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THE UTILITY OF SILICON IN ORGANIC SYNTHESIS†

ANNULATION METHODOLOGY AND APPLICATIONS EMPLOYING α-TRIMETHYLSILYL VINYL KETONES

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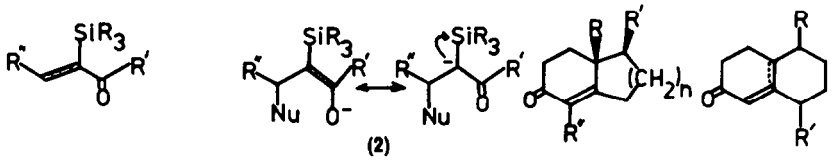
Abstract—New annulation methodology based upon the addition of diorganocuprates to α,β-unsaturated ketones and regiospecific trapping of the resulting enolate with α-trimethylsilyl vinyl ketones is presented. The stereochemical details of the process have been elucidated and are discussed. Application of this methodology to the synthesis of a variety of polycyclic ketone structures is described including applications to steroid synthesis.

The process of annulation of rings as part of the protocols for the stereoselective synthesis of complex polycyclic systems is a fundamental strategy and an enormous number of ingenious solutions to this problem have been developed over the past 40 years. Progress in the area has been nicely summarized in several reviews, one recent such summary is that of Jung.[1]

Those annulation methods which rely upon Michael addition of an enolate anion to an acceptor, however, suffer from inherent limitations which are a consequence of the reversibility of the Michael reaction and the propensity of most acceptors to undergo multiple addition and polymerization. Use of Michael acceptor equivalents which generate the acceptor *in situ* serve to reduce the problem in some instances;[2] however, for all practical purposes, use of less basic (more stabilized) enolates or protic (or effectively protic) media and excess of the annulating reagent are required to obtain useful overall yields of products. A further consequence of the multiple addition/polymerization problem is the observation that kinetically generated enolates cannot be effectively trapped with high regiospecificity with respect to the original enolate due to the fact that operations must be conducted under conditions conducive to enolate equilibration in order to avoid multiple addition.[3] Of course use of acceptor equivalents which funtion as alkylating agents (whose reactions are thus rendered irreversible) obviates the problem, but at the expense of sometimes significant numbers of additional manipulations which must be performed to complete the annulation operation.[4] Furthermore, the stereoelectronic requirements for alkylation are sometimes lower than the corresponding Michael addition process[5] leading to poorer stereoselectivity. Consequently, it was of interest to develop classes of Michael acceptors whose reactions are irreversible and whose propensity for multiple additon is low. Stork pioneered the development of one such class of reagents.[6] The α-trialkylsilyl vinyl ketones **1** fulfill the requirements in that they are usually stable showing little tendency toward polymerization, reasonable levels of reactivity toward enolates, yet no tendency toward multiple addition. Furthermore, removal of the trialkylsilyl group occurs during the second stage of the annulation process requiring no additional operations to effect removal. These favorable properties are presumably the result of the ability of Si to provide additional stabilization of the intermediate enolate by d–p π overlap facilitating the 1,4 addition and, along with the additional steric hindrance provided by the trialkyl silyl group, reducing the reactivity of the intermediate enolate **2** toward additional acceptor molecules.

Our interest in the problem arose from a need to prepare intermediates of the type **3–5** which appeared ideally suited for the synthesis of a variety of terpenes such as fukinone (**6**),[7] aristolone (**7**),[8] gascardic acid (**8**),[9] and the cadinanes (**9**). A very direct pathway appeared plausible based upon the general construction sequence illustrated for **6** in eqn (1), if a tandem conjugate addition-annulation could be accomplished with good regio

†Dedicated to Prof. Gilbert Stork on the occasion of his 60th birthday.

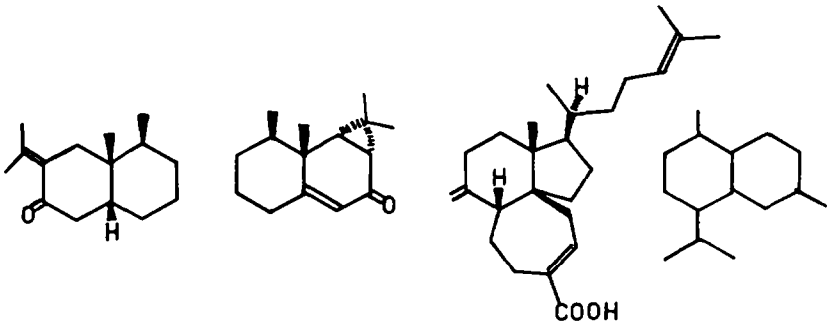


(2)

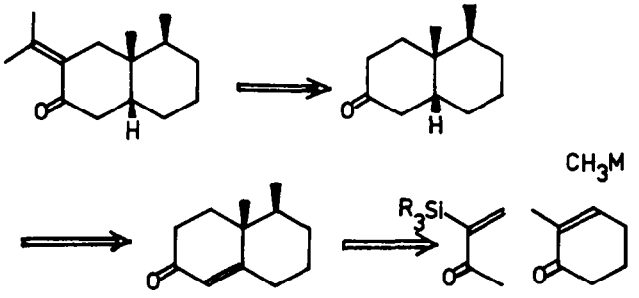
(1a) R=Me, Et; R'=R''=alkyl, H
(1b) R=Me; R'=CH_3; R''=H

(3) R=R'=R''=alkyl n=1
(4) R=R'=R''=alkyl n=2

(5) R=R';=R'' =alkylin=2



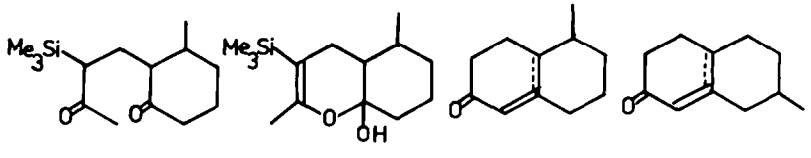
(6) (7) (8) (9)



and stereochemical control as required.[10,11] At the outset, there was some question as to whether regiospecific trapping of kinetically generated enolates would be possible,[5] but the α-trialkylsilyl vinyl ketones appeared to possess the characteristics required for the annulating agent. We had previously developed a similar tandem conjugate addition-alkylation procedure based upon the reactivity of the enolate species generated in the course of conjugate addition of diorganocuprate reagents to α,β unsaturated ketones.[5] The intermediate enolate species appeared to exhibit enhanced levels of regiostability and thus we were encouraged that regiospecific trapping of kinetically generated enolates might be possible utilizing this manner of enolate generation. At the time, the apparent higher levels of regiospecificity and lowered reactivity of the intermediate enolate species were ascribed to the intervention of copper enolate species. However, subsequent NMR studies by House strongly suggested that the intermediate enolate species should be formulated as an Li enolate.[12] Nevertheless, sufficient qualitative differences still appear to exist between the behavior of authentic Li enolates and these intermediates in some systems, that one cannot completely rule out complexes containing Cu as reactive intermediates.

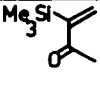
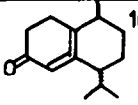
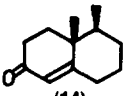
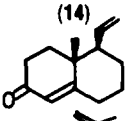
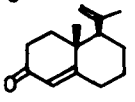
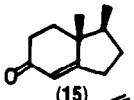
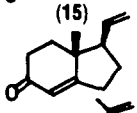
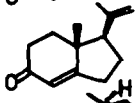
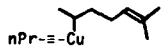
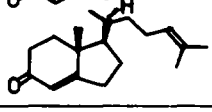
Our initial studies involved addition of 2-cyclohexen-1-one (1 eq) to a solution of $LiCu(CH_3)_2$(1 mol eq)[13] at 0° in ether (1 hr). To the intermediate enolate thus generated was added 3-trimethylsilyl-3-buten-2-one (**1b**) (1 eq)[6,13] at −78° followed by warming to −20° for 1 hr. Aqueous NH_4Cl–NH_4OH workup afforded a mixture of materials which appeared to be primarily diketone **10** and hemiketal **11** by IR and NMR analysis. The proportions of **10** and **11** varied somewhat with the workup procedure and the nature of the substrate. This mixture was directly treated with 2% KOH aq in MeOH at reflux which afforded the octalones **12** and **13** (as an equilibrium mixture of the α,β- and β,γ-isomers in each case) in a ratio of 98:2 (52%) as determined by VPC comparison with an authentic sample[14] and a 23:77 mixture of **12** and **13** prepared by treatment of the pyrrolidine enamine of 3-methyl cyclohexanone with methyl vinyl ketone.[15] Consequently, kinetic trapping of the enolate appeared feasible. We then examined several additional examples which are found in Table 1. Initially reactions were conducted at near ideal stoichiometries, but it was later found that some of the annulating agent was being consumed by reaction with the cuprate or other organometallic species present in solution. Yields of the annulated ketone could be markedly improved (generally to greater than 80%) by taking care to ensure that the conjugate addition step was complete before introduction of the annulating agent and by using a somewhat larger excess of the annulating agent (1.5–2.0 eq), see for example, case 2 in Table 1 and case 1 in Table 2.

The use of α-substituted enones as substrates introduced an additional stereochemical issue, the overall mode of addition of the two groups to the double bond. When 2-methyl-2-cyclohexen-1-one was subjected to treatment with $LiCu(CH_3)_2$ and **1b** in the usual fashion (Table 1) and the products analyzed by capillary VPC, it



(10) (11) (12) (13)

Table 1.

Enone	Annulating Agent	Cuprate	Stoichiometry[a,b]	Major Product(s)[c]	Yield(%)[d]
		$(CH_3)_2CuLi$	1:1.2:1.2	 (16)	53%
	"	$(CH_3)_2CuLi$	1:1.2:1.2		54%
"	"	"	1:1.2:1.5	(14)	85%
"	"		1:1.2:1.2		75%
"	"		1:1.2:1.2		57%
	"	$(CH_3)_2CuLi$	1:1.2:1.2	 (15)	57%
"	"		1:1.2:1.2		50%
"	"		1:1.2:1.2		58%
"	"		1:1:1.1		67%[17]

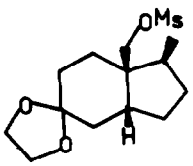
a) Reactions conducted in either mixtures of ether/thf or ether/hexane in which ether was the major component.

b) Ratio of enone:cuprate:annulating agent

c) Products examined by VPC, and were stereochemically homogeneous to >95% except for the final case which was an ~1:1 mixture of diastereomers at the side chain center.

d) Isolated yields of distilled or chromatographically pure materials.

was ascertained that the major product was the *cis*-dimethyl octalone **14** (97:3; c/t) by comparison with authentic material[18] and 3:2 mixture of the two stereoisomers prepared by annulation of 2,3-dimethylcyclohexanone with MVK.[19] This stereochemical outcome has been proved to be general for a variety of cuprate reagents, annulating reagents and enones both in our studies and those of others.[20] It is unaffected by ring size in the enone or branching in the cuprate reagent. As proof of structure, the hydrinenone **15** has been correlated with **16** whose structure has been verified by X-ray analysis.[21] The overall stereoselectivity is generally superior to comparable annulations employing alkylating agents.[5,22]



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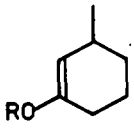


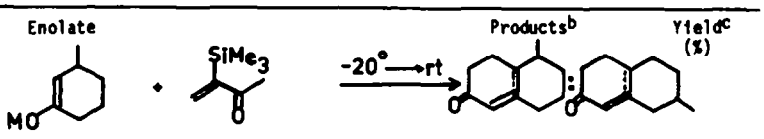
(17) R=metal
(18) R=$(CH_3)_3Si$

A plausible rationalization of the observed high stereoselectivity lies in consideration of the conformations of the intermediate enolate (Scheme 1). Reaction via the conformer B, which allows both relief of $A_{1,2}$ interactions between the Me and alkyl groups and permits the stereoelectronically favored axial approach of the annulating agent, leads directly to the observed *cis* relationship of Me and alkyl groups (R), an overall *trans* addition of the elements of R and the annulating reagent.

However, the enolates derived from the α-unsubstituted and substituted enones examined above are regiostable or only modestly prone to equilibration. In light of these results, it was of further interest to examine classes of enolates which were especially prone to equilibration since the pioneering studies of Stork suggested problems might arise in these cases.[6] It was hoped that the presence of copper species in the medium might enhance the regiostability of the enolate by inhibiting the required proton transfers. Concurrent work from Stork's laboratory also addressed these questions.[23]

Initial studies were conducted on the enolate **17** which was regenerated from the trimethylsilyl enol ether **18** by treatment with MeLi. We were interested in examining

Table 2.



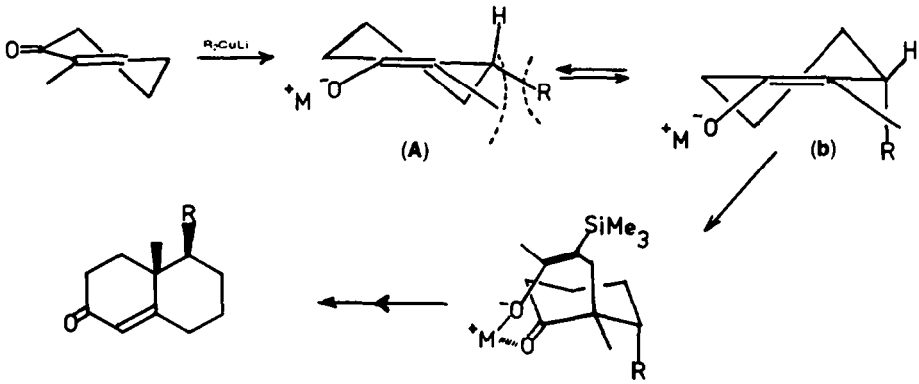
Metal	Solvent[a]				
Li	Ether	99	:	1	50(85)[d]
Li + CuI(1 eq)	"	76	:	24	30
Li + (CH_3Cu) (1eq)	"	98	:	2	50
Li + CuI(1eq) + CH_3Li(1eq)	"	74	:	26	51
Li	THF	95	:	5	48
Li	DME	80	:	20	64
In situ trapping using Li/NH_3 generation	Ether	98	:	2	55
In situ trapping using $(CH_3)_2CuLi$	Ether	99	:	1	52

a) Reactions were run under anhydrous conditions in the solvent indicated utilizing a stoichiometry of 1:1 enolate:annulating agent.

b) Product ratios determined by VPC (20% Carbowax-20-M; 10 ft; 170°C) by comparison with authentic materials.

c) Yields of distilled materials.

d) Yield of distilled materials when a stoichiometry of 1:1.33 enolate to annulating agent was utilized in parentheses.



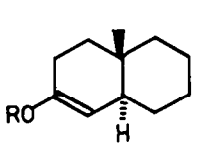
Scheme 1.

the effect of added Cu species on the regiochemical outcome of the annulation. The results are outlined in Table 2. The results suggest that Cu species, at least as external addends, are not responsible for the high regiospecificity observed, and that if Cu species are involved, they are operationally indistinguishable from Li enolates in this case. Noteworthy also is the fact that more Lewis basic solvents appear to enhance proton transfer leading to loss of regiospecificity as would be expected,[24] and that metal-ammonia reduction can be utilized to generate the enolate which is useful after solvent exchange for ether.

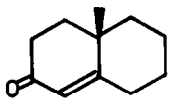
A more difficult case is the enolate **19** derived from reduction of octalone **20**, which is less stable than its counterpart **21** by ~3 kcal/mole.[25] The regiochemically pure enolate **19** was obtained from the enol silyl ether **22** with MeLi.[26] Trapping at −78→−20° with **1b** (1.5 eq) afforded the known tricyclic enone **23** (m.p. 124–126°) in 69% yield, with less than 5% of the isomeric linear tricyclic enone **24** present.[27,28] Direct trapping of **19** after Li/NH_3 reduction as described above was possible in somewhat diminished yield (60%).

We sought to demonstrate utility of the above process by application to steroid synthesis. The tetracyclic D-homoketones **25** and **26** were chosen as targets since these substances had previously been converted to (±)progesterone[29] and (±)testosterone,[30,31] respectively. In order to proceed efficiently, we required the bis-annulating agent **27**. This material was prepared as shown in Scheme 2 utilizing the route developed previously for **1b**.[5,13]

The route to ketone **25** (Scheme 3) begins with the Wieland–Miescher ketone. Conversion to enone **28** was effected by initial protection of the enone system by formation of the pyrrolidine enamine, followed by treatment with excess MeLi in ether. Acidic workup



(19) R=Li
(22) R=TMS



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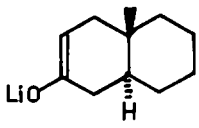

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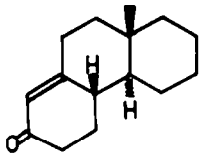

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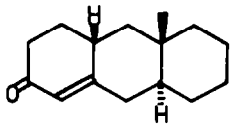

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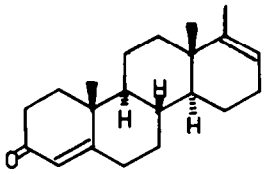

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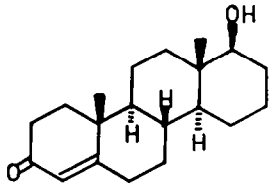

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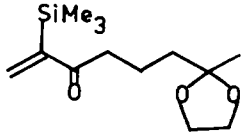
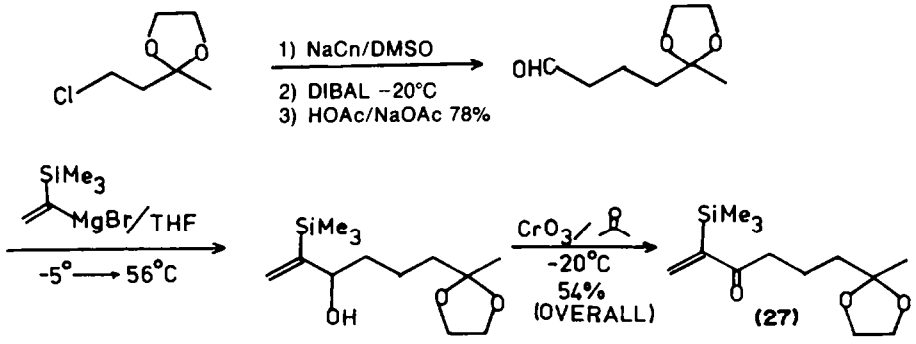


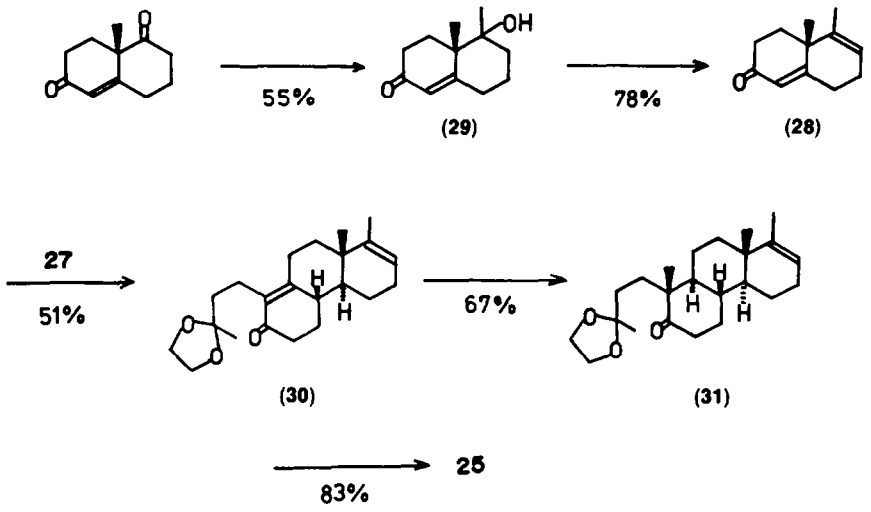
(27)

afforded the crystalline (m.p. 89–91°) alcohol **29**. Dehydration of **29** with $SOCl_2$ and pyridine in ether at 0° afforded as the product **28**, accompanied by minor amounts of the exocyclic olefin isomer. Reduction of **28** with Li/NH_3-ether and exchange of the ammonia for anhyd ether, followed by treatment of the resulting enolate solution initially at −78° with **27** (1.1 eq) and warming to −20° (2 hr) afforded on workup the crude Michael adducts. Subsequent base treatment (aq KOH/MeOH/Δ/2 hr) gave, after chromatographic purification, a single annulated product **30** in 51% yield. Reductive alkylation of **30** (Li/NH_3/ether; MeI(xs)) then provided **31** in 67% yield.[29] Exposure of **31** successively to 10% HCl in acetone and hot KOH–MeOH aq effected deketalization and cyclization to afford **25** (m.p. 141–143°) in ~83% yield from **31**.[28] In a similar manner, as outlined in Scheme 4, the known tetrahydropyranyl protected hydroxy enone **32**[32] was transformed into (±)D-homotestosterone (**26**) (m.p. 155–158°) in the indicated yields.[28,29]

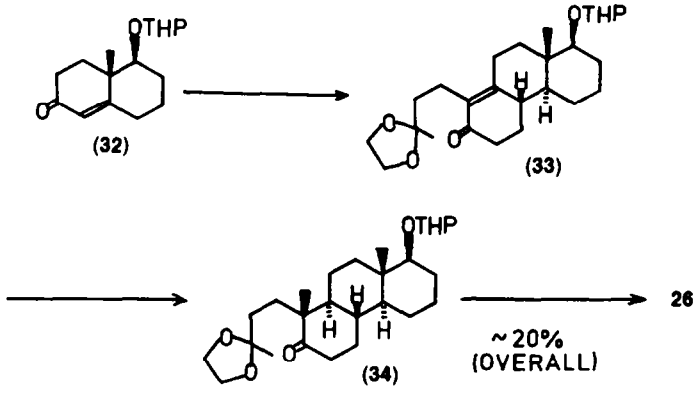
Thus, as the foregoing indicates, the combination of regiospecific generation of enolates by means of conjugate addition or reduction followed by trapping with α-silylated enones provides a powerful protocol for the



Scheme 2.



Scheme 3.



Scheme 4.

rapid and stereoselective assembly of complex polycyclic systems. Such methodology has proven valuable in the solution of the synthetic problem posed by Gascardic acid,[9] and is finding increasing use in the efficient assembly of naturally occurring substances.[33]

EXPERIMENTAL

M.ps were determined with a Thomas-Hoover capillary m.p. apparatus or on a Fisher-Johns hot stage and are uncorrected. Distillations unless otherwise specified were bulb to bulb using a Buchi Kugelrohr distillation oven and distillation temps recorded are oven temps. IR spectra were obtained on a Perkin-Elmer 137 spectrophotometer and are reported in reciprocal centimeters (cm^{-1}) using polystyrene as a standard. NMR were recorded on a Varian T60 (60 MHz) spectrometer and are reported in ppm(δ) relative to TMS. Mass spectra were recorded on an AEI MS-902 mass spectrometer. Exact mass data were obtained by peak matching and were recorded at the NIH regional mass spectrometry facility at Michigan State University. Microanalyses were performed by Midwest Microlab, Indianapolis, Indiana.

All solvents and reagents specified as anhydrous were dried by distillation from an appropriate drying agent (e.g. ethers-LAH) before use. All reactions involving bases and organometallic reagents were performed under an inert atmosphere. All other commercially available reagents and solvents were used as received unless otherwise specified.

General procedure for conjugate addition-annulation

(R,S)4a,(S,R)5 - *Dimethyl* - 4,4a,5,6,7,8 - *hexahydro*-2(3H)*naphthalenone*(14) *and* (R,S)4a,(R,S)5 - *dimethyl* - 4,4a,5,6,7,8 - *hexahydro* - 2(3H)*naphthalenone.* A soln of lithium dimethylcuprate (2 mmol) in anhyd ether (8–10 mL) was prepared as usual[13] from purified CuI[34] (456 mg; 2.4 mmol) and MeLi (2.82 mL of a 1.7 M soln in ether; 4.8 mmol) at 0°. To this soln was added dropwise a soln of 2-methyl-2-cyclohexen-1-one[35] (220 mg; 2.0 mmol) in 2 mL of anhyd ether. The resulting mixture was stirred for 35 min at 0° then cooled to −20° (dry ice/CCl_4). A soln of **1b**[13] (339 mg; 2.4 mmol) in 5 mL anhyd ether was added dropwise over 15 min. The resulting mixture was stirred at −20° for 1 hr, then quenched by addition of 3 ml 10% aq NH_4Cl–NH_4OH buffer aq (pH = 8). The whole mixture was transferred to a separatory funnel with 20 mL ether and shaken with an additional 10 mL 10% NH_4Cl–NH_4OH aq buffer until all the solids had dissolved. The organic layer was separated and the aqueous layer extracted with 3 × 10 mL ether. The combined organic phases were washed once with NH_4Cl/NH_4OH buffer (5 mL), water, dried over anhyd $MgSO_4$ and concentrated.

The residue was taken up in 25 mL MeOH and 2 mL 4% aqKOH added. The mixture was heated at reflux for ~2–3 hr under argon. After cooling, the solvents were evaporated and the residue taken up in 25 mL ether. The mixture was washed with 5 mL sat NaCl (2x), dried over $MgSO_4$ and evaporated to afford the crude annulation products. Purification by distillation at 110°/0.3 torr afforded 192 mg (54%) of a mixture of 14 and its related *trans* isomer which was determined to be in excess of 97:3 (14/*trans*) by capillary VPC (50′ column/carbowax-20-

M/160°).[18] Detection limit for *trans* ~3%. No measurable amount of the *trans* isomer was detected.

The octalone **14** had IR(film): 1685, 1620 cm^{-1}; NMR($CDCl_3$): δ5.56 (s(br), 1), 2.50–1.20(m, 11), 1.12(s, 3), 0.90(d(br), J = 7 Hz, 3). MS: 178(P^+).

4,4a,5,6,7,8 - *Hexahydro* - 5 - *methyl* - 2(3H) - *naphthalenone*(**12**) *and* 4,4a,5,6,7,8 - *hexahydro* - 7 - *methyl* - 2(3H) - *naphthalenone*(**13**). By the same procedure, lithium dimethylcuprate (3.6 mmol), 2 - cyclohexen - 1 - one (288 mg; 3 mmol) and **1b** (508 mg; 3.6 mmol) afforded 255 mg of the title octalones (52%) by distillation at 110°/0.5 torr. VPC comparison with the authentic 5-methyl isomer[14] and with a sample prepared from 3-methyl cyclohexanone (10'–20% Carbowax-20 M at 175°) showed ≤2% of the 7 isomer to be present. Small amounts of β,γ-enone isomers also present.

The mixture of octalones **12** and **13** had IR(film): 1705 (m),1682(s), 1618 cm^{-1}; NMR($CDCl_3$): δ 5.67 (s, 1), 2.70–1.0(m, 12), 1.10(s(br), 3); MS: 164(P^+).

4,4a,5,6,7,8 - *Hexahydro* - 8 - *isopropyl* - 5 - *methyl* - 2(3H)*naphthalenone.* Using a similar procedure to that described for **14**, lithium dimethyl cuprate (2.4 mmol) in ether, 6 - isopropyl - 2 - cyclohexen - 1 - one[36] (276 mg; 2.0 mmol) and **1b** (339 mg; 2.4 mmol) were combined. In this instance, the reaction of lithium dimethylcuprate was allowed to proceed for 1.5 hr at 0° before addition of the annulating agent was begun. Furthermore, in this case, the aldol closure was substantially more sluggish requiring use of 10% aqKOH in MeOH and ~18 hr at reflux to be complete (monitored by tlc). The usual purification afforded 219 mg (53%) of the title octalone (and small amounts of its β,γ-enone isomer), b.p. 120°/0.5 torr. This material was identical with authentic material by the usual criteria.[16]

The title octalone had IR(film): 1704(m), 1656(s), 1613 cm^{-1}; NMR($CDCl_3$): 5.65(s, 1), 2.60–1.20(m, 12), 1.20–0.8(m, 9); MS: 206(P^+).

(R,S) - 5 - *Ethenyl* - 4,4a,5,6,7,8 - *hexahydro* - (R,S) - 4a - *methyl* - 2(3H) - *naphthalenone.* A soln of lithium divinyl cuprate (3.0 mmol) in 10 mL anhyd THF was prepared from CuI (570 mg; 3.0 mmol) and vinyl lithium (2.75 mL of a 2.2 M soln in THF; 6.0 mmol). The mixture was warmed to −30° for 15 min and then recooled to −60°. A soln of 2 - methyl - 2 - cyclohexen - 1 - one (275 mg; 2.5 mmol) in 0.5 mL of THF added dropwise over 5 min. The soln was warmed to −20° over ~1 hr. The soln was diluted with 30 mL anhyd ether and the mixture cooled to −78°. A soln of **1b** (426 mg, 3.0 mmol) in 1 mL anhyd ether was added dropwise over 5 min. The mixture was then allowed to warm slowly to 0° over ~2 hr. The reaction was quenched with 2–3 mL of 10% $aqNH_4Cl$ soln and the whole mixture was then poured into ether—10% NH_4Cl/NH_4OH buffer (60 mL; 2:1 V/V). After the solids had dissolved, the organic phase was separated, and the aqueous phase was extracted with ether (3 × 20 mL). The combined organic solns were washed with sat aqNaCl (20 mL), dried over $MgSO_4$ and concentrated to a yellow oily residue.

The entire residue was dissolved in 20 mL MeOH (not entirely homogeneous) and 2 mL of 4% aqKOH added. The resulting mixture was heated at reflux for 2 hr under N_2. The mixture was concentrated and the residue partitioned between ether (40 mL) and water (20 mL). The organic layer was washed with sat aqNaCl, dried over $MeSO_4$ and evaporated to the crude octalone contaminated with hydrocarbon byproducts. Chromatography on SiO_2 with elution by benzene–EtOAc (4:1) followed by distillation at 90°/0.3 torr afforded 355 mg (75%) of the octalone which was >95% pure by VPC (10' Carbowax-2-M at 180°).

The title octalone had IR(film): 1667, 1613 cm^{-1}; NMR ($CDCl_3$): δ 6.07–5.50(m, 1), 5.63(d, J = 2 Hz, 1), 5.0(dd, J_1 = 16 Hz, J_2 = 1.5 Hz, 1), 4.88(dd, J_1 = 6 Hz, J_2 = 3 Hz, 1), 2.40–1.30(m, 11), 1.20(s, 3); MS: 190(P^+). (Found: C, 82.27; H, 9.49. Calc. for $C_{13}H_{18}O$: C, 82.06; H, 9.53%).

4,4a,5,6,7,8 - *Hexahydro* - (R,S) - 4a - *methyl* - (R,S) - 5 - (1 - *methyl-ethyl*) - 2(3H) - *naphthalenone.* A soln of isopropenyl lithium[37] was prepared by treatment of isopropenyl bromide (750 mg; 6.2 mmol) in 10 mL anhyd THF with t-BuLi (7.3 mL of a 1.7 M soln in pentane; 12.4 mmol) at −78° for 1 hr. This soln was added via syringe to a sitrred suspension of CuI (589 mg; 3.1 mmol) in 5 mL anhyd THF at −40°. The dark soln was stirred at −20° to −40° for 15 min then recooled to −78°. A soln of 2 - methyl - 2 - cyclohexen - 1 - one (275 mg; 2.5 mmol) in 1 mL anhyd THF was added dropwise over 5 min, and the soln warmed to −20° over ~1 hr. This mixture was diluted with 40 mL anhyd ether and a soln of **1b** (440 mg; 3.1 mmol) in 5 mL anhyd ether was added dropwise over 5 min. The soln was warmed slowly to 0° over ~1.5 hr and quenched at 0° with 3 mL 10% $aqNH_4Cl$. The whole mixture was shaken with 30 mL 10% $aqNH_4Cl/NH_4OH$ (pH = 8), sat aqNaCl, dried over $MgSO_4$, and evaporated. The crude dark residue was taken up in 25 mL MeOH and 2 mL 4% aqKOH was added. The mixture was heated at reflux for 2 hr under N_2. After cooling, the solvents were evaporated and the residue partitioned between 40 mL ether–H_2O (1:1). The organic phase was washed with sat aqNaCl, dried over $MgSO_4$ and evaporated to a dark oil.

The crude products were chromatographed on SiO_2 in hexane–benzene. Elution with benzene–EtOAc (4:1) afforded the octalone. Distillation at 100°/0.3 torr provided 290 mg of the pure title octalone (57%) which was ≥95% pure by VPC analysis (10'–20% Carbowax-20M at 180°).

The pure title octalone had IR(film): 1670, 1605 cm^{-1}; NMR($CDCl_3$): δ 5.56(d, J = 2 Hz, 1), 4.88(t, J = 1.5 Hz, 1), 4.71(s(br), 1), 2.60–1.40(m, 11), 1.79(d, J = 1.5 Hz, 3), 1.23(s, 3); MS: 204(P^+). (Found: C, 82.11; H, 9.72. Calc. for $C_{14}H_{20}O$: C, 82.30; H, 9.87%).

(R,S) - 1,(S,R) - 7a - *Dimethyl* - 2,3,7,7a - *tetrahydro* - 5(6H) - *indenone.* Using the general procedure cited above for **14**, a soln of lithium dimethyl cuprate (2.4 mmol) in ether was prepared and 2-methyl-2-cyclopenten-1-one[38] (192 mg; 2.0 mmol) was added. To the resulting enolate at −20° was added **1b** (339 mg; 2.4 mmol). After the usual workup, the residue was treated with 10% KOH in MeOH for 13 hr reflux under N_2. Extractive workup using ether and distillation afforded 187 mg of the title octalone b.p. 90°/0.7 torr (57%).

The title indenone had IR(film): 1680, 1625(sh) cm^{-1}; NMR($CDCl_3$): δ 5.51(d, J = 2 Hz, 1), 2.61–1.20(m, 9), 1.0 (s, 3), 0.95(d, 3), MS: 164(P^+). (Found: C, 80.41; H, 9.70. Calc. for $C_{11}H_{16}O$: C, 80.44; H, 9.82%).

(R,S) - 1 - *Ethenyl* - (R,S) - 7a - *methyl* - 2,3,7,7a - *tetrahydro* - 5(6H) - *indenone.* Using the general procedure outlined above for **14**, lithium divinyl cuprate (2.4 mmol) in THF was combined successively with 2 - methyl - 2 - cyclopenten - 1 - one (192 mg; 2.0 mmol) and **1b** (339 mg; 2.4 mmol). After the usual workup and base treatment with 10% aqKOH–MeOH for 18 hr at reflux under N_2, chromatography and distillation at 90°/0.5 torr afforded 190 mg of title indenone (54%).

The title indenone had IR(film): 1675, 1623(sh) cm^{-1}; NMR($CDCl_3$): δ 6.05–5.41(m, 1), 5.61(5, J = 2 Hz, 1), 5.03(dd, J_1 = 16 Hz, J_2 = 1.0 Hz, 1), 4.95(dd, J_1 = 5 Hz, J_2 = Hz, 1), 2.76–1.33(m, 9), 1.07(s, 3); MS: 176(P^+). (Found: 176.1202. Exact mass calc. for $C_{12}H_{16}O$: 176.1201).

(R,S) - 7a - *Methyl* - (R,S) - 1 - (1 - *methylethenyl*) - 2,3,7,7a - *tetrahydro* - 5(6H) - *indenone.* Using a procedure similar to that described above for the next higher homolog of the title compound, a soln of isopropenyl lithium (2.4 mmol), 2 - methyl - 2 - cyclopentene - 1 - one (192 mg; 2.0 mmol) and **1b** (399 mg; 2.4 mmol) were combined. Workup and base treatment with 10% aqKOH–MeOH, and distillation at 100°/0.5 mm afforded 220 mg of the title indenone (58%).

The title indenone had IR(film): 1658, 1620(sh) cm^{-1}; NMR($CDCl_3$): δ 5.54(t, J = 2 Hz, 1), 4.92(t, J = 1.5 Hz, 1), 4.69(s(b), 1), 2.50–1.40(m, 9), 1.81(d, J = 1.5 Hz, 3), 1.10(s, 3); MS: 190(P'). (Found: 190.1358. Exact mass calc. for $C_{13}H_{18}O$: 190.1357).

(R,S) - 1 - ((R,S) - 1',5' - *Dimethyl* - 4' - *hexenyl*) *a* (R,S) - 7a - *methyl* - 2,3,7,7a - *tetrahydro* - 5(6H) - *indenone and* R,S - 1 - ((S,R) - 1',5' - *dimethyl* - 4' - *hexenyl*) - (R,S) - 7a - *methyl* - 2,3,7,7a - *tetrahydro* - 5(6H) - *indenone.* A soln of 1,5 - dimethyl - 4 - hexenyl lithium[39] in hexane (7.4 mL; 3.7 mmol) was added dropwise over 0.5 hr to a stirred suspension of copper pentyne[40] (475 mg; 3.7 mmol) in ether (30 mL) at −78°. The mixture was allowed to warm to −40° over 1 hr and then recooled to −78°. A soln of 2 - methyl - 2 - cyclopenten - 1 - one (364 mg; 3.7 mmol) in ether (5 mL) was added dropwise over 0.5 hr and the mixture

permitted to warm to −25° over 2 hr. At −25°, **1b** (570 mg; 4.0 mmol) in 10 mL anhyd ether was added dropwise over 5 min, and after 1 hr at −25°, the mixture was poured into ice/10% NH_4Cl–NH_4OH (pH = 8). The yellow suspension was removed by filtration through celite and extractive workup with ether afforded the crude products. The mixture was taken up in MeOH (60 mL) and 10% aqKOH (4 mL) and heated at reflux for 18 hr. After cooling, the solvent was evaporated and the resue partitioned between ether and water. The ether extract was washed with sat NaCl, dried over $MgSO_4$, and evaporated. Chromatography of the residue on SiO_2 (30 g) in ether–hexane (1:9) afforded the 650 mg of the title hydrindenones (67%).

The title hydrindenones had IR(film): 1680, 1667 (sh), 1450 cm^{-1}. NMR(CCl_4): δ 5.60(s(br), 1), 5.08(t(br), 1), 2.7–0.9(m, 17), 1.66(s(br), 3), 1.60(s(br)3), 1.10(s, 3). (Found: 260.2161. Exact mass calc. for $C_{18}H_{28}O$: 260.2140).

Enolate trapping experiments

Lithium enolate **14** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**). A soln of **18**[41] (552 mg; 3.0 mmol) in 15 ml anhyd ether was treated with MeLi (2.0 mL of a 2.0 M soln in ether; 4.0 mmol) at rt under N_2. The mixture was heated to reflux for 0.5 hr and then cooled to −78°. A soln of **1b** (564 mg; 4.0 mmol) in 10 mL anhyd ether was then added dropwise over 0.5 hr, and the mixture was warmed to −15° to −20° and held at this temp for 1 hr. The mixture was quenched with 3 mL 10% aqNH_4Cl and the organic layer was separated, washed with water, dried over $MgSO_4$, and evaporated. The residue was taken up in 25 mL MeOH and 2 mL 4% aqKOH. This mixture was heated for 1 hr under N_2, and worked up with ether and water. Evaporation and distillation at 90°/0.5 torr afforded 420 mg (85%) of a mixture of **12** and **13** (99:1) identical with that prepared previously by spectroscopic criteria and VPC analysis.

Lithium enolate **17** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**) *in the presence of cuprous iodide.* A similar experiment to that described above was performed utilizing **18** (184 mg; 1.0 mmol), and MeLi (0.5 mL of 2.3 M soln in ether; 1.15 mmol). To the resulting enolate soln was added CuI (191 mg: 1.0 mmol) at rt and the mixture stirred for 3 hr at rt during which time an olive green suspension resulted. The addition of **1b** (162 mg; 1.15 mmol) was conducted as described above. Workup and base treatment as before afforded 60 mg of a mixture of products which proved to be a mixture of **12** and **13** (76:24) obtained in ~30% yield (based on recovered starting material) and 3-methylcyclohexanone (25%) by VPC analysis.

Lithium enolate **17** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**) *in presence of methyl copper.* In a similar experiment, a soln of **17** (1 mmol) was prepared from **18** (184 mg; 1.0 mmol) and MeLi (0.5 mL of 2.3 M soln; 1.15 mmol). This soln was added at 0° to a suspension of methyl copper prepared from CuI (190 mg; 1.0 mmol) and MeLi (0.44 mL of a 2.3 M soln; 1.0 mmol) at 0°. The resulting mixture was treated as usual at −78° with **1b** (142 mg; 1.0 mmol) which afforded after the usual workup and base treatment 112 mg of a mixture of products. Analysis of this mixture by VPC indicated it consisted of a mixture of **12** and **13** (68% yield) in a ratio of 98:2 and 13% of **18**. Distillation at 100°/0.5 torr provided 82 mg (50% yield; 57% based upon recovered starting material).

Lithium enolate **17** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**) *in the presence of cuprous iodide and methyl lithium.* A soln of **17** (1 mmol) was prepared as described above and CuI (190 mg; 1.0 mmol) was added and the mixture was stirred at rt under N_2 for 3 hr. The resulting suspension was cooled to −20° and treated with MeLi (0.5 mL of a 2.3 M soln; 1.15 mmol). The resulting dull yellow suspension was then treated with **1b** (162 mg; 1.15 mmol) at −20°. Workup and base treatment as described above afforded 83 mg of **12** and **13** (51%) in a ratio of 74:26. Little non-annulated material detected.

Lithium enolate **17** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**) *in THF.* A soln of **17** in 10 mL THF was prepared by stirring **18** (184 mg; 1.0 mmol) with MeLi (0.5 mL of a 2.3 M soln; 1.15 mmol) at rt for 2 hr under N_2. Treatment of this soln with **1b** (162 mg; 1.15 mmol) at −78°→−20° as described above, followed by workup and base treatment, afforded after distillation at 100°/0.5 torr 79 mg of a mixture of **12** and **13** (48%) in a ratio of 95:5.

Lithium enolate **17** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one in DME.* The identical experiment to that described above for THF was performed in DME. Workup, base treatment and distillation at 100°/0.5 torr afforted 104 mg of a mixture of **12** and **13** (64%) in a ratio of 80:20.

Generation of the lithium enolate **17** *by lithium/ammonia reduction and trapping with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**). A soln of Li metal (105 mg; 15 mmol) in 35 mL anhyd liquid NH_3 was prepared and a soln of 3 - methyl - 2 - cyclohexen - 1 - one (330 mg; 3.0 mmol) and 0.25 mL of anhyd tBuOH in 15 mL anhyd ether. After 1 hr at −33°, the excess Li was discharged with isoprene. Evaporation of the ammonia and replacement with 25 mL ether provided a soln of enolate **17** which was cooled to −78°. A soln of **1b** (568 mg; 4.0 mmol) in 10 mL anhyd ether was added dropwise, the mixture warmed to −20° for 1 hr and quenched with 3 mL 10% aqNH_4Cl. Isolation of the products with ether as usual and base treatment (1 mL of 4% aqKOH in 25 mL MeOH) for 1 hr at reflux gave, after the usual extractive workup with ether and distillation, 318 mg of crude product. Purification by chromatography on SiO_2 afforded 271 mg (55%) of a mixture of **12** and **13** (99:1).

Lithium enolate **19** *with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one* (**1b**). Utilizing a procedure similar to that described for the reaction of **17** with **1b**, a soln of **19** (2 mmol) in ether was prepared by treating the known **20**[42] with MeLi. This enolate soln was then treated with **1b** (426 mg; 3.0 mmol) at −78°→−20°. Workup and base treatment with 4% aqKOH in MeOH as before afforded, after isolation of the products by ether extraction and chromatography of the products on SiO_2 in benzene, 301 mg of **23** (69%). This material was crystallized from pentane–ether to m.p. 124–126° (lit[24] 122°) and had m.m.p. 124–125.5° with an authentic sample.[27] Enone **23** was identical by all spectral characteristics (IR, NMR, MS) with an authentic sample, and contained <5% of the linear tricyclic enone **24** (detection limit by NMR ~5%) using authentic mixtures of **23** and **24** as standards.

Generation of lithium enolate **19** *by lithium/ammonia reduction and trapping with* 3 - *trimethylsilyl* - 3 - *buten* - 2 - *one*(**1b**). Utilizing a procedure similar to that for trapping **17** generated by Li–ammonia reduction, a soln of Li (150 mg; 21.3 mmol) in 50 ml anhyd NH_3(l) and 20 mL anhyd ether was utilized to reduce **20** (820 mg; 5 mmol) for a period of 1 hr. Excess Li was discharged with isoprene. The resulting enolate soln, after exchange of the ammonia for ether, was treated with **1b** (710 mg; 5.0 mmol) in 20 mL anhyd ether as usual from −78°→rt over 12 hr. Workup and aqueous base treatment (3 mL of 4% aqKOH in MeOH at reflux for 2 hr) afforded upon isolation of the products by ether extraction and evaporation, a crude crystalline solid. Purification by fractional crystallization from pentane–ether afforded a total of 500 mg (60% based on recovered starting material; 80% conversion) of **23** which had m.p. 124–126° and was identical to the sample prepared previously and an authentic sample in all respects. No linear tricyclic ketone **24** was detected. The remainder of the material isolated was the starting Wieland–Miescher ketone (195 mg; 24%) and a small amount of *trans* 10-methyl-3-decalone (40 mg; 5%) corresponding to reduction but not trapping.

Preparation of 2 - *methyl* - 1,3 - *dioxolane* - 2 - *butanal.* A soln of 2 - methyl - 2 - (3 - chloropropyl) - 1,3 - dioxolane (1.65 g; 10 mmol in 10 mL anhyd DMSO was added dropwise over 0.25 hr to a suspension of NaCN (980 mg; 20 mmol) in 10 ml anhyd DMSO at 80° under N_2. The resulting mixture was heated at 120° for 1 hr then poured into 60 ml water. The products were extracted with ether (3 × 20 mL), and the combined etheral extracts were washed with 5 mL of water (2x), dried over $MgSO_4$, and evaporated to 1.46 g (94%) of 2 - methyl - 1,3 - dioxolane - 2 - butanenitrile pure enough for further use. A portion of the crude nitrile (310 mg; 2.0 mmol) was taken up in 10–15 mL anhyd toluene. This soln was cooled to −20° and treated with DIBAL in toluene (1.5 mL of a 2.0 M solution; 3.0 mmol). The mixture was stirred at −20°→0° for 2 hr, and quenched by successive addition of 1 mL anhyd MeOH and 2–3 mL sat aqNaCl at −20°. After stirring for 10 min, solid anhyd $MgSO_4$ was added until a granular

ppt was obtained and the salts were removed by filtration. The salts were washed well with toluene and the combined filtrates were concentrated. The residue was taken up in 15 mL of a 1:1:1 mixture of 25% aqHOAc, MeOH and THF in which 1 g NaOAc had been dissolved and stirred for 1 hr. The mixture was diluted with 40 mL ether and washed with water. The aqueous phase was extracted with ether (10 mL) twice and the combined ethereal solns were washed with 10% aqNaHCO$_3$ (10 mL) twice, sat NACl, dried over MgSO$_4$, and evaporated to afford 264 mg of the pure title aldehyde (83%). The title aldehyde[43] had IR(film): 1718 cm^{-1}.

Preparation of 2 - *methyl* - 2 - (4 - *oxo* - 5 - *trimethylsilyl* - 5 - *hexenyl*) - 1,3 - *dioxolane*(**27**). A soln of 1 - trimethylsilylvinylmagnesium bromide (25 mmol) in 35 mL anhyd THF was prepared as described previously[13] from 1-bromovinyl trimethylsilane (4.89 g; 25 mmol) and Mg metal (720 mg; 30 mmol).

The soln of the Grignard reagent was cooled to −5° in ice-MeOH and a soln of 2 - methyl - 1,3 - dioxolane - 2 - butanal (3.2 g; 20 mmol) in 10 mL anhyd THF was added dropwise over 0.5 hr. The mixture was then brought to reflux for 15 min, cooled, diluted with 80 mL ether, and quenched with 20 mL 10% aqNH$_4$Cl. The organic layer was separated, and the aqueous phase was extracted with ether (3 × 25 mL). The combined ethereal solns were dried over MgSO$_4$ and evaporated to 6.9 g of crude alcohol.

This crude material was taken up in 50 mL acetone and treated with Jones reagent[44] at −20°. This reaction must be monitored carefully to prevent loss of the ketal. After the usual ethereal extraction, the residue upon evaporation was distilled at 80°/10 mm to afford 2.7 g (54%) of **27**.

Ketone **27** had IR: 1680 cm^{-1}. NMR(CCl$_4$): δ 6.41(d, J = 2.5 Hz, 1), 6.06(d, J = 2.5 Hz, 1), 3.86(s, 4), 2.83–2.26(m, 2), 1.76–1.33(m, 4), 1.25(s, 3). (Found: C, 60.28; H, 10.07. Calc for C$_{13}$H$_{24}$O$_3$Si: C, 60.41; H, 10.14%).

Preparation of (R,S) - 4a,5 - *dimethyl* - 4,4a,7,8 - *tetrahydro* - 2(3H) - *naphthalenone*(**28**). A soln of Wieland–Miescher ketone (2.84 g; 16 mmol) in 25 mL benzene and pyrrolidine (1.136 g; 1.382 mL; 16 mmol) were combined and heated at reflux under a water separator for 2 hr. The solvent was evaporated, and the residue distilled at 100°/0.3 torr. The resulting enamine was taken up in anhyd ether (25 mL) and added dropwise at 0° to a soln of MeLi in ether (21 mL of a 2.3 M soln; 48 mmol) and the mixture allowed to stir at rt for 8 hr. The mixture was cautiously quenched with 10% aqNH$_4$Cl at 0° and the products isolated by ether extraction.

The crude material was taken up in 35 mL MeOH and 20 mL 50% aqHOAc containing 5 g NaOAc. The mixture was stirred at rt for 12 hr then made basic (pH = 11) with 40% aqKOH and the products were isolated by extraction with ether (5 × 20 mL). The combined ethereal solns were washed with 3.5% HCl (3x), dried over MgSO$_4$, and evaporated to afford the crude **29**.

The crude **29** was purified by chromatography on SiO$_2$ (30 g) in benzene with elution by benzene–EtOAc (9:1) to remove impurities then elution by EtOAc to obtain 1.7 g of **29** (55%). Alcohol **29** crystallized upon trituration with ether to m.p. 89–91° and had IR(film): 3425, 1675, 1620 cm^{-1}; NMR(CDCl$_3$): δ 5.35(s(br), 1), 3.28(s(br), 1), 2.60–1.30(m, 10), 1.30(s, 3), 1.20(s, 3).

Alcohol **29** was used without further purification. Alcohol **29** (1.70 g; 8.76 mmol) was dissolved in 25 mL anhyd ether and 2 mL anhyd pyridine added. The soln was cooled to 0° and a soln of thionyl chloride (1.785 g; 0.8 mL; 15 mmol) in 10 mL anhyd ether was added dropwise and stirring continued an additional 1 hr at rt. The mixture was cautiously treated with water and the products isolated by extraction with ether. The extracts were washed with 3.5% aqHCl, 5% aqNaHCO$_3$, dried over MgSO$_4$, and evaporated. Distillation of the residue at 90°/0.5 torr afforded 1.20 g (78%) of **28** containing small amounts of exocyclic olefin isomer.

Olefinic enone **28** had IR(film): 1672, 1625 cm^{-1}; NMR(CDCl$_3$): δ 5.63(s(br), 1), 5.38(m, 1), 2.67–1.83(m, 8), 1.67(d, J = 2 Hz, 3), 1.35(s, 3). (Found: C, 81.60; H, 8.93. Calc. for C$_{12}$H$_{16}$O: C, 81.77; H, 9.15%).

Tricyclic enone **30**. A soln of Li (35 mg; 5 mmol) in 25 mL anhyd NH$_3$ (l) was treated dropwise with a soln of **28** (176 mg; 1.0 mmol) and anhyd t-BuOH (63 mg; 0.08 mL; 0.85 mmol) in 10 mL ether. An additional 10 mL ether was added to ensure complete addition. After 0.75 hr, the excess Li was discharged by addition of isoprene and the ammonia was evaporated. The soln was heated briefly to expel residual ammonia. The resulting light yellow suspension was cooled to −78° and a soln of **27** (256 mg; 1.0 mmol) in 10 mL anhyd ether was added dropwise over 0.5 hr followed by warming slowly to −20°. After 1 hr at −20°, the mixture was quenched with 5 mL 10% aqNH$_4$Cl, the layers seqarated and the aqueous layer extracted with ether (2 × 20 mL). The combined organic phases were washed with water, sat aqNaCl, dried over MgSO$_4$, and evaporated.

The residue was taken up in a mixture of 25 mL MeOH and 2 mL 4% aqKOH and the mixture heated at reflux for 3 hr. The solvents were evaporated and the residue partitioned between 30 mL ether and 5 mL water. The layers were separated and the aqueous phase was extracted with ether (2 × 20 mL). The combined organic phases were washed with water, sat aqNaCl, dried over MgSO$_4$, and evaporated to afford 330 mg of crude products.

The crude material was purified by chromatography on SiO$_2$(15 g) in hexane and elution with benzene–EtOAc (9:1) afforded 176 mg of **30** (51%).

Enone **30** had IR(film): 1665, 1625 cm^{-1}; NMR (CDCl$_3$): δ 5.22 (m, 1), 3.85(s, 4), 3.00–1.00(m, 18), 1.62(d, J = 2 Hz, 3), 1.27(s, 3), 1.10(s, 3); MS: 344(P$^+$). (Found: 344.2357. Exact mass calc. for C$_{22}$H$_{32}$O$_3$: 344.2352).

Tricyclic ketone **31**. A soln of Li (84 mg; 12 mmol) in 40 mL NH$_3$(l) (distilled from Na) was treated dropwise at −33° over 0.5 hr with a soln of **30** (176 mg; 0.51 mmol) in 10 mL anhyd ether, and the mixture stirred an additional 1 hr at −33°. A soln of MeI (3.42 g; 1.5 mL; 24.2 mmol) in 5 mL anhyd ether was added dropwise over 10 min. The mixture was stirred at −33° for 2–3 hr and the ammonia allowed to evaporate overnight. Ether (50 mL) and 10% aqNH$_4$Cl (10 mL) were added, the layers separated, and the aqueous phase extracted with 20 mL ether. The combined organic phases were washed with water, dried over MgSO$_4$ and evaporated to 167 mg of crude products.

The crude material was purified by chromatography on SiO$_2$ (5 g) in hexane, and elution with benzene–EtOAc (20:1) provided 120 mg of **31** (67%).

Ketone **30** had IR(film): 1718, 1615(w) cm^{-1}; NMR(CDCl$_3$): δ 5.13(m, 1), 3.83(s, 4), 2.60–0.8(m, 19), 1.58(d, J = 2 Hz, 3), 1.27(s, 3), 1.07(s, 3), 1.00(s, 3); MS: 360(P$^+$). (Found: 360.2671. Exact mass calc. for C$_{23}$H$_{36}$O$_3$: 360.2665).

(±)*Tetracyclic enone* **25**. A soln of **31** (110 mg; 0.3 mmol) in 3 mL acetone and 1 mL 10% aqHCl was stirred at rt for 12 hr. The majority of the acetone was evaporated and ether (30 mL) and sat aqNaCl (10 mL) were added. The layers were separated and the aqueous phase was extracted with ether (2 × 10 mL). The combined organic phases were washed with 5% aqNaCHO$_3$, dried over MgSO$_4$ and evaporated to 100 mg of a yellow oily residue.

The crude residue was dissolved in 20 mL MeOH and 1 mL 4% aqKOH added. The mixture was treated at reflux for 3 hr and the reaction progress monitored by tlc. The solvent was evaporated after cooling and the products isolated by ether extraction to afford 74 mg (83%) of **25** (1 spot/tlc). This material was further purified by filtration through SiO$_2$ (2 g) in benzene–EtOAc (9:1) and crystallization from ether–pentane to m.p. 140–143° (lit[29] m.p. 145°) identical to an authentic sample by IR, NMR, MS and mixed m.p.

Tricyclic enone **33**. By a procedure similar to that described for the preparation of **30**, a noncrystalline sample of the known THP protected **32**[32] (660 mg; 2.5 mmol) was reduced with Li (105 mg; 15 mmol) in liquid ammonia. After exchange of solvents for ether, the resulting enolate was treated with **27** (768 mg; 3.0 mmol) in ether at −78° → −20°. Workup and base treatment as before with 4% aqKOH in MeOH provided upon isolation of the products by ether extraction and chromatography on SiO$_2$ with elution by benzene–EtOAc (20:1), 536 mg of **33** as a yellow oil (50%).

The tricyclic enone **33** had IR(film): 1667, 1620 cm^{-1}; NMR(CDCl$_3$): δ 4.53 (m, 1), 4.20–3.40(m, 3), 3.90(s, 4), 2.60–1.00(m, 26), 1.33(s, 3), 1.00(s, 3); MS: 432(P$^+$). (Found: 432.2877. Exact mass calc. for C$_{26}$H$_{40}$O$_5$: 432.2876).

Tricyclic ketone **34**. By a procedure similar to that described for the preparation of **31**, **33** (536 mg; 1.24 mmol) was reduced with Li (105 mg; 15 mmol) in liquid NH_3. The resulting enolate was treated with MeI (9.12 g; 4 mL; 64.7 mmol). Workup afforded 527 mg of tricyclic ketone which was sufficiently pure for further use.

Tricyclic ketone **34** had IR(film): 1720 cm^{-1}; NMR($CDCl_3$): δ 4.57(m, 1) 4.20–3.40(m, 3), 3.93(s, 4), 2.80–0.9(m, 27), 1.35(s, 3), 1.10(s, 3), 0.90(s, 3). (Found: 448.3201. Exact mass calc. for $C_{27}H_{44}O_5$: 448.3189).

(±)-*Homotestosterone*(**26**). By a similar procedure to that described for the preparation of **25**, **34** (527 mg; 1.18 mmol) was treated successively with 1 mL 10% aqHCl in 4 mL acetone for 18 hr at rt and then a mixture of 2 mL of 4% aqKOH in 20 mL MeOH at reflux for 3 hr. Isolation of the products by ether extraction and chromatography on SiO_2 (15 g) with elution by benzene–EtOAc (4:1) provided 125 mg of **26** (20%). Crystallization of **26** from ether–hexane afforded material m.p. 155–158° (lit[29] 158°) which was identical to an authentic sample by m.m.p. and had the expected spectral characteristics.

The yields of this series of experiments was influenced by the presence of initially undetected impurities in the THP enone **32**. The overall yield should be considerably improved when crystalline **32** is utilized.

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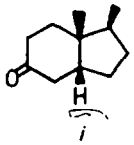

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