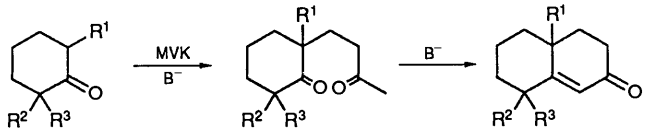
Lewis Acid Catalysed Michael-type Addition. A New Regio- and Diastereoselective Annulation Method using Methyl Vinyl Ketone

Pierre Duhamel,* Gilles Dujardin, Laurent Hennequin and Jean-Marie Poirier
URA n°464 du CNRS, Faculté des Sciences et des Techniques de Rouen et IRCOF, BP 118 F-76134 Mont Saint Aignan Cedex-France

A new annulation method is presented, involving a boron trifluoride catalysed Michael addition of trialkylsilyl enol ethers to methyl vinyl ketone (MVK) in the presence of a hydroxylic compound. This methodology allows regiospecific 3-oxobutylation of either of the two isomeric enol ethers of mono or di-substituted cyclanones. Octalones **2d, e** and hydrindenones **17** with the two alkyl groups in a *cis* relationship can thus be specifically obtained. This method has been applied to a short and efficient preparation of (±)-dehydrofukinone **10**.

The work reported in this paper is focused on the synthesis of octalones and hydrindenones which are very important building blocks for synthesis in the sesquiterpenic, diterpenic and triterpenic families. The literature provides little access to these compounds. Indeed, the original well-known Robinson annulation procedure,[1] while of great interest, suffers from severe drawbacks especially in terms of yields, regioselectivity and stereoselectivity.[2] Good results are obtained with relatively acidic β-dicarbonyl compounds, but there is a sharp decrease in the yields with monoketones. In these cases, the more basic monoketone enolates[2a,b] induce polymerization of MVK (methyl vinyl ketone) (Scheme 1).



B^- = RONa/ROH
1a; R^1 = Me, R^2 = R^3 = H
1b; R^1 = R^2 = Me, R^3 = H
1c; R^1 = R^2 = R^3 = Me

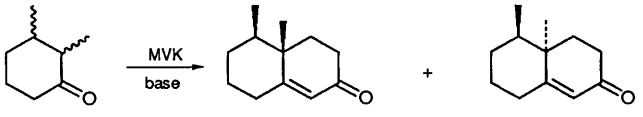
Yields(%)
2a 40
2b 10
2c 0

Scheme 1

In order to try to increase the yield of reactions, several improvements have been proposed regarding reaction conditions and/or structure of the electrophilic reagents. For less hindered ketones such as cyclohexanone or 2-substituted cyclohexanones, lower temperatures and a catalytic amount of base were used.[3] This procedure allowed the isolation of an intermediate ketol which was then dehydrated in poor overall yield.[4] Numerous modifications of the structures of the electrophilic reagents have also been made. For example, in aprotic medium, replacement of MVK by Stork silylenone[5] raised the yield from 5 to *ca.* 70%.[5,6] Modifications of Wichterle type[7] alkylating reagents bearing new masked carbonyl groups have also been proposed. Among them, the trimethylsilylbutenyl iodide,[8] the iodotiglate,[9] and the halomethylisoxazole[10] gave the best results. However, while condensing well, these reagents require unmasking of the carbonyl function in a multistep procedure.

Another aspect of the annulation concerns steric hindrance. For instance, classical methods[1,2] do not give access to polymethylated octalones **2b** and **2c** which are very important building blocks for the synthesis of a number of natural products such as widdrol,[11] thujopsene,[12] nimbiol,[13] sugiol[13] and ferruginol.[13] To overcome these synthetic failures, multistep procedures have been proposed,[14,15] which in the case of **2c** gave yields ranging from 10 to 40%.[11-13] Concerning the regioselectivity, it is well known that conventional procedures, under equilibrating conditions, lead to reactions of the more substituted enolates. Quenching the regio-unstable kinetically-generated enolates with MVK or the Wichterle reagent fails because of the equilibration of these enolates prior to reaction. However, regiospecificity can be observed in multistep procedures[6,8-10] when, under non-equilibrating conditions, the electrophilic reagents are reactive enough to trap the regio-unstable enolates.

The lack of stereoselectivity is another drawback of the Robinson annulation. A classical example of this failure is illustrated by the annulation of 2,3-dimethylcyclohexanone which led to a mixture of the two diastereoisomers with a very low yield[16-18] (10–15%), and with a *cis*:*trans* ratio of 60:40 (Scheme 2).



1d *cis*-**2d** *trans*-**2d**

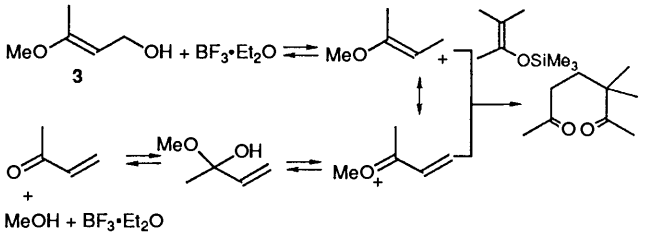
Scheme 2

Due to the importance of the *cis*-**2d** isomer for synthesis in the sesquiterpene field (the eremophilane group, for instance) and given that Robinson annulation gives unsatisfactory results, multistep procedures[19] have been proposed towards *cis*-**2d**, no one procedure being satisfactory for both yield and diastereoselectivity. One of the most recent has been disclosed by Torii's group[19b] and is a sixteen-step, 16% overall yield procedure.

Robinson annulation *via* acid catalysed Michael type addition has only been described recently. First introduced by Heathcock[20] using sulfuric acid catalysis, this procedure has further been improved by Still,[21] who lowered the temperature, thus allowing the isolation of the intermediate diketone. While this procedure is generally successful, it leads, when applied to 2,3-dimethylcyclohexanone, to a 33% yield[22] and low stereoselectivity (**2d**; *cis*:*trans* ratio = 3:1).[23] Another approach using a Lewis acid catalysed Michael type addition was described by Mukaiyama.[24] This well-known procedure is based on the reaction of silyl enol ethers with vinyl ketones at low temperature (−78 °C) in the presence of titanium derivatives as catalysts. However, according to Huffman,[23] this procedure is quite unsuccessful with MVK which must be replaced by its dioxolane derivative, and in addition the reaction must be run at a very low temperature (−95 °C).

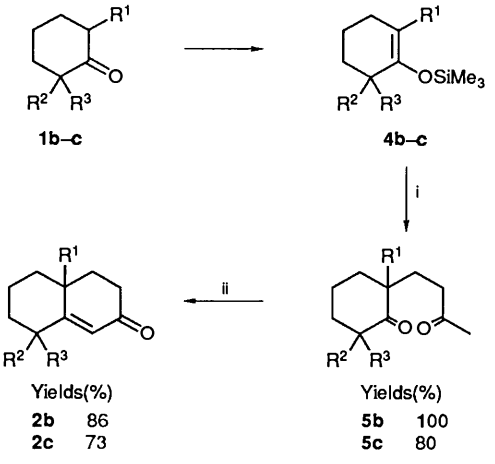
Results and Discussion

In the course of our recent studies on Lewis acid catalysed Michael-type additions to silyl enol ethers, we have previously shown that a hemiacetal vinylogue such as **3*** can be used as a MVK equivalent.[25] A mechanistic approach led us to consider that the same intermediate carbocation could be generated by using MVK in the presence of methanol (Scheme 3).



Scheme 3

These considerations led us to discover that the Michael-type addition of silyl enol ethers to MVK may become nearly quantitative when using BF_3•Et_2O as a catalyst, in the presence of one equiv. of an alcohol. This procedure is efficient even with silyl enol ethers of sterically hindered ketones[26] such as **4b–c** (Scheme 4).



Scheme 4 *Reagents:* i, MVK, PhCH(OH)Me, BF_3•Et_2O; ii, base

In order to obtain the results presented in this paper which is mainly devoted to the synthetic aspects of this new annulation method, *i.e.*, regio- and stereo-selective controls, alcohols as well as carboxylic acids have been used as the hydroxylic compounds. In the case of tetrasubstituted silyl enol ethers, the use of alcohols or carboxylic acids [acetic, chloracetic, benzoic, dipivaloyltartaric or dibenzoyltartaric acid (DBTA)][27] led to virtually similar yields. However, the simplicity of the separation during aqueous work-up led us to the routine use of an acid as the hydroxylic reagent. In the case of trisubstituted silyl enol ethers which are more sensitive to hydrolysis, the use of alcohols (Pr^iOH, Bu^sOH, 1-phenylethanol, menthol†) proved to give better yields. In all cases, use of MVK in the absence of a hydroxylic compound caused a dramatic decrease in the yields, all other reaction conditions being equal.

Octalone Synthesis.—Regiochemistry. We first chose to test the condensation of both isomeric silyl enol ethers **4a** and **6a** of 2-methylcyclohexanone **1a** with MVK, in the presence of BF_3•Et_2O and menthol (Scheme 5). The trisubstituted enol ether **6a** was easily prepared by trapping the kinetically generated enolate of ketone **1a** with TMSCl, while the tetrasubstituted enol ether **4a** was prepared by Duboudin's method[28] leading to a mixture of regioisomers **4a** and **6a** in a 90:10 ratio. With silyl enol ether **4a** the same procedure led exclusively to the diketone **5a** in 92% yield.† The trisubstituted silyl enol ether **6a** led exclusively to the regioisomeric diketone **7a**.‡ These two diketones were classically cyclized to the corresponding octalones **2a** and **8a**.§ It has been noted that octalone **8a** has also been prepared without purification of the intermediate diketone **7a**.§

Similarly, we have applied this condensation to the trisubstituted trimethylsilyl enol ether **6d** and to the tetrasubstituted *tert*-butyldimethylsilyl enol ether **4d′** (the starting material for eremophilane skeleton). Silyl enol ether **6d** was classically obtained by trapping the kinetically generated enolate of ketone **1d** with TMSCl. Regiocontrolled synthesis of the unknown tetrasubstituted silyl enol ether **4d′** was achieved through addition of dimethyl cuprate to 2-methylcyclohexenone, followed by trapping the intermediate enolate using *tert*-butyldimethylsilyltriflate (TBDMSTf). Regiopurity of the enol ethers **6d** and **4d′** thus obtained is 97:3 or higher (Scheme 6). All our attempts to use methods from the literature[25,28,29] to prepare enol ether **4d** ($SiMe_3$) or **4d′** ($SiMe_2Bu^t$) starting from ketone **1d** yielded a mixture of the two regioisomers.¶

Applied to enol ether **6d**, our method led to diketone **7d** (as a mixture of four diastereoisomers) in a regiospecific manner. In the case of silyl enol ether **4d′**, this new method gave a regiospecific access to diketone **5d** (Scheme 6) in good yield (72%). The use of other acids (benzoic or dipivaloyltartaric acid) does not change the yield. Under these conditions, diketone **5d** is accompanied by traces of diketone **7d** (2%) resulting from the minor regioisomeric silyl enol ether **6d′** (3%). In another experiment, a mixture of silyl enol ethers **4d**:**6d** = 77:23 ratio gave a mixture of diketones **5d** and **7d** in 82% total yield with a **5d**:**7d** = 84:16 ratio. The proportion of diketone **5d** is increased probably because of the higher sensitivity of the silyl enol ether **6d** to Lewis acid cleavage.

These two series of results show that the condensation conditions do not lead to the isomerization of the enol ethers **4** and **6**, and thus the quantity of isomeric diketones **5** and **7** obtained is only dependent on the regioisomeric purity of the starting silyl enol ether.

Stereochemistry. Concerning the stereocontrol of the diketone **5d** formation, a remarkable selectivity is observed. Diketone **5d** is obtained essentially with the two methyl groups in a *cis* relationship (Fig. 1) as shown by NOE effects.**,†† ^1H NMR spectroscopy shows a *cis*:*trans* ratio of 92:8.

The selectivity in the preparation of diketone **5d** may be

* Hemiacetal vinylogues **3** present some analogies with hemiacetals, hemiacetal phenylogues and furfuryl alcohol in the presence of a Lewis acid.

† Use of (−)-menthol gave no enantiomeric excess in the formation of diketones **5**.

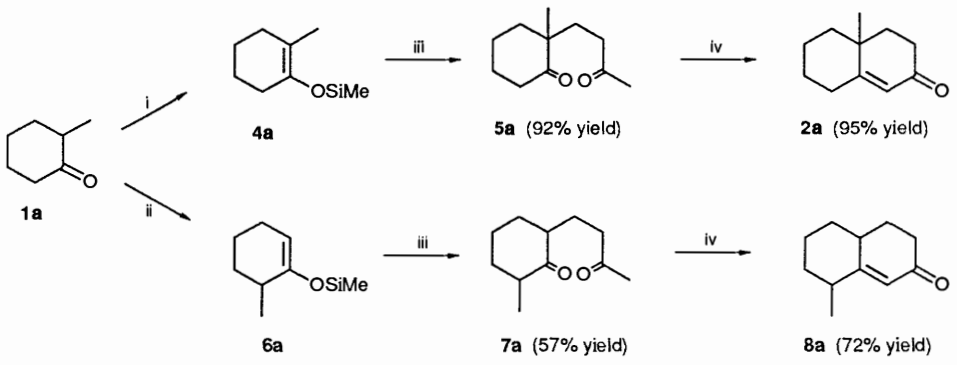
‡ This process allows high stereocontrol in favour of the *cis*-isomer (*cis*:*trans* ratio for **7a**; 90:10).

§ *cis*:*trans* ratio for **8a**; 80:20. This ratio is somewhat lower than for the dicarbonyl compound **7a**, possibly due to partial epimerization.

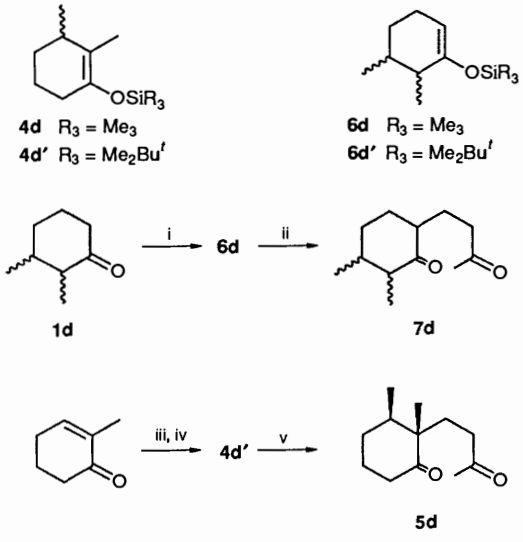
¶ See Experimental section. Isomeric ratios were determined by ^1H NMR and GC analysis.

** '*cis*' and '*trans*' for diketone **5d** refers to the methyl groups relationship.

†† The *cis* relationship for the two methyl groups was demonstrated by the NOE effect. Irradiating the methyl in the 2-position (0.88 ppm) gave no NOE effect on the proton in the 3-position. The chemical shift of the second methyl is too close to allow observation of an NOE. The diastereoisomeric ratio was determined by GC and 400 MHz ^1H NMR analysis. The *cis* relationship was confirmed by the ^{13}C NMR spectrum of the corresponding octalone.[33]



Scheme 5 *Reagents:* i, NEt_3, NaI, TMSCl; ii, LDA, TMSCl; iii, MVK, menthol, BF_3·Et_2O; iv, KOH, EtOH



Scheme 6 *Reagents:* i, LDA, TMSCl; ii, MVK, Pr^iOH, BF_3·Et_2O; iii, Me_2CuLi, HMPA; iv, TBDMSTf; v, MVK, AcOH, BF_3·Et_2O

Fig. 1

explained by the conformation of the starting enol ether **4d** or **4d'**. Due to a $A^{1(2)}$ strain,[30] conformation **B** is preferred and electrophilic attack takes place from the less hindered face of the double bond, thus leading preferentially to the methyl groups in a *cis* relationship (Fig. 2).

Placing a more hindered alkyl group in the 3-position of the starting enol ether, as in **4e*** (Scheme 7), led selectively to diketone **5e** as a single diastereoisomer in which the two alkyl groups are in a *cis* relationship.†,‡ This observation agrees well with the proposed hypothesis.

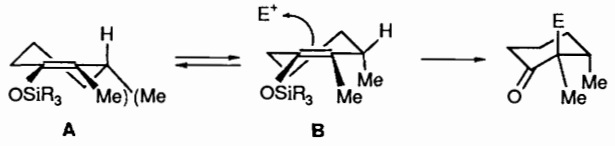
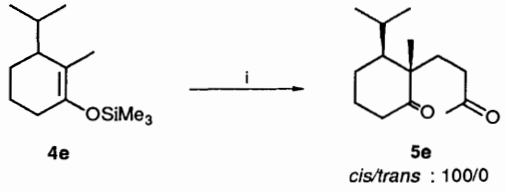


Fig. 2



Scheme 7 *Reagents:* i, MVK, DBTA, BF_3·Et_2O

Diketones **5** are easily cyclized in basic medium to give octalones **2** in high yields (Table 1). Diketone **5d**, when treated in 3 mol dm^{-3} basic medium (KOH or NaOMe), led to octalone **2d** in a *cis*:*trans* ratio similar to the starting diketone (Table 1, entries 1, 2). However we have shown that the diastereoselectivity of this method may be enhanced by using sodium methoxide in methanol in more dilute conditions; using these conditions, almost pure octalone *cis*-**2d** may be obtained (*cis*:*trans* ratio = 99:1§) starting from a mixture of diketones **5d** (*cis*:*trans* ratio = 92:8) (Table 1, entry 3).

This improvement in diastereoselectivity may be explained by the intermediate formation of ketols *cis*-**9d** (R = Me, R' = H) and *trans*-**9d** (R = H, R' = Me)[5,31] which do not have the same subsequent behaviour; dehydration being easier for the first one as previously observed.[32] Indeed, ketol *trans*-**9d**¶ was easily separated from octalone **2d**. Upon oxalic acid treatment[3] *trans*-**9d** led essentially to octalone *trans*-**2d** as identified by its ^{13}C NMR spectrum.[33] Finally, we have also prepared octalone **2d** (*cis*:*trans* = 98:2) from enol ether **4d'** (**4d'**:**6d'** = 96:4) without purification of the intermediate diketone **5d** with an overall yield of 62%. Compared with the known procedures of Kelly[34] (yield: 10%, no *cis*:*trans* ratio given), Ourisson,[16] Piers,[17] Pinder[18] (yield: 15%, *cis*:*trans* ratio = 60:40), Zoretic[22] (yield: 33%, *cis*:*trans* ratio = 90:10) and Huffman[23] (no yield given, *cis*:*trans* ratio from 75:25 to 86:14),** this method appears to be a short and efficient procedure since the overall yields are good (up to 62%) and the diastereoisomeric ratios excellent (99:1). It appears to be an alternative synthesis

* Enol ether **4e** was obtained by trapping, with Me_3SiCl, the intermediate enolate which was prepared by Li/NH_3 reduction of 3-isopropyl-2-methyl-cyclohex-2-enone.

† Identification of diastereoisomer **5e** as *cis* was done as follows: irradiating the 2-methyl gave no NOE effect on 3-H but gave an NOE effect (7%) on the hydrogen of the isopropyl group.

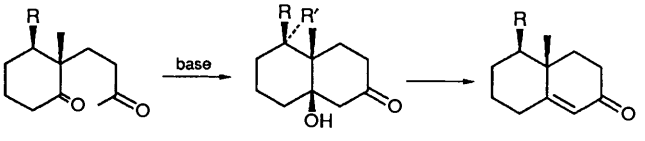
‡ The use of the enol ether of 3-alkylcyclohexanone in the same reaction conditions yielded the corresponding diketone which is a potential starting material for the cadinane series. Work in this area is in progress.

§ See Experimental section. Isomeric ratios were determined by ^1H NMR and GC analysis.

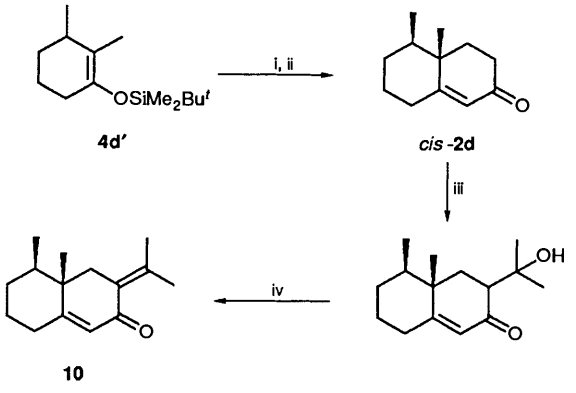
¶ Ketol *trans*-**9d** is accompanied by a small quantity of ketol *cis*-**9d** and starting diketones **5d** and **7d**.

** Ratio *cis*-**2d**:*trans*-**2d** depending on the determination method used.

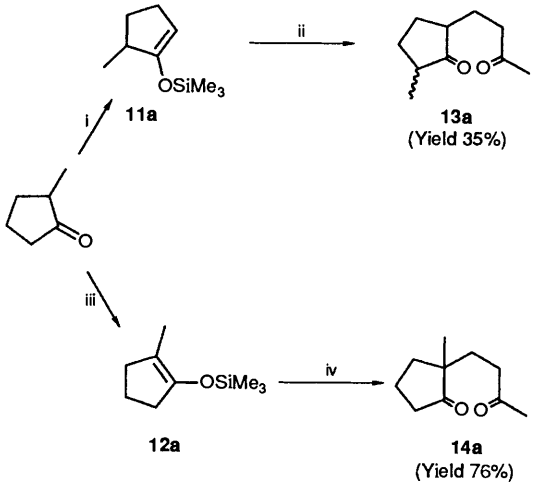
Table 1 Preparation of octalones **2** from diketones **5**



Entry	Diketone R		*cis*:*trans*	Base (conditions)	Octalone	*cis*:*trans*	Yield (%)
1	Me	**5d**	90:10	KOH/EtOH (3 mol dm^{-3}, 20 °C, 3 h)	**2d**	90:10	78
2	Me	**5d**	90:10	MeONa/MeOH (3 mol dm^{-3}, 20 °C, 1 h)	**2d**	90:10	90
3	Me	**5d**	92:8	MeONa/MeOH (0.3 mol dm^{-3}, 40 °C, 1 h)	**2d**	99:1	80
4	Pr^i	**5e**	99:1	MeONa/MeOH (3 mol dm^{-3}, 20 °C, 1 h)	**2e**	100:0	85



Scheme 8 *Reagents:* i, MVK, AcOH, BF_3·Et_2O; ii, MeONa, MeOH; iii, LDA, $ZnCl_2$, MeCOMe; iv, PTSA, C_6H_6



Scheme 9 *Reagents:* i, LDA, TMSCl; ii, MVK, PhCH(OH)Me, BF_3·Et_2O; iii, NaI, TMSCl, NEt_3; iv, MVK, menthol, BF_3·Et_2O

to that of Boeckman Jr. and co-workers[6] who used silylenones in basic medium. By comparison, our method also presents the advantage of using the cheaper and commercially available starting enone (MVK).

The efficiency of this new procedure has been illustrated by a two step synthesis of (±)-dehydrofukinone **10** starting from octalone *cis*-**2d** (Scheme 8).

Starting from the silyl enol ether **4d'**, only four steps are required to obtain dehydrofukinone in a 44% overall yield. This procedure is thus considerably shorter and the yield much higher than those proposed previously.[19,35]

Hydrindenone Synthesis.—As for six-membered rings, silyl enol ethers **11a** and **12a** led regiospecifically to the corresponding diketones **13a** and **14a** (Scheme 9) and as previously observed the regioselectivity of this condensation is dependent only on the regioisomerism of the starting enol ether.

With 2,3-disubstituted enol ethers such as **12b–e**, a regiospecific reaction is also observed. In these cases diastereoselectivity depends dramatically on the bulkiness of the alkyl group (Table 2).

With hindered alkyl groups (silyl enol ethers **12b, c**) the diastereoselectivity of the reaction is excellent. The **14** *cis*:*trans* ratio, as determined by ^{1}H NMR * and capillary GC, is at least 99:1, and the yield is high and depends slightly on the nature of the hydroxylic compound used. Decrease in the bulkiness (R = Me or vinyl; enol ethers **12d, e**) seems to imply a lowering of the diastereoselectivity.

Diastereoselective control may also be due to the influence of steric strain on the conformers of the enol ether.[30] In agreement with this statement is the observation that the bulkier is R, the higher is the diastereocontrol (Table 2).

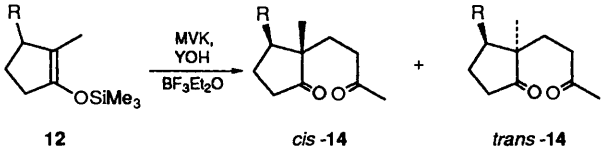
Hydrindenone structure can constitute the basic synthon of the CD part of vitamin D_3 (cholecalciferol) or its metabolites, provided that the methyl and the alkyl groups are in a *cis* relationship.

In order to determine whether the method is also suitable in this area, silyl enol ether **12f** was prepared from the corresponding enone **15** *via* ketone **16**, using TBDMSCl/NaI/NEt_3. This procedure led to a mixture of the two regioisomeric (tri- and tetra-substituted) silyl enol ethers. This mixture, heated in the presence of a catalytic amount of triethylamine hydrochloride, undergoes, in high yield and without hydrolysis (Scheme 10),† a rapid and efficient migration of the double

* Identification of diastereoisomer *cis*-**14b** was done as follows: irradiating the 2-methyl group does not give an effect on 3-H but does give a 6% NOE on the hydrogen of the isopropyl group.

† This isomerization method, also available for various enol ethers, will be published elsewhere.

Table 2 Preparation of diketones **14**

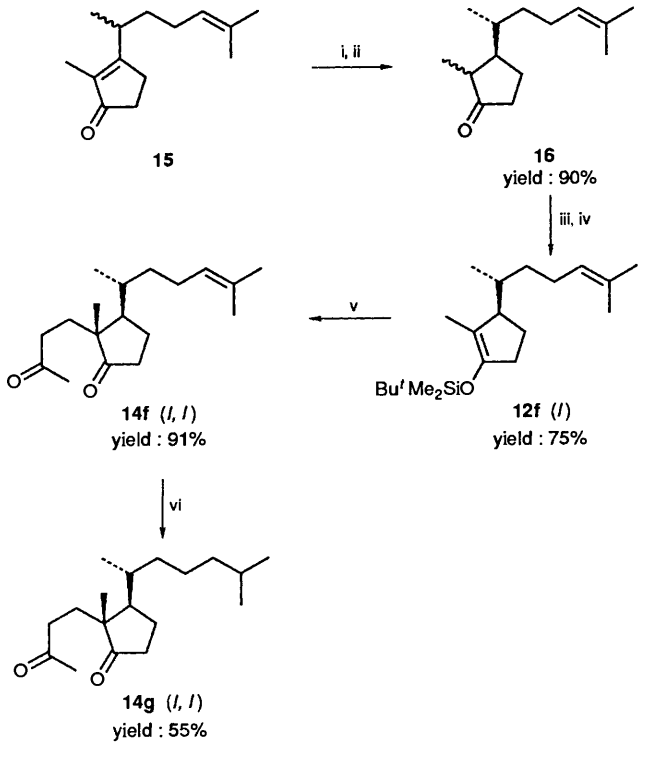


12 *cis*-**14** *trans*-**14**

R	Enol ether **12**	Y–OH	Diketone **14**	Ratio *cis*:*trans*	Yield (%)
Pr^i	**12b**	DBTA	**14b**	99:1	82
Pr^i	**12b**	AcOH	**14b**	99:1	80
Pr^i	**12b**	Pr^iOH	**14b**	97:3	75
Isopropenyl	**12c**	AcOH	**14c**	99:1	76
Me	**12d**	DBTA	**14d**	78:22	56
Vinyl	**12e**	AcOH	**14e**	79:21	64

bond of the trisubstituted enol ether into silyl enol ether **12f** (tetrasubstituted:trisubstituted enol ether = 98:2, *l*:*u*[36] = 70:30).

When applied to enol ether **12f**, reaction with MVK in the presence of BF_3·Et_2O and acetic acid afforded diketone **14f** with the methyl and alkyl groups in a *cis* relationship (Scheme 10). To confirm the relative configuration of the three asymmetric centres,[36] the double bond of the diketone **14f** thus obtained was hydrogenated leading to diketone **14g** (Scheme 10). The ^{13}C NMR spectrum of the major isomer of this

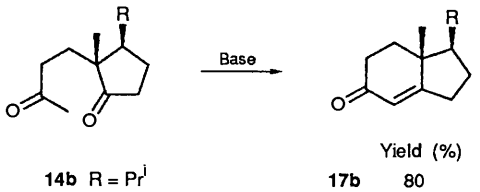


Scheme 10 *Reagents:* i, Li/NH_3; ii, NH_4Cl; iii, Bu^tMe_2SiCl, NEt_3, NaI; iv, NEt_3HCl; v, MVK, AcOH, BF_3·Et_2O; vi, H_2, Pd

diketone (70%) is fully compatible with that described for the corresponding isomer precursor of cholecalciferol.[37]

When treated in basic medium, diketones **14b, f, g** undergo cyclization into *cis*-hydrindenones **17b, f, g** (Scheme 11) in (unoptimized) good yields. To our knowledge, our method is the first permitting stereocontrolled hydrindenone syntheses using MVK as the Michael acceptor.

Conclusion.—The Lewis acid catalysed Michael-type addition proposed here, represents the key step of a new and efficient synthetic access to substituted octalones and hydrindenones with a high degree of regio- and stereo-selectivity. In this important area, this method is the first to successfully employ MVK as an annulating reagent* towards monoketonic species in acidic medium. The utilization of this method in the syntheses of natural products has been demonstrated with an expeditious preparation of (±) dehydrofukinone and of various hydrindenones, potential precursors to vitamin D metabolites. Its applicability has been recently illustrated for asymmetric synthesis of Sporogen AO-1[38b] and is now being investigated in asymmetric steroid syntheses starting from chiral D ring.



Scheme 11

Experimental

General.—IR spectra were recorded on a Perkin-Elmer 377 infrared spectrophotometer as pure liquid films, or in $CHCl_3$ or CCl_4 solution. ^1H NMR spectra were obtained with a Bruker AW 80 (80 MHz) or AM 400 (400 MHz) or WM 500 (500 MHz) spectrometer in $CDCl_3$ solution, with TMS as internal standard, unless otherwise noted. ^{13}C NMR spectra were recorded on a Varian CFT 20 (20 MHz) or a Bruker AM 400 (100 MHz) in $CDCl_3$ solutions unless otherwise noted. *J* values are given in Hz. Mass spectra were recorded on JEOL JMS AX 500 mass spectrometer (EI: Electronic Impact; CI: Chemical Ionisation with CH_4). GC analyses were performed on a Hewlett-Packard 5890 gas chromatograph, using a H-P.-5.1 column [16 ft 1/50″ (i.d.)]. Flash chromatography[39] was performed with Merck Kieselgel 60 (230–400 mesh ASTM) support with light petroleum (b.p. <60 °C) and diethyl ether (Et_2O) as eluent. Microanalyses were performed by INSA laboratories, Rouen. All reactions involving organometallic reagents or silyl enol ethers were conducted under a dry argon atmosphere.

Reagents and solvents. Anhydrous tetrahydrofuran (THF) and diethyl ether were distilled from sodium–benzophenone ketyl prior to use. Nitromethane, stored over molecular sieves, was distilled prior to use. Acetic acid was dried by addition of acetic anhydride (5% in volume) at least one day before use. 2-Methylcyclohexenone was prepared by Warnhoff's method[40] and isolated from 6-methyl regioisomer by flash chromatography prior to use.

Preparation of Silyl Enol Ethers.—*2-Methyl-1-trimethylsilyoxycyclohex-1-ene* **4a**.[25,29] To a mixture of 2-methylcyclohexanone (1.12 g, 10 mmol), triethylamine (1.26 g, 12.5 mmol) and chlorotrimethylsilane (1.36 g, 12.5 mmol) was added dropwise a solution of sodium iodide (1.88 g, 12.5 mmol) in acetonitrile (13 cm^3). After stirring for 3 h at room temperature, the suspension was filtered, washed with pentane, and the acetonitrile phase was extracted with pentane (6 × 5 cm^3). After evaporation of the solvent, distillation afforded the product **4a**

* Recently Sato *et al.*[38a] have obtained a good regioselectivity with MVK in the presence of $Bu_2Sn(OTf)_2$ (prepared from Bu_2SnCl_2 + AgOTf) but yields are generally lower.

(1.66 g, 90%) (b.p. 72 °C/13 mmHg); δ_H(60 MHz; $CDCl_3$) 0.18 (9 H, s), 1.6 (3 H, s) and 1.45–2.1 (8 H, m); ν_{max}(neat)/cm^{-1} 1690 (C=C). ^1H NMR spectroscopy showed the presence of 10% of regioisomer **6a**.

6-*Methyl*-1-*trimethylsiloxycyclohex*-1-*ene* **6a**. Enol ether **6a** was prepared according to Fleming and Paterson's procedure,[29a] starting from 2-methylcyclohexanone (2.24 g, 20 mmol). Flash chromatography afforded the silyl enol ether **6a** (1.53 g, 83%) (b.p. 76–78 °C/16 mmHg); δ_H(80 MHz; CCl_4) 0.20 (9 H, s), 1.05 (3 H, d, *J* 6.8), 1.15–2.25 (7 H, m) and 4.80 (1 H vinylic, t, *J* 4); δ_C(20 MHz; C_6D_6) 0.5 (3 C), 19.0, 20.9, 24.8, 32.2, 34.2, 102.7 and 154.7; ν_{max}(neat)/cm^{-1} 1650 (C=C). GC analysis showed the presence of 4% of regioisomer **4a**.

2,3-*Dimethyl*-1-*trimethylsiloxycyclohex*-1-*ene* **4d**. 2,3-Dimethylcyclohexanol (1.28 g, 10 mmol) in CH_2Cl_2 (5 cm^3) was added to a suspension of pyridinium chlorochromate (PCC) (4.3 g, 20 mmol) in CH_2Cl_2 (25 cm^3). After 2.5 h at room temperature, diethyl ether (100 cm^3) was added and the mixture was filtered on Florisil, evaporated and distilled, giving 2,3-dimethylcyclohexanone **1d** (1.22 g, 95%); (b.p. 71–75 °C/13 mmHg). GC analysis showed two diastereoisomers in the ratio *cis*:*trans*, 65:35 (60 °C, 10 cm^3 min^{-1}): 4.0 min (*trans*, 35%) and 4.7 min (*cis*, 65%).

To a solution of 2,3-dimethylcyclohexanone **1d** (0.78 g, 6.2 mmol) and hexamethyldisilylazane (HMDS) (9.5 mmol) in CH_2Cl_2 (15 cm^3) was added dropwise at 0 °C trimethyliodosilane (1.68 g, 8.4 mmol).[29b] After stirring for 10 min at 0 °C, and then 1 h at 20 °C, hexane (50 cm^3) was added. The mixture was filtered on Florisil and concentrated. Silyl enol ether **4d** was purified by flash chromatography (eluent: light petroleum) (1.12 g, 91%): b.p. 83–85 °C/13 mmHg (Found: C, 66.25; H, 11.05. $C_{11}H_{22}OSi$ requires C, 66.60, H, 11.18%); GC analysis (70 °C, 10 cm^3 min^{-1}): 10.0 min; δ_H(400 MHz; C_6D_6) 0.12 (9 H, s), 0.98 (3 H, d, *J* 7), 1.22 (1 H, m), 1.45 (1 H, m), 1.6 (2 H, m), 1.69 (3 H, s), 1.98 (2 H, m) and 2.06 (1 H, m); ν_{max}(neat)/cm^{-1} 1680 (C=C). GC and ^1H NMR spectroscopy showed the presence of 14% of regioisomer **6d**. Other procedures have been involved starting from ketone **1d**, leading to the following results: Duboudin's method[28] (as described for **4a**): yield: 86%, **4d**:**6d** = 77:23; Fleming's method[29a] (TMSCl, NEt_3, DMF, reflux) yield: 87%, **4d**:**6d** = 73:27; Krafft's method[29c] (TMSCl, NEt_3, bromomagnesiumdiisopropylamide) yield = 56%, **4d**:**6d** = 94:6.

3,4-*Dimethyl*-2-*trimethylsiloxycyclohex*-1-*ene* **6d**. To a solution of diisopropylamine (3.08 cm^3, 22 mmol) in anhydrous THF (10 cm^3) was added, at −20 °C with stirring, butyllithium (14.7 cm^3, 1.5 mol dm^{-3}, 22 mmol) in hexane. After 20 min, at −20 °C, the LDA solution was cooled to −70 °C and ketone **1d** (2.52 g, 20 mmol) in THF (10 cm^3) was added dropwise. After 1.5 h at this temperature, chlorotrimethylsilane (3.6 g, 33 mmol) was added and the mixture was allowed to warm to room temperature, filtered and the solvents were removed. Enol ether **6d** was purified by flash chromatography (eluent: light petroleum) (3.29 g, 83%). GC analysis (70 °C; 10 cm^3 min^{-1}) showed two diastereoisomers: 7.9 min (*cis* isomer, 68%) and 9.3 min (*trans* isomer, 32%) (Found: C, 66.35; H, 11.05. $C_{11}H_{22}OSi$ requires C, 66.60; H, 11.18%); δ_H(400 MHz; C_6D_6) *cis* isomer 0.18 (9 H, s); 0.93 (3 H, d, *J* 7), 1.18 (3 H, d, *J* 7), 1.0–2.2 (6 H, m) and 4.88 (1 H, t, *J* 3.7); *trans* isomer: 0.19 (9 H, s), 0.83 (3 H, d, *J* 7), 1.03 (3 H, d, *J* 7), 1.0–2.2 (6 H, m) and 4.82 (1 H, t, *J* 3.7); ν_{max}(neat)/cm^{-1} 1665 (C=C *cis*) and 1655 (C=C *trans*). ^1H NMR spectroscopy showed the presence of less than 3% of regioisomer **4d**.

1-tert-*Butyldimethylsiloxy*-2,3-*dimethylcyclohex*-1-*ene* **4d′**. Cuprous iodide (7.6 g, 40 mmol) was dried by heating at 0.5 mmHg. After cooling, the white powder was vigorously stirred with methyl sulfide (5–10 cm^3) until complete dissolution was achieved. To the clear solution were added at −70 °C THF (100 cm^3), and a solution of methyllithium (1.6 mol dm^{-3}; 50 cm^3, 80 mmol) in diethyl ether. Stirring was continued for 1 h after which HMPA (7.2 g, 40 mmol) was introduced, followed by 2-methylcyclohexenone (2.2 g, 20 mmol) and *tert*-butyldimethylsilyltrifluoromethanesulfonate (10.56 g, 40 mmol). The mixture was stirred at −70 °C for 4 h, allowed to warm, stirred for an additional 0.5 h and poured into a separatory funnel containing cold (0 °C) 0.1 mol dm^{-3} HCl and pentane. After separation, the combined organic layers were washed with cold saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. The enol ether was obtained by flash chromatography (eluent: light petroleum) combined with the *tert*-butyldimethylsilanol. After distillation of this mixture, the silanol was collected at 60–80 °C/10 mmHg and the residue contained pure enol ether **4d′** (3.5 g, 73%) b.p. 115 °C/10 mmHg; (Found: C, 70.0; H, 12.0. $C_{14}H_{28}OSi$ requires C, 69.96; H, 11.74%); GC analysis (100 °C, 6.8 cm^3 min^{-1}): 17.1 min; δ_H(400 MHz; C_6D_6) 0.11 (6 H, s), 0.98 (3 H, d, *J* 7), 1.01 (9 H, s), 1.20 (1 H, m), 1.43 (1 H, m), 1.60 (2 H, m), 1.70 (3 H, s), 1.97 (2 H, m) and 2.07 (1 H, m). Regioisomers **6d′** were also detected by vinylic protons (3%): 4.81 and 4.86 (t, *J* 3.5 or 3.8); ν_{max}(neat)/cm^{-1} 1675 (C=C). GC and ^1H NMR spectroscopy showed the presence of 3% of regioisomer **6d′** (2 diastereoisomers). δ_H 4.81 and 4.86 (1 H, vinylic, t, *J* 3.5 and 3.8). GC analysis (100 °C, 6.8 cm^3 min^{-1}): 12.3 and 14 min.

3-*Isopropyl*-2-*methyl*-1-*trimethylsiloxycyclohex*-1-*ene* **4e**. Isopropyl magnesium chloride was prepared by reaction between isopropyl chloride (3.6 g, 46 mmol) and magnesium (1.25 g, 52 mmol) in diethyl ether (60 cm^3). After this compound had been cooled to −70 °C, the mono ethyl enol ether of 2-methylcyclohexane-1,3-dione (25 mmol) (prepared according House's procedure[41]) was added dropwise in diethyl ether (10 cm^3). After stirring for 3.5 h at −20 °C, the mixture was poured into a separating funnel containing cold (4 °C) ethyl acetate (120 cm^3) and cold (4 °C) 3 mol dm^{-3} hydrochloric acid (60 cm^3), and shaken until completely homogenized. After decantation and extraction with ethyl acetate (3 × 60 cm^3), the organic layers were washed with saturated aq. NaCl (4 × 10 cm^3), dried ($MgSO_4$) and evaporated. 3-Isopropyl-2-methylcyclohex-2-en-1-one **4e** was purified by flash chromatography (eluent: Et_2O–light petroleum, 5:100) (2.28 g, 60% yield); δ_H(80 MHz; $CDCl_3$) 1.04 (6 H, d, *J* 7), 1.76 (3 H, s), 2.03 (2 H, m), 2.35 (4 H, m) and 2.98 (1 H, m); ν_{max}(neat)/cm^{-1} 1665 (C=O) and 1620 (C=C); δ_C(20 MHz; $CDCl_3$) 9.8, 19.5 (2 C), 22.5, 24.5, 31.2, 37.7, 130.0, 163.3 and 199.5.

Lithium (0.84 g, 120 mmol) was dissolved in liquid ammonia (105 cm^3) and then at −35 °C a solution containing 3-isopropyl-2-methylcyclohex-2-enone (2.61 g, 17.2 mmol) and *tert*-butanol (1.58 g) in THF (70 cm^3) was added. After 0.5 h, butadiene was introduced until complete decolouration was obtained and the ammonia was evaporated. Complete elimination of ammonia was achieved at 0.5 mmHg, and the resulting enolate was dissolved in anhydrous THF (15 cm^3), then the solvent was removed at low pressure. This operation was repeated three times. Finally, an equimolar mixture of trimethylsilylchloride and triethylamine free from triethylamine hydrochloride (separated by centrifugation) (7.7 cm^3) was added to a solution of the enolate in THF (60 cm^3) at −10 °C. After filtration and evaporation, enol ether **4e** was purified by flash chromatography (eluent: light petroleum) (2.26 g, 83% yield); (Found: C, 69.3; H, 11.6. $C_{13}H_{26}OSi$ requires C, 68.96; H, 11.57%); δ_H(80 MHz; CCl_4, standard $CHCl_3$) 0.20 (9 H, s), 0.73 (3 H, d, *J* 7.6), 0.96 (3 H, d, *J* 6), 1.58 (3 H, s) and 1.0–2.4 (8 H, m); ν_{max}(neat)/cm^{-1} 1675 (C=C); δ_C(20 MHz; C_6D_6) 0.8 (3 C), 14.1, 16.3, 21.3, 22.7 (2 C), 28.8, 31.1, 44.9, 114.4 and 145.7. ^1H NMR spectroscopy showed no regioisomer **6e** was present.

2-*Methyl*-1-*trimethylsiloxycyclopent*-1-*ene* **12a**. The same

procedure described for enol ether **4a** was used, starting from 2-methylcyclopentanone (1.96 g, 20 mmol) yielding enol ether **12a** (2.21 g, 65%) after distillation (b.p. 60–62 °C/13 mmHg); δ_H(60 MHz; CCl_4) 0.18 (9 H, s), 1.50 (3 H, s) and 1.5–2.4 (6 H, m); ν_{max}(neat)/cm^{-1} 1695 (C=C). ^{1}H NMR spectroscopy showed the presence of 5% of regioisomer **11a**.

3-*Methyl*-2-*trimethylsiloxycyclopent*-1-*ene* **11a**. The same procedure described for enol ether **6a** was used starting from 2-methylcyclopentanone (0.98 g, 10 mmol) yielding enol ether **11a** (1.02 g, 60%) after flash chromatography (b.p. 63–65/13 mmHg); δ_H(60 MHz; CCl_4) 0.20 (9 H, s), 1.0 (3 H, d, *J* 6.8), 1.50–2.70 (5 H, m) and 4.48 (1 H, br s); δ_C(20 MHz; C_6D_6) 0.2 (3 C), 18.9, 27.1, 30.9, 39.8, 100.1 and 158.9. ^{1}H NMR spectroscopy showed the presence of 5% of regioisomer **12a**.

3-*Isopropyl*-2-*methyl*-1-*trimethylsiloxycyclopent*-1-*ene* **12b**. 3-Isopropyl-2-methylcyclopent-2-enone was prepared as described above for compound **4e** from 2-methylcyclopenta-1,3-dione (72% yield); δ_H(80 MHz; $CDCl_3$) 1.10 (6 H, d, *J* 7.0), 1.62 (3 H, s), 2.2 (2 H, m), 2.45 (2 H, m) and 2.98 (1 H, m); ν_{max}(neat)/cm^{-1} 1645 (C=C) and 1705 (C=O); δ_C(20 MHz; C_6D_6) 7.9 20.2, 24.8, 29.5, 33.7, 134.7, 176.3 and 208.0.

The same procedure described for compound **4e** was used with 3-isopropyl-2-methylcyclopent-2-en-1-one (2.37 g, 17.2 mmol), and pure enol ether **12b** was obtained (2.14 g, 58%) (Found: C, 68.0; H, 11.25. $C_{12}H_{24}OSi$ requires C, 67.86; H, 11.39%); δ_H(80 MHz; CCl_4) 0.18 (9 H, s), 0.7 (3 H, d, *J* 6.5), 0.88 (3 H, d, *J* 6), 1.0–2.65 (6 H, m) and 1.48 (3 H, s). ^{1}H NMR spectroscopy showed no regioisomer **11b** was present.

3-*Isopropenyl*-2-*methyl*-1-*trimethylsiloxycyclopent*-1-*ene* **12c**. To a solution of isopropenyl magnesium bromide (1 mol dm^{-3}; 30 cm^3) in THF, was added at −60 °C a mixture of 2-methylcyclopent-2-enone (1.92 g, 20 mmol) and cuprous iodide (0.19 g, 1 mmol) in THF (10 cm^3). Stirring was continued for 3 h at −40 °C and an equimolar mixture of trimethylsilylchloride and triethylamine (free from triethylamine hydrochloride) (8 cm^3) was added at −15 °C. The resulting mixture was allowed to warm to room temperature. The same work-up as above was used to yield enol ether **12c** (3.21 g, 75%); (Found: C, 68.6; H, 10.7. $C_{12}H_{26}OSi$ requires C, 68.51; H, 10.54%); δ_H(80 MHz; CCl_4, standard $CHCl_3$) 0.18 (9 H, s), 1.37 (3 H, s), 1.57 (3 H, s), 1.75–2.45 (4 H, m), 3.00 (1 H, t) and 4.65 (2 H, s); ν_{max}(neat)/cm^{-1} 1645 (C=C) and 1690 (C=O). ^{1}H NMR spectroscopy showed no regioisomer **11c** was present.

2,3-*Dimethyl*-1-*trimethylsiloxycyclopent*-1-*ene* **12d**. Prepared by the same method as above using methyl magnesium bromide (30 mmol) and 2-methylcyclopent-2-enone (20 mmol) (16 h at −20 °C), followed by the same treatment and work up, 2,3-dimethyl-1-trimethylsiloxycyclopent-1-ene **12d** (1.86 g, 50%) was obtained. δ_H(80 MHz; CCl_4, standard $CHCl_3$) 0.16 (9 H, s), 0.98 (3 H, d, *J* 6), 0.8–2.4 (5 H, m) and 1.46 (3 H, s); ν_{max}(neat)/cm^{-1} 1690 (C=C). ^{1}H NMR spectroscopy showed no regioisomer **11d** was present.

2-*Methyl*-1-*trimethylsiloxy*-3-*vinylcyclopent*-1-*ene* **12e**. Obtained according to Funk and Vollhardt's procedure[42] (50% yield); δ_H(80 MHz; CCl_4, standard $CHCl_3$) 0.15 (9 H, s), 1.40 (3 H, s), 1.5–2.4 (4 H, m), 2.98 (1 H, m), 4.87 (1 H, dd, *J* 2.3 and 9), 4.98 (1 H, dd, *J* 17.5 and 2.3) and 5.61 (1 H, ddd, *J* 17.5, 9 and 8); ν_{max}(neat)/cm^{-1} 1640 (C=C) and 1690 (C=C). ^{1}H NMR spectroscopy showed no regioisomer **11e** was present.

1-tert-*Butyldimethylsiloxy*-3-(1,5-*dimethylhex*-4-*enyl*)-2-*methylcyclopent*-1-*ene* **12f**. 3-(1,5-Dimethylhex-4-enyl)-2-methylcyclopentanone **16** was obtained from 3-(1,5- dimethylhex-4-enyl)-2-methylcyclopent-2-enone **15**[43] by a reduction procedure similar to that described for the preparation of compound **4e** from the corresponding enone: in this case, the final treatment was carried out using an excess of saturated aqueous NH_4Cl, yielding, from enone **15** (5.15 g, 25 mmol), ketone **16** (4.68 g, 90%) as a mixture of diastereoisomers; δ_H(80 MHz; $CDCl_3$) 0.75–1.05 (6 H, dd), 1.55 (3 H, s), 1.63 (3 H, s), 1.0–2.4 (11 H, m) and 5.02 (1 H, t, *J* 7); ν_{max}(neat)/cm^{-1} 1740 (C=O).

To a mixture of 3-(1,5-dimethylhex-4-enyl)-2-methylcyclopentanone **16** (4.16 g, 20 mmol), *tert*-butyldimethylsilyl chloride (3.75 g, 25 mmol) and triethylamine (2.55 g, 25 mmol), was added dropwise a solution of sodium iodide (3.75 g, 25 mmol) in acetonitrile (26 cm^3), then stirring was continued for 24 h at 20 °C. The suspension was filtered, washed with pentane and the filtrate was extracted with pentane (5 × 10 cm^3). After removal of the solvent, the crude product was heated at 200 °C with triethylamine hydrochloride (0.2 g) for 2–3 h until the IR absorption band at *v* 1645 cm^{-1} (cyclic C=C of the regioisomer **11f**) had completely disappeared. After cooling and dilution with pentane, the silyl enol ether and the siloxane were separated by flash chromatography (eluent: light petroleum). After evaporation of the siloxane at 20–65 °C at 0.5 mmHg, product **12f** was obtained (4.9 g, 75%) as a couple of diastereoisomers (*l*) and (*u*) (ratio *l*:*u* = 75:25 determined by ^{1}H NMR spectroscopy), b.p. 115 °C/0.5 mmHg; (Found: C, 74.1; H, 12.15. $C_{20}H_{38}OSi$ requires C, 74.46; H, 11.87%); δ_H(400 MHz; C_6D_6) 0.11 (*u*) and 0.12 (*l*) [6 H, s, $(CH_3)_2Si$], 0.75 (*u*) and 0.93 (*l*) (3 H, d, *J* 7, 1′-Me), 1.0 (*l*) and 1.01 (*u*) (9 H, s, Me_3CSi), 1.07 (1 H, m), 1.2–1.55 (3 H, m), 1.56–1.70 (9 H, 3 s, 2-Me and two 5′-Me), 1.75 (1 H, m), 1.97 (1 H, hept), 2.12 (1 H, m), 2.23 (2 H, m), 2.52 (*l*) and 2.62 (*u*) (1 H, m, 3-H), 5.21 (*l*) and 5.26 (*u*) (1 H, tt, *J* 7.0 and 1.4, 4′-H); ν_{max}(neat)/cm^{-1} 1690 (C=C); δ_C(100 MHz; C_6D_6) (*l* isomer) −3.8 (Me_2CSi), 11.0 (Me-C_2), 17.8 (C-6′), 18.3 (Me_3CSi), 21.8, 25.9 (1-Me, 5′-Me), 26.8, 31.3, 33.5, 34.5, 51.2, 114.6 (C-2), 125.7 (C-4′), 130.7 (C-5′), 148.0 (C-1). ^{1}H NMR spectroscopy showed the presence of less than 3% of the regioisomer **11f**: 4.56 (1 H, m, H vinylic).

General Procedure for Preparation of 1,5-*Diketones*.—Into a two-necked, 25 cm^3 round bottomed flask, were introduced, under argon, the silyl enol ether in nitromethane (3 cm^3) at 20 °C, then at −20 °C a solution of methyl vinyl ketone (MVK) in nitromethane (3 cm^3) and, dropwise, a solution of boron trifluoride–diethyl ether (0.1 cm^3) and hydroxylic compound (acid or alcohol) in nitromethane (0.5 cm^3). For each compound, the nature of the hydroxylic compound and the quantities of reagents used are specified below. The mixture was stirred at −20 °C for 1 h, then allowed to warm to 0 °C and saturated aq. $NaHCO_3$ (6 cm^3) was added. After extraction with CH_2Cl_2 (4 × 10 cm^3), the combined layers were dried ($MgSO_4$), filtered and evaporated, the ketone resulting from the hydrolysis of the starting enol ether was first eluted by flash chromatography (Et_2O:light petroleum, 5:95) and then the diketone (Et_2O:light petroleum, 15:85).

2-*Methyl*-2-(3-*oxobutyl*)*cyclohexanone* **5a**.[25,44] Enol ether **4a** (0.79 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and menthol (0.47 g, 3 mmol) to yield diketone **5a** (0.7 g, 92%); (Found: C, 72.3; H, 10.2. Calc. for $C_{11}H_{18}O_2$: C, 72.48; H, 9.88%); δ_H(60 MHz; $CDCl_3$) 1.07 (3 H, s), 1.50–2.55 (12 H, m) and 2.15 (3 H, s); δ_C(20 MHz; $CDCl_3$) 21.1, 22.6, 27.5, 29.9, 31.2, 38.4, 38.8, 39.5, 47.9, 208.2 and 215.2; ν_{max}(neat)/cm^{-1} 1710 (C=O). ^{1}H NMR spectroscopy showed no presence of the diketone **7a**.*

6-*Methyl*-2-(3-*oxobutyl*)*cyclohexanone* **7a**.[44] Enol ether **5a** (0.79 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and menthol (0.47 g, 3 mmol) and yielded diketone **7a** (0.34 g, 57%) (2 diastereoisomers *cis*:*trans*, 89:11); δ_H(400 MHz; $CDCl_3$) *cis* isomer: 1.05 (3 H, d, *J* 6.8), 2.11 (3 H, s), 1.45–2.05 (8 H, m), 2.3–2.5 (3 H, m) and 2.55 (1 H, m). The *trans* isomer was detected by the signal at δ_H 0.99 (3 H, d, *J* 6.4); δ_C(20 MHz; $CDCl_3$) *cis* isomer: 14.8, 19.8, 24.1, 29.2, 32.3, 34.4, 40.5, 42.0, 47.5, 207.2 and 215.2; *trans* isomer: 13.7, 23.0, 24.8, 29.2, 30.5,

34.8, 36.8, 44.9, 49.1, 207.8 and 214.4. ^{1}H NMR spectroscopy showed the presence of 3% of the diketone **5a**.*

cis-2,3-*Dimethyl*-2-(3-*oxobutyl*)*cyclohexanone* **5d**. *tert*-Butyldimethylsilyl enol ether **4d'** (0.72 g, 3 mmol, 1 equiv.) was reacted with MVK (0.21 g, 3 mmol) and anhydrous dibenzoyl tartaric acid (DBTA) (1.07 g, 3 mmol) to yield diketone **5d** (0.42 g, 72%, 89% based on unrecovered ketone **1d**). GC (100 °C, 11 cm^3 min^{-1}) indicated major product *cis*-**5d** (92%, R_t = 14.5 min) and the minor isomer *trans*-**5d** (8%, R_t = 13.4 min); δ_H(400 MHz; [$^2H_5$]-pyridine) *cis* isomer: 0.74 (3 H, d, *J* 7), 0.88 (3 H, d, *J* 1.45), 1.3–1.9 (7 H, m), 2.03 (3 H, s) and 2.22–2.55 (4 H, m); irradiation at 0.74 ppm (Me doublet) caused the multiplet at 1.65 ppm to narrow (H on C_3 axial, *J* 4 and 10); irradiation at 0.88 ppm (Me singlet) caused no NOE effect at 1.65 ppm on C_3 axial proton, consistent with the *cis* relationship of the two methyl groups. Diastereoisomer *trans* **5d** was detected by the following signals δ_H(400 MHz; [$^2H_5$]-pyridine) 0.79 (3 H, d, *J* 6.4) and 1.03 (3 H, d, *J* 1.45); δ_C(20 MHz; C_6D_6) *cis* isomer 15.4, 18.6, 24.6, 29.0, 29.5, 29.7, 38.2 (2 C), 38.7, 51.3, 206.6 and 213.3. ν_{max}(neat)/cm^{-1} 1710 (C=O); *m/z* (70 eV, CI) 197 (M^+ + 1); (Found: C, 73.3; H, 10.25. $C_{12}H_{20}O_2$ requires C, 73.43; H, 10.27%). ^{1}H NMR spectroscopy showed the presence of 2% of the diketone **7d**.

5,6-*Dimethyl*-2-(3-*oxobutyl*)*cyclohexanone* **7d**. Enol ether **6d** (0.79 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and isopropyl alcohol (0.18 g, 3 mmol) to yield diketone **7d** (0.175 g, 30%, 57% based on unrecovered ketone). ^{1}H NMR spectra and GC analysis (100 °C, 10 cm^3 min^{-1}) showed the presence of the four diastereoisomers (A–D) of diketone **7d** (A:B:C:D = 50:23:20:7); δ_H(400 MHz; [$^2H_5$]-pyridine) A: 0.80 (3 H, d, *J* 6.0) and 0.98 (3 H, d, *J* 6.7); B: 0.68 (3 H, d, *J* 7) and 0.86 (3 H, d, *J* 7.2); C: 0.84 (3 H, d, *J* 6.0) and 0.94 (3 H, d, *J* 6.5); D: 0.56 (3 H, d, *J* 7.2) and 0.87 (3 H, d, *J* 6.7), A–D: 1.05–2.05 (7 H, m), 1.99 (3 H, s) and 2.1–2.5 (4 H, m); ν_{max}(neat)/cm^{-1} 1715 (C=O); (HRMS: Found: M^+ 196.1467. Calc. for $C_{12}H_{20}O_2$: *M*, 196.1463) ^{1}H NMR spectroscopy showed the presence of 3% of the diketone **5d**.

cis-3-*Isopropyl*-2-*methyl*-2-(3-*oxobutyl*)*cyclohexanone* **5e**. Enol ether **4e** (0.18 g, 3 mmol) was reacted with MVK (0.21 g, 3 mmol) and DBTA (1.07 g, 3 mmol) to yield diketone **5e** (0.41 g, 60%, 74% based on unrecovered ketone). GC analysis (135 °C, 9.2 cm^3 min^{-1}) showed only one *cis* isomer (R_t = 7.9 min); (Found: C, 74.85; H, 11.0. $C_{14}H_{24}O_2$ requires C, 74.95; H, 10.78%); δ_H(500 MHz; $CDCl_3$) 0.86 (3 H, d, *J* 6.5), 0.89 (3 H, d, *J* 6.5), 1.06 (3 H, s), 1.43 (1 H, dt), 1.50 (1 H, m), 1.64 (3 H, m), 1.88 (1 H, dt), 2.00 (2 H, m), 2.12 (3 H, s), 2.25 (2 H, m) and 2.41 (2 H, m). Irradiation at 1.06 ppm (Me singlet) caused no NOE effect at 1.43 (H on C_3) but caused an NOE effect (7%) at 1.88 (H on $C_{1''}$), consistent with the *cis* relationship of methyl and isopropyl groups. ν_{max}(neat)/cm^{-1} 1720–1725 (C=O); δ_C($CDCl_3$; 20 MHz) 18.5, 20.0, 20.2, 24.0, 24.8, 25.8, 28.4, 29.2, 38.0, 38.4, 47.7, 52.0, 208.1 and 214.2.

2-*Methyl*-2-(3-*oxobutyl*)*cyclopentanone* **14a**.[25] Enol ether **12a** (0.68 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and menthol (0.47 g, 3 mmol) to yield diketone **14a** (0.38 g, 76%); (Found: C, 71.2; H, 9.8. Calc. for $C_{10}H_{16}O_2$: C, 71.33; H, 9.51%); δ_H(60 MHz; $CDCl_3$) 1.0 (3 H, s), 1.5–2.65 (10 H, m) and 2.15 (3 H, s); δ_C(20 MHz; C_6D_6) 18.7, 21.5, 29.6, 30.3, 36.2, 37.3, 38.3, 47.1, 206.9 and 212.2; ν_{max}(neat)/cm^{-1} 1715 (C=O). ^{1}H NMR spectroscopy showed no presence of diketone **13a**.

5-*Methyl*-2-(3-*oxobutyl*)*cyclopentanone* **13a**. Enol ether **11a** (0.68 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and 2-phenylethanol (0.37 g, 3 mmol) to yield diketone **7a** (0.18 g, 35%) (2 diastereoisomers: 65:35). δ_H(80 MHz; $CDCl_3$) 1.04 and 1.08 (3 H, d, *J* 8 and 6.5), 2.13 (3 H, s), 1.20–2.10 (6 H, m), 2.20–2.70 (2 H, m) and 2.55 (2 H, t, *J* 7.5); δ_C(20 MHz; $CDCl_3$) major isomer: 14.1, 24.0, 27.4, 29.5 (2 C), 40.8, 43.8, 47.3, 207.0 and 221.7; minor isomer: 14.8, 24.0, 26.5, 28.6, 29.5, 40.8, 42.5, 46.5, 208.0 and 222.0; ν_{max}(neat)/cm^{-1} 1725–1740 (C=O). ^{1}H NMR spectroscopy showed the presence of 5% of the diketone **14a**.

cis-3-*Isopropyl*-2-*methyl*-2-(3-*oxobutyl*)*cyclopentanone* **14b**. Enol ether **12b** (0.86 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and DBTA (1.07 g, 3 mmol) to yield diketone **14b** (0.52 g, 82%, 95% based on unrecovered ketone). GC (135 °C; 9 cm^3 min^{-1}) showed a single isomer (R_t = 3.9 mm); δ_H(500 MHz; [$^2H_5$]-pyridine) 0.79 (3 H, d, *J* 6.4), 0.84 (3 H, s), 0.87 (3 H, d, *J* 6.4), 1.27 (1 H, m), 1.49 (1 H, dq), 1.55 (1 H, dt), 1.81 (1 H, hept), 1.84 (1 H, m), 2.03 (3 H, s), 2.07 (2 H, m), 2.12 (1 H, hept), 2.26 (1 H, m) and 2.54 (1 H, hept). Irradiation at 0.84 ppm (Me singlet) caused no NOE effect on the signal of H on C_3 at 1.55 ppm but an NOE effect is observed (6%) on the signal of H on $C_{1''}$ at 1.49 ppm consistent with a *cis* relationship of methyl and isopropyl groups; δ_C($CDCl_3$; 20 MHz) 17.3, 20.8, 21.9, 22.9, 28.8, 29.4, 30.7, 36.8, 38.5, 49.0, 50.5, 207.6 and 222.8; ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1740 (C=O); *m/z* (70 eV, C.I.) 211 (M^+ + 1), 193, 141 and 75. (HRMS: Found: M^+ 210.1620. Calc. for $C_{13}H_{22}O_2$: *M*, 210.1599.)

cis-3-*Isopropenyl*-2-*methyl*-2-(3-*oxobutyl*)*cyclopentanone* **14c**. Enol ether **12c** (0.84 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and acetic acid (0.18 g, 3 mmol) yielding *diketone* **14c** (0.475 g, 76%). GC (135 °C; 9.2 cm^3 min^{-1}) showed a single *cis* isomer (R_t 4.2 min). (Found: C, 74.55; H, 9.65. $C_{13}H_{20}O_2$ requires C, 74.96; H, 9.68%); δ_H(400 MHz) 0.82 (3 H, s); 1.75 (3 H, s), 1.76 (1 H, m), 1.88 (2 H, m), 2.03 (1 H, m), 2.12 (3 H, s), 2.18 (1 H, dt, *J* 18 and 9.2), 2.33 (1 H, hept), 2.39 (1 H, ddd, *J* 18 and 8.5), 2.53 (1 H, hept), 2.61 (1 H, ddd, *J* 6 and 10.5), 4.75 (1 H, s) and 4.93 (1 H, t, *J* 1.7); ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1735 (C=O).

cis-2,3-*Dimethyl*-2-(3-*oxobutyl*)*cyclopentanone* **14d**. Enol ether **12d** (0.74 g, 4 mmol, 1.33 equiv.) was reacted with MVK (0.21 g, 3 mmol) and DBTA (1.07 g, 3 mmol) yielding diketone **14d** (0.305 g, 56%, 71% based on unrecovered ketone) as a pair of diastereoisomers; *cis*:*trans* = 78:22 from GC analysis. δ_H(80 MHz; [$^2H_5$]-pyridine) *cis* isomer: 0.79 (3 H, s), 0.88 (3 H, d, *J* 6.4), 1.5–2.6 (9 H, m) and 2.07 (3 H, s); *trans* isomer was detected by the following signal: 0.95 (3 H, s).

cis-2-*Methyl*-2-(3-*oxobutyl*)-3-*vinylcyclopentanone* **14e**. Enol ether **12e** (0.735 g, 3.75 mmol, 1.25 equiv.) was reacted with MVK (0.21 g, 3 mmol) and acetic acid (0.18 g, 3 mmol) to yield diketone **14e** (0.37 g, 64%, 70% based on unrecovered ketone). GC (110 °C, 10 cm^3 min^{-1}) showed the presence of 2 diastereoisomers: 6.6 min (79%, *cis*) and 5.5 min (21%, *trans*); δ_H(80 MHz; $CDCl_3$) *cis* isomer 0.84 (3 H, s), 1.5–2.75 (9 H, m), 2.10 (3 H, s), 5.02 (1 H, d), 5.19 (1 H, s) and 5.70 (1 H, m); *trans* isomer was observed by the signal at 0.95 (3 H, s); δ_C(100 MHz; $CDCl_3$) *cis* isomer 17.2, 24.2, 29.0, 29.7, 36.7, 38.2, 48.4, 50.4, 116.7, 136.7, 208.2 and 222.1; *trans* isomer: 19.3, 23.6, 29.7, 30.0, 35.9, 37.3, 50.2, 52.4, 116.7, 136.3, 208.2 and 221.7; ν_{max}(neat)/cm^{-1} 1730 (C=O), 1715 (C=O) and 1645 (C=C).

3-(1,5-*Dimethylhex*-4-*enyl*)-2-*methyl*-2-(3-*oxobutyl*)*cyclopentanone* **14f**. Enol ether **12f** (0.72 g, 3 mmol) was reacted with MVK (0.28 g, 4 mmol, 1.33 equiv.) and acetic acid (0.18 g, 3 mmol), yielding pure *cis*-diketone **14f** (0.46 g, 55%, 85% based on uncovered ketone). GC analysis (150 °C, 10 cm^3 min^{-1}) indicated a major product (*l,l*) (15.5 min, 70%), and its diastereoisomer (*l,u*) (17.8 min, 30%). No trace of *trans* isomers (*u,l* or *u,u*) was found from GC analysis and NMR spectroscopy; δ_H(400 MHz; $CDCl_3$) major isomer (*l,l*): 0.90 (3 H, s), 0.97 (3 H,

* Enol ether **6a** was more sensitive to hydrolysis in the reaction conditions than was enol ether **4a**. This property explains the reason that no diketone **7a** was obtained when preparing diketone **5a** from a mixture of enol ethers **4a** and **6a** (**4a**:**6a** = 90:10) and is also the reason that a small quantity of diketone **5a** was observed when preparing diketone **6a** from a mixture of enol ethers **6a** and **4a** (**6a**:**4a** > 95:5).

d, *J* 6.6), 1.09 (1 H, m), 1.40 (1 H, m), 1.55 (1 H, m), 1.56 (1 H, m), 1.58 (3 H, s), 1.66 (3 H, s), 1.66 (1 H, m), 1.73 (1 H, hept), 1.90 (1 H, hept), 1.91 (1 H, m), 2.03 (1 H, m), 2.05 (1 H, m), 2.10 (1 H, m), 2.10 (3 H, s), 2.23 (1 H, hept), 2.32 (1 H, m), 2.42 (1 H, hept) and 5.06 (1 H, t, *J* 7); minor isomer (*l,u*) was detected by the following signal: 0.84 (3 H, d, *J* 6.6) and 0.89 (3 H, s); δ_C(100 MHz; $CDCl_3$) major isomer (*l,l*) 17.4, 17.5, 18.3, 22.8, 24.8, 25.5, 29.7, 31.0, 33.4, 33.9, 37.0, 38.7, 48.1, 50.9, 124.3, 131.4, 208.0 and 223.3; minor isomer (*l,u*); 16.8, 17.4, 17.5, 21.8, 25.4, 25.5, 29.7, 31.1, 32.8, 35.8, 37.0, 38.6, 47.7, 50.8, 124.1, 131.4, 208.0 and 223.1; ν_{max}(neat)/cm^{-1} 1720 (C=O) and 1740 (C=O) (HRMS: Found M^+ 278.2248. Calc. for $C_{18}H_{30}O_2$: *M*, 278.2246).

3-(1,5-*Dimethylhexyl*)-2-*methyl*-2-(3-*oxobutyl*)*cyclopentanone* **14g**.[37] To a suspension of 10% palladium-on-charcoal (0.17 g) in ethyl acetate (11 cm^3) was added a solution of diketone **14f** (0.83 g, 3 mmol) in ethyl acetate (2 cm^3) under hydrogen atmosphere and the mixture was vigourously stirred for 24 h at room temperature. After filtration and evaporation, purification by flash chromatography gave pure *cis*-diketone **14g** (0.76 g, 91%). GC analysis (150 °C, 10 cm^3 min^{-1}) indicated a major product (*l,l*) (10.7 min, 70%), and its diastereoisomer (*l,u*) (11.4 min, 30%). No trace of *trans* isomers (*u,l* or *u,u*) was found from GC analysis and NMR spectroscopy; δ_H(400 MHz; $CDCl_3$) 0.86 (6 H, d, *J* 6.6), 0.91 (3 H, s), 0.84 (30%, *l,u*) and 0.96 (70%, *l,l*) (3 H on C″$_1$, d, *J* 6.8), 1.13 (4 H, m), 1.30–2.35 (12 H, m), 2.11 (3 H, s), 2.43 (70%, *l,l*) and 2.47 (30%, *l,u*) (1 H, q); δ_C(100 MHz; $CDCl_3$) major isomer (*l,l*): 17.2, 18.2, 22.2, 22.4, 22.7, 23.7, 27.6, 29.5, 30.8, 33.5, 33.9, 36.6, 38.5, 39.0, 47.7, 50.6, 207.8 and 223.0; minor isomer (*l,u*); 16.7, 17.2, 21.6, 22.2, 22.3, 24.4, 27.6, 29.5, 30.8, 32.9, 35.7, 36.6, 38.3, 38.5, 47.5, 50.6, 207.6 and 223.0; ν_{max}(neat)/cm^{-1} 1715 (C=O) and 1740 (C=O).

Cyclization of 1,5-*Diketones into Bicyclic Enones*.—4a-*Methyl*-4,4a,5,6,7,8-*hexahydronaphthalen*-2(3H)-*one* **2a**.[5,6,20] To diketone **5a** (0.36 g, 2 mmol), was added an ethanolic solution (3 mol dm^{-3}; 1.1 cm^3) of potassium hydroxide. After stirring for 1 h at 20 °C, saturated aqueous NaCl (3.3 cm^3) was added at 20 °C. The mixture was extracted with diethyl ether (7 × 10 cm^3), and the combined organic layers were dried ($MgSO_4$) and evaporated. Octalone **2a** was obtained after flash chromatography (eluent; Et_2O:light petroleum, 10:100); (0.31 g, 95% yield); b.p. 87–88/0.25 mmHg; GC (80 °C, 9 cm^3 min^{-1}): 29.6 min. δ_H(60 MHz; $CDCl_3$) 1.25 (3 H, s), 1.30–2.60 (12 H, m) and 5.73 (1 H, s); δ_C(20 MHz; $CDCl_3$) 21.6, 22.1, 27.2, 32.8, 34.0, 36.0, 38.1, 41.6, 124.2, 170.3 and 199.5; ν_{max}(neat)/cm^{-1} 1625 (C=C) and 1680 (C=O). ^1H NMR spectroscopy showed no presence of enone **8a**.

8-*Methyl*-4,4a,5,6,7,8-*hexahydronaphthalen*-2(3H)-*one* **8a**.[45] The same procedure (reaction time: 5 h) as above was applied to diketone **7a** yielding product **8a**, (0.24 g, 72%). GC (80 °C, 9 cm^3 min^{-1}) showed 2 diastereoisomers: 30.7 min (*trans*, 80%) and 37.0 min (*cis*, 20%); δ_H(400 MHz; $CDCl_3$) *trans* isomer: 1.09 (3 H, d, *J* 6.5), 1.15 (1 H, m), 1.32 (1 H, td), 1.63 (3 H, m), 1.80 (1 H, m), 1.92 (2 H, m), 2.02–2.52 (4 H, m) and 5.83 (1 H, s); *cis* isomer was detected by the following signals: 1.17 (3 H, d, *J* 6.5) and 5.72 (1 H, s); δ_C(100 MHz; $CDCl_3$) *trans* isomer: 17.4, 25.4, 28.5, 34.5, 35.5, 36.3, 38.2 (2 C), 121.0, 171.0 and 200.3; *cis* isomer: 19.8, 20.4, 29.2, 32.2, 33.8, 34.4, 36.5, 37.8, 124.0, 171.9 and 200.3; ν_{max}(neat)/cm^{-1} 1610 (C=C) and 1680 (C=O). ^1H NMR spectroscopy showed the presence of 6% of the enone **2a**.

cis-4a,5-*Dimethyl*-4,4a,5,6,7,8-*hexahydronaphthalen*-2(3H)-*one* **2d**.[6,22,33] To a 92:8 mixture of *cis* and *trans* diketones **4d** (0.42 g, 2.16 mmol, also containing 2% of regioisomers **6d**) was added a methanolic solution (0.3 mol dm^{-3}; 8 cm^3) of sodium methoxide (prepared prior to use from sodium and anhydrous methanol). This solution was stirred at 45 °C for 45 min. Then, saturated aqueous NaCl (4.3 cm^3) was introduced at 20 °C. The mixture was extracted with diethyl ether (7 × 10 cm^3), and the combined organic layers were dried ($MgSO_4$) and evaporated. *cis*-Octalone **2d** was obtained after flash chromatography (eluent; Et_2O:light petroleum, 10:100) (0.327 g, 85%). GC analysis (100 °C, 11 cm^3 min^{-1}): 17.4 min; (Found: C, 80.3; H, 10.45. Calc. for $C_{12}H_{18}O$: C, 80.87; H, 10.17%); δ_H(400 MHz; $CDCl_3$) 0.82 (3 H, d, *J* 6), 1.01 (3 H, s), 1.35 (3 H, m), 1.43 (1 H, m), 1.63 (1 H, td, *J* 4.9 and 13.9), 1.77 (1 H, m), 1.94 (1 H, ddd, *J* 4.9, 3.4 and 13.5), 2.1–2.4 (4 H, m) and 5.63 (1 H, d, *J* 0.3); δ_C(100 MHz; $CDCl_3$) 15.0, 15.7, 26.3, 30.2, 33.1, 33.8, 35.3, 38.8, 42.9, 123.8, 170.9 and 199.1; ν_{max}(neat)/cm^{-1} 1620 (C=C) and 1680 (C=O); *m/z* (70 eV, EI) 178 (M^+), 163, 149, 136, 121 and 57. Diastereoisomer *trans*-**2d**[33,46] (2%) was detected by GC (100 °C, 11 cm^3 min^{-1}): 18.3 min, by ^1H NMR spectroscopy (400 MHz; $CDCl_3$) 5.70 (1 H, d, *J* 0.3, H vinylic) and by ^{13}C NMR spectroscopy (100 MHz; $CDCl_3$) 16.1, 20.5, 23.5, 28.3, 31.6, 31.8, 34.1, 39.1, 39.2, 126.0, 169.9 and 199.0. ^1H NMR spectroscopy showed the presence of 1% of the enone **8d**: 5.73–5.75 (1 H, s, H vinylic).

cis-5-*Isopropyl*-4a-*methyl*-4,4a,5,6,7,8-*hexahydronaphthalen*-2(3H)-*one* **2e**. To diketone **5e** (0.45 g, 2 mmol), was added an ethanolic solution (3 mol dm^{-3}; 1.1 cm^3) of potassium hydroxide. After stirring at 20 °C for 3 h, work up and purification were the same as described above, giving the pure desired *cis*-product **2e** (0.35 g, 85%); m.p. 58 °C (Found: C, 81.3; H, 10.9. $C_{14}H_{22}O$ requires C, 81.49; H, 10.95%); GC (135 °C, 9.2 cm^3 min^{-1}): 10.1 min; δ_H(80 MHz; $CDCl_3$) 0.88 (3 H, d, *J* 6.9), 0.93 (d, *J* 6.9), 1.19 (3 H, s), 1.1–2.55 (12 H, m) and 5.67 (1 H, s); ν_{max}(neat)/cm^{-1} 1610 (C=C) and 1680 (C=O).

cis-1-*Isopropyl*-7a-*methyl*-2,3,7,7a-*tetrahydroinden*-5(6H)-*one* **17b**. To diketone **14b** (0.42 g, 2 mmol), was added a methanolic solution (0.3 mol dm^{-3}; 1.1 cm^3) of sodium methoxide (prepared prior to use from sodium and anhydrous methanol). After stirring at 20 °C for 1 h, work up and purification were the same as described above, giving the pure desired *cis* product **17b** (0.31 g, 80%); δ_H(80 MHz; $CDCl_3$) 0.94 (3 H, d, *J* 6.3), 0.99 (3 H, d, *J* 6.3), 1.19 (3 H, s), 1.0–2.8 (10 H, m) and 5.73 (1 H, br s); δ_C(20 MHz; $CDCl_3$) 15.8, 22.1, 22.4, 26.7, 28.4, 29.3, 33.1, 36.6, 44.5, 57.2 , 121.0, 179.5 and 198.5; ν_{max}(neat)/cm^{-1} 1660 (C=C and C=O); *m/z* (70 eV, C.I.) 193 (M^+ + 1), 175 and 165. (HRMS: Found: M^+ 192.1527. Calc. for $C_{13}H_{20}O$: *M*, 192.1514.)

cis-1-(1,5-*Dimethylhex*-4-*enyl*)-7a-*methyl*-2,3,7,7a-*tetrahydroinden*-5(6H)-*one* **17f**.[6] By the same procedure as described for **2a** and **2e**, from a mixture (70:30) of diketones **14f** (*l,l*) and (*l,u*) (0.556 g, 2 mmol), a mixture (70:30) of the desired hydrindenones **17f** (*l,l*) and (*l,u*) was obtained (0.37 g, 71%). GC (160 °C, 10 cm^3 min^{-1}): 15.1 min (*l,u*), 30%, 16.9 min (*l,l*), 70%; δ_H(400 MHz; $CDCl_3$) major isomer (*l,l*): 0.95 (3 H, d, *J* 6.6), 1.06 (3 H, s), 1.12 (1 H, m), 1.36–1.58 (4 H, m), 1.58 (3 H, s), 1.66 (3 H, s), 1.75–2.08 (4 H, m), 2.22 (1 H, m), 2.31 (1 H, m), 2.37 (1 H, dt), 2.47 (1 H, dd), 2.57 (1 H, dt), 5.05 (1 H, m), 5.70 (1 H, s). Diastereoisomer (*l,u*) was detected by the following signals: 0.89 (3 H, d, *J* 6.6) and 1.05 (3 H, s); δ_C(100 MHz; $CDCl_3$) major isomer (*l,l*): 15.9, 17.4, 18.4, 24.4, 25.4, 26.5, 28.6, 33.2, 33.8, 35.4, 36.8, 44.8, 55.6, 121.2, 124.4, 131.1, 179.7 and 198.9. Diastereoisomer (*l,u*) was detected by the following signal: 55.0; *m/z* (70 eV, EI) 260 (M^+), 245, 218, 175, 149 and 69; ν_{max}(neat)/cm^{-1} 1655 (C=C) and 1665 (C=O).

cis-1-(1,5-*Dimethylhexyl*)-7a-*methyl*-2,3,7,7a-*tetrahydroinden*-5(6H)-*one* **17g**.[37] The procedure described by Ficini and co-workers[37] was used with a mixture (70:30) of diketones **14g** (*l,l*) and (*l,u*) (0.556 g, 2 mmol). A mixture (70:30) of the desired hydrindenones **17g** (*l,l*) and (*l,u*) was obtained (0.435 g, 83%); δ_H(400 MHz; $CDCl_3$) major isomer (*l,l*): 0.87 (6 H, d, *J* 6.3), 0.96 (3 H, d, *J* 6.3), 1.07 (3 H, s), 1.05–2.65 (17 H, m) and 5.72 (1 H, br s). Diastereoisomer (*l,u*) was detected by the following signals: 0.85 (3 H, d, *J* 6.3) and 1.08 (3 H, s); ν_{max}(neat)/cm^{-1} 1660 (C=C and C=O).

Preparation of Octalone **2d** *Without Purification of the Intermediate Diketone.*—Into a two-necked, 25 cm^3 round bottomed flask, was introduced under argon, enol ether **4d** (0.72 g, 3 mmol) in nitromethane (3 cm^3) at 20 °C. Then at −20 °C a solution of methyl vinyl ketone (0.21 g, 3 mmol) in nitromethane (3 cm^3) and, dropwise a solution of boron trifluoride–diethyl ether (0.1 cm^3) and acetic acid (0.18 g, 3 mmol) in nitromethane (0.5 cm^3) were added. The mixture was stirred at −20 °C for 1 h, then allowed to warm to 0 °C and saturated aqueous $NaHCO_3$ (6 cm^3) was added. After extraction with CH_2Cl_2 (4 × 10 cm^3) the organic layers were dried ($MgSO_4$), filtered and evaporated. To the crude product obtained was added a methanolic solution of freshly prepared methoxide (0.3 mol dm^{-3}; 8 cm^3). This solution was stirred at 45 °C for 45 mins. Then saturated aqueous NaCl (4.3 cm^3) was introduced at 20 °C. The mixture was extracted with diethyl ether (7 × 10 cm^3) and the combined layers were dried ($MgSO_4$), filtered and evaporated. Octalone **2d** was purified by flash chromatography (Et_2O:light petroleum, 10:100) (0.34 g, 62%).

cis-4a,5-*Dimethyl*-3-*isopropylidene*-4,4a,5,6,7,8-*hexahydronaphthalen*-2(3H)-*one* **10** (*Dehydrofukinone*).[19,35]—*cis*-Octalone **2d** (0.32 g, 1.8 mmol, purity: 97%) was treated by acetone according to Hagiwara's procedure[19c] to furnish the intermediate alcohol (0.387 g, 91% yield); δ_H(80 MHz; $CDCl_3$) 0.89 (3 H, d), 1.10 (3 H, s), 1.19 (6 H, s), 1.2–2.7 (10 H, m), 5.13 (1 H mobile, s) and 5.68 (1 H, s); ν_{max}(neat)/cm^{-1} 3450 (OH), 1660 (C=O) and 1640 (C=C); *m/z* (70 eV, EI) 236 (M^+), 218, 203, 178, 163 and 150. The tertiary alcohol (0.354 g, 1.5 mmol) was dehydrated by Hagiwara's method[19c] using PTSA in refluxing benzene leading to dehydrofukinone **10** (0.262 g, 80%); δ_H(400 MHz; $CDCl_3$) 0.92 (3 H, d, *J* 6.4), 0.94 (3 H, s), 1.10–1.55 (5 H, m), 1.81 (3 H, d, *J* 1.4), 2.05 (3 H, d, *J* 1.9), 2.10 (1 H, d, *J* 13.6), 2.24 (2 H, m), 2.84 (1 H, d, *J* 13.6) and 5.71 (1 H, t, *J* 1.0); δ_C(100 MHz; $CDCl_3$) 15.3, 15.9, 21.9, 22.5, 26.4, 30.4, 32.4, 40.9, 41.8, 42.4, 126.0, 128.1, 142.1, 168.6 and 192.3; *m/z* (70 eV, EI) 218 (M^+), 203, 189, 175 and 161. *trans*-Isomer[35] (2%) was detected in the ^1H NMR spectrum ($CDCl_3$; 400 MHz) by the following signal: 5.78 (1 H, d, *J* 2).

Acknowledgements

We are gratefully indebted to Prof. D. Davoust and to Dr. G. Ple for performing 400 and 500 MHz ^1H NMR spectra and for providing helpful discussion.

References

1 (*a*) W. S. Rapson and R. Robinson, *J. Am. Chem. Soc.*, 1935, 1285; (*b*) E. C. Du Feu, F. J. MacQuillin and R. Robinson, *J. Chem. Soc.*, 1937, 53.
2 For reviews see: (*a*) R. E. Gawley, *Synthesis*, 1976, 777; (*b*) M. E. Jung, *Tetrahedron*, 1976, **32**, 3.
3 J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, 1964, **29**, 2501.
4 H. O. House and M. J. Lusch, *J. Org. Chem.*, 1977, **42**, 183.
5 G. Stork and B. Ganem, *J. Am. Chem. Soc.*, 1973, **95**, 6152.
6 (*a*) R. Boeckman Jr, *Tetrahedron*, 1983, **39**, 925; (*b*) R. Boeckman Jr, D. M. Blum, B. Ganem and N. Halvey, *Org. Synth.*, 1978, **58**, 152.
7 O. Wichterle, J. Prochaska and J. Hoffman, *Coll. Czech. Chem. Comm.*, 1948, **13**, 300.
8 (*a*) G. Stork and M. E. Jung, *J. Am. Chem. Soc.*, 1974, **96**, 3682; (*b*) G. Stork, M. E. Jung, E. Colvin and Y. Noel, *J. Am. Chem. Soc.*, 1974, **96**, 3684.
9 P. Stotter and K. A. Hill, *J. Am. Chem. Soc.*, 1974, **96**, 6524.
10 (*a*) G. Stork, S. Danishefsky and M. Ohashi, *J. Am. Chem. Soc.*, 1967, **89**, 5459; (*b*) G. Stork and J. E. McMurry, *J. Am. Chem. Soc.*, 1967, **89**, 5463, 5464.
11 C. Enzell, *Acta Chem. Scand.*, 1962, **16**, 1553; *Tetrahedron Lett.*, 1962, 185.
12 W. C. Dauben and A. C. Ashcraft, *J. Am. Chem. Soc.*, 1963, **85**, 3673.
13 W. L. Meyer, G. B. Clemans and R. A. Marming, *J. Org. Chem.*, 1975, **40**, 3686.
14 J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, 1965, **30**, 3642.
15 D. Caine and T. N. Tuller, *J. Org. Chem.*, 1969, **34**, 222.
16 C. Berger, M. Franck-Neumann and G. Ourisson, *Tetrahedron Lett.*, 1968, 3451.
17 E. Piers, R. W. Britton and W. De Waal, *Can. J. Chem.*, 1969, **47**, 4307.
18 A. R. Pinder and A. K. Torrence, *J. Chem. Soc. C*, 1971, 3410.
19 (*a*) M. Ohashi, *Chem. Commun.*, 1969, 893; (*b*) S. Torii, T. Inokuchi and T. Yamafuji, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 2640; (*c*) H. Hagiwara, H. Uda and T. Kodama, *J. Chem. Soc., Perkin Trans. 1*, 1980, 963.
20 C. H. Heathcock, J. E. Ellis, J. E. McMurry and A. Coppolino, *Tetrahedron Lett.*, 1971, **52**, 4995.
21 W. C. Still and F. L. Van Middlesworth, *J. Org. Chem.*, 1977, **42**, 1258.
22 P. Zoretic, J. A. Golen and M. D. Saltzman, *J. Org. Chem.*, 1981, **44**, 3554.
23 J. W. Huffman, S. M. Potnis and A. V. Satish, *J. Org. Chem.*, 1985, **50**, 4266.
24 See for example: (*a*) N. Narasaka, R. Soai and T. Mukayaima, *Chem. Lett.*, 1976, 1223; (*b*) N. Narasaka, R. Soai, Y. Aiwacha and T. Mukayaima, *Bull. Chem. Soc. Jpn.*, 1976, 49.
25 (*a*) P. Duhamel, J. M. Poirier and G. Tavel, *Tetrahedron Lett.*, 1984, **25**, 43; (*b*) P. Duhamel, L. Hennequin, J. M. Poirier, G. Tavel and C. Vottero, *Tetrahedron*, 1986, **42**, 4777; (*c*) L. Hennequin, Ph.D. Thesis, University of Rouen (France), 1986; (*d*) J. M. Poirier and A. Deyine, unpublished work.
26 P. Duhamel, L. Hennequin, J. M. Poirier and N. Poirier, *Tetrahedron Lett.*, 1985, **26**, 6201.
27 G. Dujardin, Ph.D. Thesis, University of Rouen (France), 1990.
28 P. Cazeau, F. Duboudin, F. Moulines, O. Babot and J. Dunogues, *Tetrahedron*, 1983, **43**, 2075, 2089.
29 (*a*) I. Fleming and I. Paterson, *Synthesis*, 1979, 736; (*b*) R. D. Miller and D. R. McKean, *Synthesis*, 1979, 730; (*c*) M. E. Krafft and R. A. Holton, *Tetrahedron Lett.*, 1983, **24**, 1345 and *J. Org. Chem.*, 1984, **49**, 3669.
30 F. Johnson, *Chem. Rev.*, 1968, **68**, 375.
31 C. Nussbaumer, *Helv. Chim. Acta.*, 1990, **73**, 1621.
32 (*a*) J. A. Marshall and H. Roebke, *J. Org. Chem.*, 1968, **33**, 840; (*b*) B. J. M. Janssen, J. A. Kreuger and A. De Groot, *Tetrahedron*, 1989, **45**, 1447.
33 G. I. Birnbaum, A. Stoessl, S. H. Grover and J. B. Stothers, *Can. J. Chem.*, 1974, **52**, 993.
34 R. B. Kelly, J. A. Zamenick and B. A. Beckett, *Can. J. Chem.*, 1972, 3455.
35 H. J. Reich, E. K. Eisenhart, R. E. Olson and M. J. Kelly, *J. Am. Chem. Soc.*, 1986, **108**, 7791.
36 D. Seebach and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 654.
37 (*a*) D. Desmaeles, J. Ficini, G. Guinguant and A. M. Touzin, *Tetrahedron Lett.*, 1983, **24**, 3083; (*b*) D. Desmaeles, Ph.D. Thesis, University Pierre et Marie Curie, Paris, 1984.
38 (*a*) T. Sato, Y. Wakahara, J. Otera and H. Nozaki, *Tetrahedron Lett.*, 1990, **31**, 1581; (*b*) T. Kitahara, H. Kurata and K. Mori, *Tetrahedron*, 1988, **44**, 4339.
39 W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
40 E. W. Warnhoff, D. G. Martin and W. S. Johnson, *Org. Synth., Coll. Vol. IV*, 1963, 162.
41 W. F. Gannon and H. O. House, *Org. Synth.*, 1977, **40**, 41.
42 R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 1977, **99**, 483.
43 S. J. Alward and A. G. Fallis, *Can. J. Chem.*, 1984, **62**, 121.
44 E. Negishi, F. Luo, A. J. Pecora and A. Silveira Jr, *J. Org. Chem.*, 1983, **48**, 2427.
45 (*a*) W. M. B. Konst, J. G. Witteveen and H. Boelens, *Tetrahedron*, 1976, **32**, 1415; (*b*) G. Stork, A. Brizzolara, H. Landesman, J. Smuszkovic and R. Terell, *J. Am. Chem. Soc.*, 1963, **85**, 207.
46 H. Wu, H. Nakamura, J. Kobayashi, M. Kobayashi, Y. Ohizumi and Y. Hirata, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 2495.

Paper 1/03697A
Received 19*th July* 1991
Accepted 15*th October* 1991