ^{1}H NMR showed to be a 1:1 mixture of diastereomers which could not be separated; IR: 2950, 1745, 1270, 1167cm^{-1}; ^{1}H NMR: 7.60-7.15 (m, 5H), 5.08 [5.06] (t, 1H, J = 6.4 Hz), 3.46 [3.45] (s, 3H), 2.78 (m, 1H), 2.63-2.40 (m, 1H), 2.1 (m, 1H), 1.90-1.25 (m, 12H).

Compounds 11[18], 12[19], and (+)-13[19] were prepared as outlined in the literature. Recrystallization of (+)-13 from hexane was necessary to raise the rotation to an acceptable value.

(2S,5R,6R) 5-(3-oxopropyl)-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one propylene ketal (14). The Grignard reagent from 2-(3-bromopropyl)-1,3-dioxolane was prepared by refluxing 3.9g (2 mmol) of the acetal with 0.5 g (2 mmol) of Mg metal and a catalytic amount of iodine in 15 mL of dry THF for 1 h. The turbid solution was cooled to 0 °C an 0.1g. of CuCl (5 mol% based on Mg) was added. After stirring 15 min, a solution of (+)-13 (2 g, 14 mmol) in 15 mL of THF was added dropwise. After stirring 1 h at 0 °C , tlc (1:1 pet ether:ether) showed there was none of the starting enone remaining. The reaction was poured into 20 mL of sat. NH_4Cl solution, filtered through Hyflow and the aqueous layer was extracted with ether. After drying

and evaporation, 3.4 g of a colorless oil was obtained. Column chromatography (1:1 pet. ether:ether) gave 3.3 g of **14** (94%) as a thick colorless oil: IR: 2960, 1732, 1145 cm^{-1}; ^1H NMR: 6.15 (m, 2H), 4.44 (t, 1H, J = 5.3 Hz), 4.12 (m, 2H), 3.75 (m, 2H), 3.18 (m, 1H), 3.05 (m, 1H), 2.92 (m, 1H), 2.61 (m, 1H), 2.31 - 1.90 (m, 3H), 1.75 - 1.31 (m, 8H); ^{13}C NMR: 220.51(s), 136.16(d), 135.24(d), 102.01(d), 66.88(t), 54.9(d), 52.32(t), 48.66(d), 48.28(t), 47.05(d), 46.01(d), 36.79(t), 33.40(t), 31.81(t), 25.77(t).

Anal. Calcd. ($C_{16}H_{22}O_3$). C, 73.26; H, 8.45. Found. C, 73.48; H 8.30

(2S,5R,6R) 5-(3-hydroxypropyl)-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one t-butyldimethylsilyl ether ((+)-**15**). To a suspension of 1 g of lithium wire in 20 mL of ether was added 17 g (67 mmol) of the TBDMS derivative of 3-bromopropanol[26] in 5 mL of ether in portions under an argon atmosphere. The exothermic reaction was allowed to cool before each subsequent addition. After the addition was complete, the reaction was stirred for 1 h at room temperature.

A solution of 6.6 g (32 mmol) of CuBr.Me_2S in 40 mL of ether was cooled to 0 ^oC in an ice bath. To this was added, via syringe, the solution of the lithium compound. The reaction turned orange and then dark. The mixture was stirred for 10 min and then 60 mL of Me_2S was added. After stirring for 30 min at 0 ^oC, a solution of (+)-**13** (2.7 g, 18.5 mmol) in 40 mL of ether was added dropwise. After 1 h, tlc (3:1 pet. ether:ether) indicated that the reaction was complete. The mixture was poured into 40 mL of sat. NH_4Cl solution and filtered. The layers were separated, the aqueous layer was washed with ether and the combined organic extracts were dried and concentrated to give 9 g of a yellow oil. Column chromatography (3:1 pet ether: ether) gave 5.5 g (94%) of **15** as a colorless oil; $[\alpha]_D^{24}$ +56 (c=1.04, MeOH); IR: 2954, 1733, 1252, 1100, 838, 776 cm^{-1}; ^1H NMR: 6.15 (bs, 2H), 3.54 (m, 2H), 3.14 (m, 1H), 3.02 (m, 1H), 2.92 (ddd, 1H, J = 1.6, 4.6, 9.6 Hz), 2.61 (m, 1H), 2.20 (dd, 1H, J = 8.9, 18.5), 1.92 (ddd, 1H, J = 1.8, 6.9, 18.5 Hz), 1.73 - 1.35 (m, 7H), 0.84 (s, 9H), 0.02 (s, 6H); ^{13}C NMR: 220.90(s), 136.28(d), 135.34 (d), 63.13(t), 54.98(d), 52.43(t), 48.91(d), 48.42(t), 47.22(d), 46.22(d), 36.80(d), 34.22(t), 30.96(t), 26.07(q), 18.47(s), -5.18(q).

Anal. Calcd. ($C_{19}H_{32}O_2Si$): C, 71.19; H, 10.06. Found: C, 71.31; H, 10.37.

(2S,8S,9R)Tetracyclo[8.2.1.$0^{2,9}$.$0^{4,8}$]trideca-4,11-dien-3-one (**17**) Acetal **14** (3.15 g, 12 mmol) was refluxed overnight in 90% aqueous acetone containing 0.8 mL of conc. HCl. The acetone was evaporated and the aqueous layer extracted with 3 x 30 mL of ether, and the combined organic layers were dried and evaporated to give a brown oil which gave 2.3 g (85%) of **16** on chromatography using 2:1 pet. ether:ether. NMR analysis showed this to be a 5:1 mixture of the epimers (at the carbinol carbon).

IR: 3404 (br), 2961, 1721, 1184 cm^{-1}; ^1H NMR: 6.19 (m, 1H), 6.01 (m, 1H), 4.28 (m, 1H), 3.18 (m, 1H), 3.07 (m, 1H), 2.86 (m, 1H), 2.68 (m, 2H), 2.54 (m, 1H), 2.41 - 2.05 (m, 4H), 1.70 - 1.28 (m, 3H); ^{13}C NMR: 223.23, 135.43, 135.14, 77.01 [76.58], 65.80, 55.71, 51.61, 48.33, 47.56, 47.50, [42.31] 41.73, [35.38] 35.33, 33.23.

Compound **16** (1.7 g, 8.5 mmol) was added to 3 mL of dry pyridine and cooled to 0 ^oC . Methanesulfonyl chloride (0.8 mL 10 mmol) was added dropwise and the reaction was allowed to warm to room temperature and stirred for 10 h. The mixture was poured into 10 mL of 10% HCl, the phases separated, the aqueous phase extracted with ether and the combined organic phases dried and evaporated. The crude

mesylate was dissolved in 10 mL of dry THF, cooled to 0 ^{o}C, 1.1 equivalents of DBU were added and the reaction was allowed to warm to room temperature. After stirring for 5 h the mixture was poured into 10% HCl, the layers separated, the aqueous phase extracted with ether and the combined organic layers dried and evaporated. There remained 1.0g of a yellow oil which was purified by column chromatography (5:1 pet. ether:ether) to give 0.97 g (62%) of **17** as a colorless oil; IR: 2966, 1704, 1214 cm^{-1}; ^{1}H NMR: 6.28 (m, 1H), 6.10 (m, 2H), 3.18 (m, 2H), 3.02 (s, 1H), 2.55 (m, 4H), 2.35 (m, 1H), 1.72 (pent. 1H), 1.58 (ABq, 1H, J = 8.3 Hz), 1.39 (ABq, 1H, J = 8.3 Hz); ^{13}C NMR: 203.55(s), 153.96(s), 135.99(d), 135.87(d), 133.12(d), 60.02(d), 52.22(t), 49.15(d), 46.18(d), 45.84(d), 45.42(d), 37.43(t), 36.60(t).

Anal. Calcd. ($C_{13}H_{14}O$): C, 83.83; H, 7.58. Found: C, 83.41; H, 7.53.

(2S,4S,8S,9R)Tetracyclo[8.2.1.0^{2,9}.0^{4,8}]tridec-11-en-3-one (**18**). To a solution of 75 mg of Li wire in 20 mL of liq. NH_3 was added **17** (0.85 g, 4.5 mmol) as a solution in 10 mL of dry THF. After 20 min the blue color had disappeared and the ammonia was allowed to evaporate. Water (5 mL) was added and the aqueous phase was extracted with ether. The crude reduction product was stirred with 1 equiv of pyridinium dichromate in methylene chloride overnight. Ether was added, the mixture filtered through Hyflow and the residue from solvent removal was chromatographed (2:1 pet. ether:ether) to give 0.53 g (61%) of **18** as an oil; bp 110-120 ^{o}C (4 mm, Kugelrohr); IR: 2948, 1727 cm^{-1}; ^{1}H NMR: 6.16 (dd, 1H, J = 3.0, 5.6 Hz), 6.01 (dd, 1H, J = 2.9, 5.6 Hz), 3.15 (bs, 1H), 3.04 (bs, 1H), 2.85 (dd, 1H, J = 4.8, 8.6 Hz), 2.52 (ddd, 1H, J = 1.6, 4.1, 8.6 Hz), 2.29 - 2.10 (m, 2H), 1.95 - 1.54 (m, 3H), 1.52 - 1.24 (m, 5H); ^{13}C NMR: 225.00(s), 135.69 (d), 135.07(d), 55.93(d), 55.90(d), 51.64(t), 48.10(d), 47.48(d), 47.27(d), 43.20(d), 36.21(t), 30.36(t), 26.57(t).

Anal. Calcd. ($C_{13}H_{16}O$); C, 82.93; H, 8.56. Found: C, 82.58; H, 8.78.

(1S,5S) Bicyclo[3.3.0]oct-3-en-2-one (**20**). Enone **18** was converted to **19** in 65% yield using Grieco's method[22]; IR: 2965, 1727, 1147 cm^{-1}; ^{1}H NMR: 4.53 (m, 1H), 4.05 (m, 2H), 3.72 (m, 2H), 2.64 (m, 1H), 2.48 (m, 2H), 2.01 (m, 2H), 1.92 - 1.22 (m, 12H); ^{13}C NMR: 221.73(s), 102.37(d), 102.15(d), 66.98(t), 52.20(d), 47.53(d), 45.55(t), 40.60(d), 35.32(t), 33.88(t), 30.42(t), 29.55(t), 25.087(t), 23.97(t).

Compound **20** was obtained from **19** using the same four steps and conditions as were utilized in the conversion of (+)-**13** to **17**. The yield over the four steps was 30%: IR: 2960, 1700, 1620 cm^{-1}; ^{1}H NMR: 6.42 (t, 1H, J = 5.5 Hz), 2.84 (m, 2H), 2.75 (m, 2H), 2.63 (m, 2H), 1.93 - 1.41 (m, 7H); ^{13}C NMR: 205.38(s), 151.40(s), 138.60(d), 58.80(d), 53.16(d), 47.81(d), 37.82(t), 35.69(t), 32.55(t), 29.01(t), 26.24(t).

Calcd.($C_{11}H_{14}O$): C, 81.43; H, 8.68. Found: C, 81.74; H, 8.98.

(4S) 4-(3-*tert*-butyldimethylsilyloxypropyl)-2-cyclopenten-1-one ((+)-**21**). A solution of **15** (5.4 g, 16.8 mmol) in 1,2-dichlorobenzene was refluxed for 4-5 h. The reaction was monitored by tlc using 3:1 pet. ether:ether. The resulting solution was added to the top of a dry silica gel column and eluted successively with pet. ether, 8:1 pet. ether:ether, then 2:1 pet ether:ether to give 3.3 g (77%) of **21** as a yellow oil; $[\alpha]_D^{25}$ +39.6 (c=0.9, MeOH); IR: 2929, 1745, 836 cm^{-1}; ^{1}H NMR: 7.62 (dd, 1H, J = 2.4, 5.6 Hz), 6.13 (dd, 1H, J = 1.8, 5.6 Hz), 3.61 (t, 2H, J = 6.0 Hz), 2.92 (m, 1H), 2.52 (dd, 1H, J = 6.3, 18.8), 1.98 (dd, 1H, J = 2.1, 18.8 Hz), 1.65 - 1.20 (m, 4H), 0.88 (s, 9H), 0.02 (s, 6H); ^{13}C NMR: 209.83, 168.35, 133.68, 62.31, 41.94, 41.00, 31.09, 30.67, 25.90, 18.29, -5.35.

Anal. Calcd. ($C_{14}H_{26}O_2Si$): C, 66.08; H, 10.29. Found: C, 66.37; H, 10.54.

(3S,4S) 3,4-bis(3-tert-butyldimethylsilyloxypropyl)-2-cyclopenten-1-one ((-)-**22**) This ketone was prepared by the method given for ketone **15**. The yield of **22** after chromatography was 82%; $[\alpha]_D^{25}$ -47.7 (c=0.5, MeOH); IR: 2932, 1745, 1102, 837 cm^{-1}; ^1H NMR: 3.59 (t, 4H, *J* = 6.4 Hz), 2.43 (m, 2H), 1.80 (m, 6H), 1.45 (m, 4H), 1.21 (m, 2H), 0.87 (s, 18H), 0.03 (s, 12H); ^{13}C NMR: 218.60(s), 63.11(t), 45.24(t), 42.66(d), 31.34(t), 30.25(t), 26.04(q), 18.43 (s), -5.19(q)

Anal. Calcd. ($C_{23}H_{48}O_3Si_2$): C, 64.42; H, 11.28. Found: C, 64.75; H, 11.59.

(3S,4S) 3,4-bis(3-hydroxypropyl)cyclopentanone ((-)-**23**). A solution of **22** (3.7 g, 8.7 mmol) in a mixture consisting of 2 mL of THF, 2 mL of H_2O and 6 mL of HOAc was stirred at 25 °C for 24 h. The solvents were evaporated and the residue chromatographed on Florisil (EtOAc) to afford 1.6 g (94%) of **23** as a thick oil; $[\alpha]_D^{25}$ -90.0 (c=0.58, MeOH); IR: 3404 (br), 1735, 1245, 1055 cm^{-1}; ^1H NMR: 3.62 (t, 4H, *J* = 6.2 Hz), 2.45 (m, 2H), 2.00 (bs, 2H, exchange with D_2O), 1.82 (m, 6H), 1.55 (m, 4H), 1.23 (m, 2H); ^{13}C NMR: 218.72(s), 62.68(t), 45.15(t), 42.60(d), 31.11(t), 30.14(t)

Diol **23** was converted to dibromide **24** in the following manner. To 15 mL of dry CH_2Cl_2 were added 1.5 g (7.5 mmol) of **23** and 5.9 g (17.8 mmol) of CBr_4. The solution was cooled in ice and 4.7 g (17.8 mmol) of triphenylphosphine in 15 mL of CH_2Cl_2 was added dropwise. The reaction was allowed to stir and warm to room temperature overnight. The solvents were evaporated and the residue triturated with 2:1 pet. ether:ether. The solution was filtered, evaporated and chromatographed (3:1 pet. ether:ether) to give **24** as a yellow oil (1.8 g, 75%) which was used without further purification; IR: 2973, 1738 cm^{-1}; ^1H NMR: 3.41 (m, 4H), 2.42 (m, 2H), 1.85 (m, 10H), 1.38 (m, 2H); ^{13}C NMR: 217.15, 44.93, 42.10, 33.57, 32.52, 31.24

cis,anti,cis-tricyclo[6.3.0.0^{3,7}]undecan-2-one (**3**) from dibromide **24**. Dibromide **24** (1.7 g, 5.2 mmol) was refluxed in 100 mL of ethanol containing 5.2 g (8 equiv.) of K_2CO_3 for 18 h. The ethanol was evaporated, 10 mL of water was added and the aqueous solution extracted with ether. The ethereal solution was dried and evaporated to give 0.9 g of a yellow oil which was purified by Kugelrohr distillation (80-90 °C, 0.2 mmHg)to give 0.75 g (86%) of **3** as a colorless oil, identical in all respects except its optical activity to the racemic material; $[\alpha]_D^{25}$ +166 (c=1.20, MeOH) .

cis,anti,cis-tricyclo[6.3.0.0^{3,7}]undecan-2-one (**3**) from **20**. A solution of 27 mg of **20** in 1 mL of ethyl acetate was hydrogenated over 10 mg of 10% Pd/C overnight. Filtration and evaporation afforded 28 mg of a clear oil. ^1H NMR showed the product to be a 4:1 mixture of ketones **3** and **6**.

(S,S,S,S) cis,anti,cis-Tricyclo[6.3.0.0^{3,7}]undecan-2-ol (**4**) Reduction of (-)-**3** in the same manner as was used for the racemic ketone afforded alcohol **4** whose spectroscopic properties were identical with the racemic material; $[\alpha]_D^{25}$ +153 (c=1.03, MeOH).

References and Footnotes.

1. (a) Chemical Abstracts Name: 3aα,3bβ,6aβ,7aα-decahydro-7H-cyclopenta[a]pentalen-7-one; (b) Chemical Abstracts Name: 3aα,3bβ,6aβ,7aα-decahydro-7H-cyclopenta[a]pentalen-7-ol.
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