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1,5-DICARBONYL COMPOUNDS

A GENERAL PREPARATION METHOD

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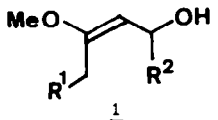
Abstract - In this report, a general method for the preparation of 1,5-dicarbonyl compounds and six membered ring annelation is described. This method involves the reaction of hemiacetal vinylogs 1 with enol ethers 2 or 3 in the presence of a Lewis acid. This reaction was successfully applied to the enol ethers of α and α,α'-hindered ketones such as 2,2,6-trimethyl cyclohexanone. α-Cyperone and 6-epi-α-cyperone were obtained using this process.

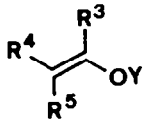
1,5-Dicarbonyl compounds[1,2] are an important class of building blocks for many natural substances such as terpenoids. Many modifications of the classical Robinson[3] and Wichterle[4] reactions have been proposed, involving in many cases multistep procedures.[5,6,7]

We describe in this report a new method for six membered ring annelation which involves the reaction of hemiacetal vinylogs 1 with enol ethers 2 or 3 in the presence of a Lewis acid. Some preliminary results were reported in a previous paper.[8] Reaction of non-functionalized allyl-alcohols with silyl enol ethers was previously described.[9]



1

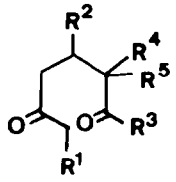
	R^1	R^2
1a	H	H
1b	Me	H
1c	Et	H
1d	H	Me



2 R^3 = alkyl
3 R^3 = H

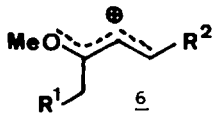
Y = $SiMe_3$, $SiMe_2tBu$, $SitBuPh_2$, Me

R^4,R^5 : see tables 1,2



4 R^3 = alkyl
5 R^3 = H

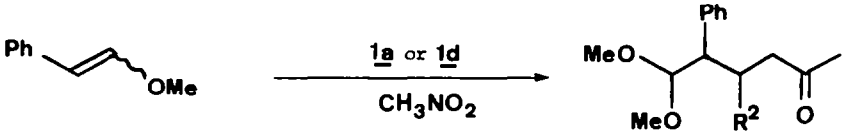
In the presence of boron trifluoride etherate,[10] hemiacetal vinylogs 1 generate the delocalized carbocation 6 which reacts rapidly with enol ethers 2 or 3 to yield 1,5-dicarbonyl compounds 4 or 5 (tables 1,2).[11]



6

The reaction may be carried at - 78 °C in dichloromethane (3 h) or at - 20 °C in nitromethane (1 h). Yields of 1,5-dicarbonyl compounds are generally better with nitromethane (tables 1, 2) as the solvent. In this solvent we observed that there was not as much cleavage of the starting silyl enol ether 2 or 3 (in the experimental conditions).

When the methyl enol ether 3i is used instead of the silyl enol ether 3h in nitromethane, the ketoacetal 7h is obtained quantitatively (scheme 1).



3i
Z/E : 80/20

7h R^2 = H : 100 %
7i R^2 = Me : 90 %

Scheme 1

Ketoacetals 7h,i are rapidly hydrolysed by acidic treatment into the corresponding keto-aldehydes 5h and 5i (table 2). The same reaction of enol ether 3i with 1a failed in dichloromethane. The use of alkyl enol ethers (instead of silyl enol ethers) does not always increase the yields. With alkyl enol ethers 2c and 2o lower yields are observed for 1,5- diketones 4b and 4n (table 1).[12]

When hemiacetal vinylogs with a primary allylic hydroxyle (1a-c, R^2 = H) are used, the yields of the reaction are better than for hemiacetal vinylog with a secondary allylic hydroxyle (1d, R^2 = Me) (table 1). This result is probably due to the higher steric hindrance of the reactional center of the secondary carbocation 6d.

In the literature, some 1,5-ketoaldehydes are described but are often obtained in poor yields.[13-19]

It is noteworthy that 1,5-diketones 4h and 4i are easily obtained in yields $\geqslant$ 50 % from silyl enol ethers 2h and 2i of hindered cyclohexanones (2,2,6-trimethylcyclohexanone and 2,6-dimethyl-cyclohexanone). These two diketones are important intermediates in the synthesis of natural compounds (ferruginol, numbiol[5]) but difficult to prepare because Michaël Robinson annulation of these α and α,α'-hindered cyclohexanones proceeds poorly.[5]

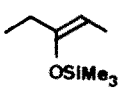
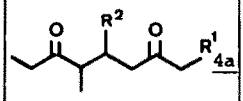
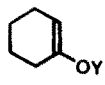
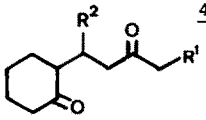
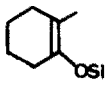
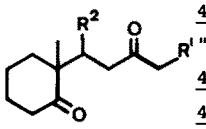
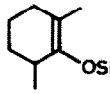
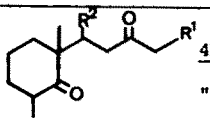
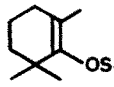
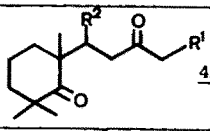
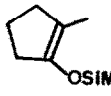
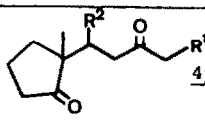
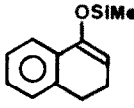
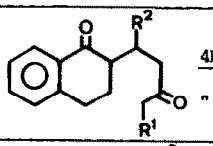
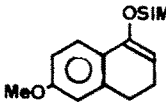
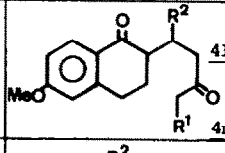
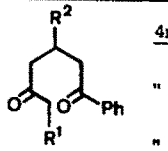
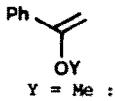
1,5-Diketones 4 were classically cyclized in ethanolic potassium hydroxyde medium[20] to give the corresponding cyclohexenones 8 in high yields (table 3) (scheme 2). A similar procedure applied to 1,5-ketoaldehydes 5 does not give the corresponding cyclohexenones 9 . However, in basic medium cyclohexenones 9 can be obtained in low yields using sodium methylate in methanol. Nevertheless, in acidic medium (scheme 2) satisfactory yields were obtained for the cyclization of ketoaldehydes 5 (R^3 = H) (table 4).

4 R^3 = alkyl, aryl KOH/EtOH 8

5 R^3 = H HCl 3M/Δ 9

Scheme 2

Table 1. 1,5-Diketones 4

Starting Materials		Reaction Conditions a	1,5-Diketones	R^1	R^2	Yields % b	Literature
 2a	1a	A	 4a	H	H	57	-
Y = $SiMe_3$: 2b 	1a	A	 4b	H	H	50	6, 20 , 21
Y = Et : 2c	1a	B	"	H	H	36	6, 20 , 21
 2d	1a	A	 4d	H	H	68 c	6, 18
	1a	B d	"	H	H	68	-
	1b	A	4e	Me	H	41	22
	1c	A	4f	Et	H	36	-
	1d	A	4g	H	Me	35	-
 2h	1a	A	 4h	H	H	55	6, 20
	1a	B d	"	H	H	65	6, 20
 2i	1a	B	 4i	H	H	50	23
 2j	1a	B d	 4j	H	H	70	24
 2k	1a	A	 4k	H	H	45	25
	1a	B d	"	H	H	56	25
 2l	1a	B d	 4l	H	H	72	-
	1d	B d	4m	H	Me	30	-
Y = $SiMe_3$: 2n	1a	A	 4n	H	H	48	26
	1a	B	"	H	H	40	26
Y = Me : 2o	1a	B	"	H	H	23	26

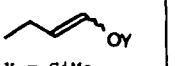
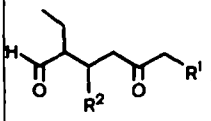
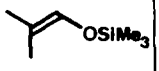
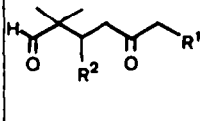
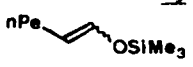
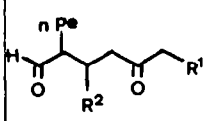
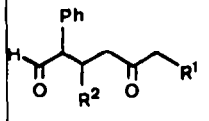
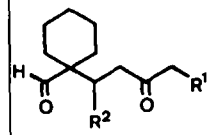
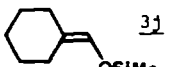
a : Ratio 2/1 : 1/1 unless otherwise noted. Method A : CH_2Cl_2, - 78 °C, 3 h; method B : CH_3NO_2, - 20 °C, 1 h.

b : Yield of product purified by flash chromatography unless otherwise noted.

c : Distilled compound.

d : Ratio 2/1 : 1.7/1

Table 2. 1,5 Ketoaldehydes 5

Starting Materials		Reaction Conditions *a*	1,5-Ketoaldehydes		R^1	R^2	Yields % *b*	Literature
 Y = $SiMe_3$ Z/E = 75/25 3a	1a	A		5a	H	H	48	-
	1a	B		"	H	H	40	-
Y = $SiMe_2tBu$; Z/E = 100/0 3b	1a	A		"	H	H	48	-
3c	1a	A		5c	H	H	66	9, 15, 17
	1a	B		"	H	H	44	9, 15, 17
	1b	A		5d	Me	H	30	9
	1c	A		5e	Et	H	41	-
	1d	B		5f	H	Me	31	16
3g	1a	A		5g	H	H	35	-
	1a	A [c]		"	H	H	54	-
Z/E = 90/10								
								
Y = $SiMe_3$; 3h	1a	A		5h	H	H	38	-
Z/E = 70/30	1a	A [c]		"	H	H	51	-
	1a	B		"	H	H	58	-
Y = Me 3i	1a	A		"	H	H	0	-
Z/E = 80/20	1a	B		"	H	H	95 [d]	-
	1d	B		5i	H	Me	80 [d]	-
3j	1a	A		5j	H	H	40	14
	1a	B		"	H	H	57	14

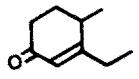
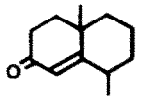
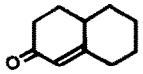
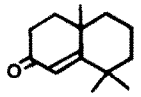
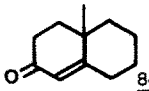
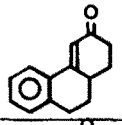
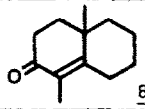
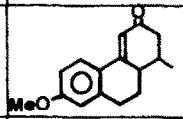
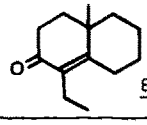
a : Ratio 3/1 : 1/1 unless otherwise noted. Method A : CH_2Cl_2, - 78 °C, 3 h; method B : CH_3NO_2, - 20 °C, 1 h.

b : Yields of product purified by flash chromatography based on starting silyl enol ether.

c : Ratio 3/1 : 1/1.6.

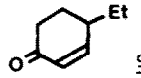
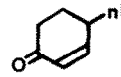
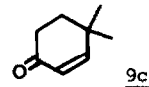
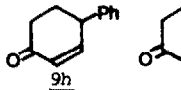
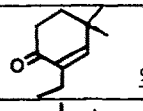
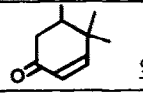
d : Obtained after hydrolysis of ketoacetals 7.

Table 3. Cyclohexenones 8 from 1,5-diketones 4

1,5-Diketones 4	Cyclohexenones 8	Lit.	Yields % a	1,5-Diketones 4	Cyclohexenones 8	Lit.	Yields % a
4a	 8a	27	65	4h	 8h	20, 28	86
4b	 8b	20	78	4i	 8i	23	73
4d	 8d	6,22	95	4k	 8k	25	85
4e	 8e	22	68	4m	 8m		69
4f	 8f		60				

a : Yield of product purified by flash chromatography based on the starting 1,5-diketone 4.

Table 4. Cyclohexenones 9 from 1,5-ketoaldehydes 5

Ketoaldehydes 5	Cyclohexenones 9	Lit.	Yields % a	Ketoaldehydes 5	Cyclohexenones 9	Lit.	Yields % a
5a	 9a	29	35	5g	 9g		60
5c	 9c	13, 30	71	5h	 9h 10		67 [c]
5e	 9e		74	5j	 9j	14	70
5f	 9f	31	26 [b]				

a : Yield of purified product (by flash chromatography) based on starting 1,5-ketoaldehyde 5 otherwise noted.

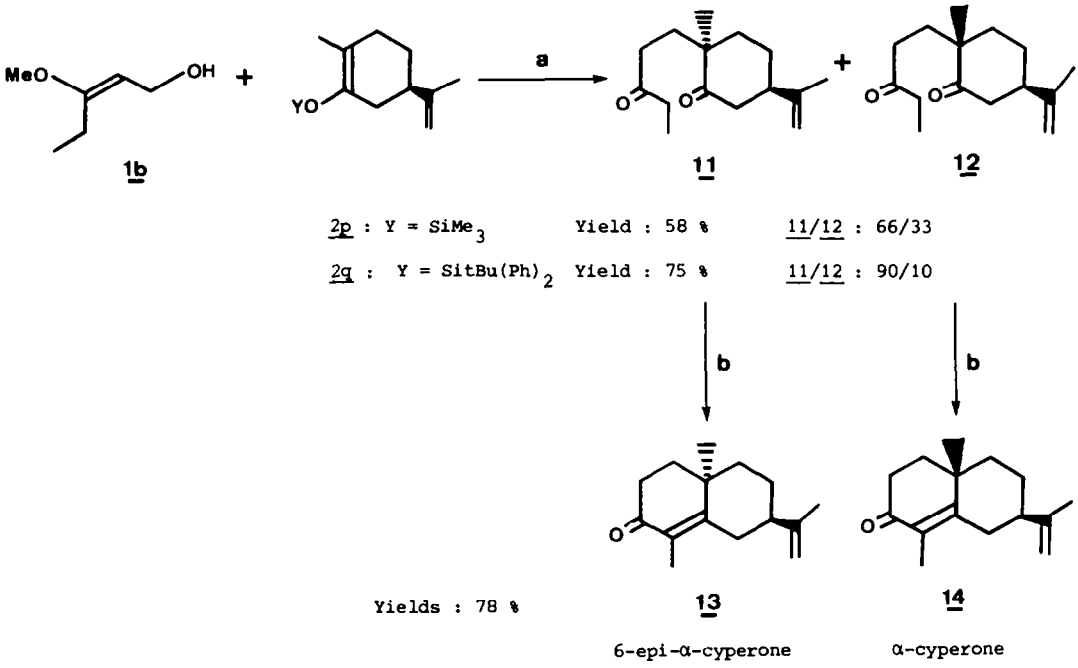
b : Yield of purified product based on the starting silyl enol ether without isolation of the intermediate 1,5-ketoaldehyde.

c : Total yield of separated products(9h : 20 %; 10 : 47 %). The cyclohexenone 10 is due to the conjugaison of the carbon-carbon double bond with the phenyl group.

Our interest in the field of natural compounds lead us to investigate, in a model sequence, a short synthesis of a D-homo-Nor-19 steroid[8] and of sesquiterpenes.

This process was thus applied to the synthesis of 6-épi-α-cyperone and α-cyperone (scheme 3). Starting from the hemiacetal vinylog 1b by reaction with the silyl enol ether 2p (prepared from (-) carvone), the corresponding 1,5-diketones 11 and 12 were obtained in good yields as a mixture.

With the enol ether 2q (Y = $SitBu(Ph)_2$), the reaction become more stereospecific (11/12 = 9/1). This result is due to the bulkiness of the tertbutyldiphenyl silyl group. By flash chromatography the diketone 12 was obtained in a pure form whereas the isomer 11 was always contaminated by a minor amount of diketone 12 .



a) BF_3,Et_2O 0.25 eq. , CH_3NO_2 - 20 °C, ratio 2/1 : 1/1.4, 1 h.

b) KOH, EtOH, 3 M, 25 °C.

Scheme 3

In basic medium, cyclization of the diketone 12 yields the corresponding α-cyperone 14. A minor by product was the intermediate hydroxyketone. This compound was easily separated (yield : 28 %) and dehydrated in acidic medium to give the corresponding cyclohexenone 14. Thus the total yield of the cyclization is 78 %. The same process was applied to the diketone 11 (contaminated by a minor amount of the diketone 12) and the 6-epi-α-cyperone 13 was prepared with the same total yield.

During this reaction, the optical activity of the starting (-) carvone was preserved.

We have described in this report a general preparation method for 1,5-dicarbonyl compounds with good yields from hemiacetal vinylogs 1 and enol ethers. This method is especially suitable for the synthesis of 1,5-diketones starting from hindered cyclohexanones such as 2,6-dimethyl and 2,2,6-trimethylcyclohexanone. 1,5 Diketones may be conveniently cyclized in basic medium whereas 1,5-ketoaldehydes require acidic medium to lead to the corresponding cyclohexenones. Using this method, 6-epi-α-cyperone and α-cyperone were prepared. Some other syntheses of natural compounds are in progress.

EXPERIMENTAL

^1H NMR spectra were recorded on a Perkin Elmer R 12 60 MHz.
^{13}C NMR were recorded on a Varian CFT 20. All chemical shifts are given in δ unit down field from internal tetramethylsilane in $CDCl_3$ solutions otherwise noted. I.R. spectra were obtained with a Perkin Elmer Infracord 277. Flash chromatography [32] was performed on silica gel (230 - 400 mesh) (Et_2O/petroleum ether). Nitromethane was dried on molecular sieves 4 Å and purified by distillation. Dichloromethane was purified by distillation on P_2O_5. The reaction progress is monitored by thin layer chromatography (ether/petroleum ether : 50/50).

Preparation of hemiacetal vinylogs 1a-d
The hemiacetal vinylogs 1a-d were prepared from the corresponding ketoesters by reaction of methylorthoformate [33] and the resulting enemethoxyesters were reduced by $LiAlH_4$. [34] The hemiacetal vinylog 1d with a secondary alcohol function (R^2 = Me) was prepared by the same reaction procedure from acetylacetone. [35] Analysis and spectral data of the compounds 1a, 1d are in good agreement with the literature. [33-35]

3-Methoxy-2-pentene-1-ol 1b
Yield : 75 %; bp : 75 °C/13 mmHg; IR : 1670 cm^{-1} (νC=C), 3350 cm^{-1} (νOH); NMR ^1H (CCl_4) : 1.05 (t, 3 H); 2.2 (q, 2 H); 3.1 (s, 1 H, OH); 3.5 (s, 3 H); 4.0 (d, 2 H); 4.55 (t, 1 H); NMR ^{13}C (C_6D_6) : 12.90 (q); 24.05 (t); 54.15 (q); 58.35 (t); 96.2 (d); 162.10 (s).

3-Methoxy-2-hexene-1-ol 1c
Yield : 87 %; bp : 83-86 °C/13 mmHg; IR : 1660 cm^{-1} (νC=C), 3350 cm^{-1} (νOH); NMR ^1H (CCl_4) : 0.9 (t, 3 H); 1.5 (m, 2 H); 2.15 (t, 2 H); 2.5 (s, 1 H, OH); 3.5 (s, 3 H); 4.0 (d, 2 H); 4.6 (t, 1 H); NMR ^{13}C (C_6D_6) : 13.85 (q); 21.50 (t); 32.60 (t); 54.05 (q); 58.45 (t); 97.20 (d); 160.40 (s).

Preparation of silyl enol ethers 2 from ketones
To a solution of 12.6 g of triethylamine (0.125 mol) and of 0.1 mol of ketone (table 1) was added 15.9 ml of chlorotrimethylsilane (0.125 mol) then 18.8 g of NaI (0.125 mol) in 130 ml of CH_3CN dropwise. The reaction mixture was stirred at 20 °C. The reaction progress was monitored by G.C. or T.L.C. (petroleum ether/ether : 50/50). Upon completion, the reaction mixture was diluted with pentane, filtered and the filtrate extracted with pentane (5 x 100 ml). For methylcycloalkanones, the more substituted double bond is obtained (>90 %). The extracts were evaporated under reduced pressure and the trimethylsilyl enol ether was distilled.

Preparation of silyl enol ethers 3 from aldehydes
To a solution of 18.8 g of NaI (0.125 mol) in 130 ml of CH_3CN was added 15.9 ml of chlorotrimethylsilane (0.125 mol) and 12.6 g (0.125 ml) of triethylamine. The solution was cooled to 10 °C and 0.1 mol of aldehyde (table 2) was added dropwise (temperature $\leq$ 10 °C). The reaction mixture was stirred for an additionnal 12 h at 20 °C. The reaction mixture was diluted with pentane, filtered and the filtrate extracted with pentane (5 x 100 ml). The combined extracts were evaporated under reduced pressure and the enol ether was distilled.
Analysis and spectral data of the silyl enol ethers 2b, 2d, 2j-l, 2n, 3c, 3h, prepared from ketones and aldehydes, are in good agreement with the literature. [36-39] Spectral data of unknown products are described below.

3-Trimethylsiloxy-2-pentene 2a
Yield : 55 %; bp : 132-134 °C/760 mmHg; IR : 1685 cm^{-1} (νC=C); NMR ^1H : 0.19 (s, 9 H); 1.02 (t, 3 H). 1.5 (m, 3 H); 2.0 (q, 2 H); 4.52 (q, 1 H).

2,6-Dimethyl-1-trimethylsiloxycyclohexene 2h
Yield : 93 %; bp : 86-88 °C/18 mmHg; IR : 1680 cm^{-1} (νC=C); NMR ^1H : 0.2 (s, 9 H); 1.0 (s, 3 H); 1.1 (s, 3 H); 1.5-2.3 (m, 6 H).

2,2,6-Trimethyl-1-trimethylsiloxycyclohexene 2i
IR : 1675 cm^{-1} (νC=C); NMR ^1H (C_6D_6) : 0.07 (s, 9 H); 0.92 (s, 6 H); 1.2-1.9 (m, 9 H); NMR ^{13}C (C_6D_6) : 1.2 (q); 18.0 (q); 20.0 (t); 27.8 (q); 31.95 (t); 35.4 (s); 40.35 (t); 109.6 (s); 150.4 (s).

1-Trimethylsiloxy-1-butene 3a
Yield : 47 %; bp : 113-115 °C/760 mmHg; IR : 1655 cm^{-1} (νC=C); NMR ^1H : isomer Z : 0.15 (s, 9 H); 0.9 (t, 3 H); 2.0 (q, 2 H); 4.3 (q, 1 H); 6.0 (dd, 1 H); isomer E : 0.05 (s, 9 H); 0.9 (t, 3 H); 1.9 (q, 2 H); 4.85 (q, 1 H); 6.1 (dd, 1 H).

1-Dimethyltertbutylsiloxy-1-butene 3b
Yield : 45 %; bp : 59-61 °C/16 mmHg; IR : 1660 cm^{-1} (νC=C); NMR ^1H (CCl_4) : 0.1 (s, 6 H); 0.95 (s, 9 H); 0.95 (t, 3 H); 2.0 (q, 2 H); 4;35 (q, 1 H); 6.1 (d, 1 H).

1-Trimethylsiloxy-1-heptene 3g
Yield : 40 %; bp : 72 °C/12 mmHg; IR : 1660 cm^{-1} (νC=C); NMR ^1H : isomer Z : 0.15 (s, 9 H); 0.9 (m, 3 H); 1.3 (m, 6 H); 2.05 (m, 2 H); 4.45 (q, 1 H); 6.1 (d, 1 H); isomer E : 0.15 (s, 9 H); 0.9 (m, 3 H); 1.3 (m, 6 H); 2.05 (m, 2 H); 4.95 (q, 1 H); 6.2 (d, 1 H).

1-Trimethylsiloxymethylenecyclohexane 3j
Yield : 53 %; bp : 87-90 °C/26 mmHg; IR : 1685 cm^{-1} (νC=C); NMR ^1H : 0.15 (s, 9 H); 1.3-1.7 (m, 6 H); 1.9 (m, 2 H); 2.2 (m, 2 H); 6,0 (s, 1 H).

Preparation of 1,5-dicarbonyl compounds 4 and 5
To a stirred solution of 5 mmol of silyl enol ether 2 or 3 in 5 ml of CH_3NO_2 (CH_2Cl_2) and 5 mmol of hemiacetal vinylog 1 (tables 1 and 2) in 5 ml of solvent cooled at - 20 °C (- 78 °C), was

added dropwise 0.2 ml of a solution of boron trifluoride etherate (0.25 eq.) and ether (volumic ratio $BF_3,Et_2O/Et_2O$: 4/1). The reaction mixture was stirred for 1 h (3h) at - 20 °C (- 78 °C) and then hydrolyzed at 0 °C (- 30 °C) with 5 ml of an aqueous saturated solution of $NaHCO_3$. The solution was stirred for 15 min at - 20 °C. The mixture was then extracted with 7 x 15 ml of CH_2Cl_2. Organic layers were dried ($MgSO_4$) and evapored. 1,5-Dicarbonyl compounds 4 or 5 were purified by flash chromatography[32] (ether/petroleum ether : 10/100) or distilled. For 1,5-dicarbonyl compounds 4b, d, e, h-k, n, 5c, d, f, j, see references in tables 1 and 2.

5-Methyl-2,6 octanedione 4a
bp : 85-88 °C/0.3 mmHg; IR : 1715 cm^{-1} (νC=O); NMR ^1H : 1.03 (t, 3 H); 1.1 (d, 3 H); 1.75 (m, 2 H); 2.12 (s, 3 H); 2.41 (t, 4 H); 3.2 (m, 1 H).

2-Methyl-2(3-oxo hexyl)cyclohexanone 4f
IR : 1720 cm^{-1} (νC=O); NMR ^1H : 0.9 (t, 3 H); 1.2 (q, 2 H); 1.5-2;0 (m, 8 H); 2.1-2.5 (m, 6 H); NMR ^{13}C : 13.75 (q); 17.3 (t); 21.05 (t); 22.6 (q); 27.45 (t); 31.2 (t); 37.4 (t); 38.75 (t); 39.6 (t); 44.75 (t); 47.85 (s); 210.08 (s); 214.9 (s).

2-Methyl-2(1-methyl-3-oxo butyl)cyclohexanone 4g
IR : 1705 cm^{-1} (νC=O); NMR ^1H : 0.9 (s, 3 H); 0.9 (d, 3 H); 1.15-2.8 (m, 11 H); 2.1 (s, 3 H).

6-Methoxy-2(3-oxo butyl) α-tetralone 4l
IR : 1680-1720 cm^{-1} (νC=O); NMR ^1H : 1.5-3.0 (m, 9H); 2.05 (s, 3H); 3.7 (s, 3H); 6.65 (m, 2H); 7.85 (d, 1 H); NMR ^{13}C : 23.5 (t); 28.3 (t); 28.4 (t); 29.3 (q); 40.65 (t); 45.7 (d); 54.8 (q); 111.85 (d); 112.65 (d); 125.4 (s); 129.07 (d); 145.8 (s); 162.9 (s); 197.97 (s); 208.0 (s).

6-Methoxy-2(1-methyl-3 oxo butyl) α-tetralone 4m
IR : 1600 cm^{-1} (νC=C); 1670-1705 cm^{-1} (νC=O); NMR ^1H : 0.85-0.95 (2 d, 3 H); 2.1 (s, 3 H); I.6-3.0 (m, 8 H); 3.8 (s, 3 H); 6.7 (m, 2 H); 7.9 (d, 1 H); NMR ^{13}C (C_6D_6) : 2 diastéréoisomères: 16.65; 17.1; 24.15; 25.33; 27.97; 28.85; 29.25; 29.75; 47.7; 48.25; 51.5; 52.2; 55.1; 112.75; 113.2; 129.9; 146.4; 163.55; 196.95; 206.6.

2-Ethyl-5-oxo-hexanal 5a
IR : 1720 cm^{-1} (νC=O); NMR ^1H : 1.25-1.9 (m, 2 H); 1.85 (q, 2 H); 2.15 (s, 3 H); 2.0-2.3 (m, 1 H); 2.45 (t, 2 H); 9.65 (d, 1 H); NMR^{13}C : 11.34 (q); 22.0 (2 t); 29.9 (q); 40.7 (t); 52.6 (d); 204.65 (d); 207.7 (s).

2,2-Dimethyl-5-oxo octanal 5e
IR : 1720 cm^{-1} (νC=O); NMR ^1H : 0.9 (t, 3 H); 1.0 (s, 6 H); 1.15-1.95 (m, 4 H); 2.1-2.55 (m, 4 H); 9.5 (s, 1 H).

2,2-3-Trimethyl-5-oxo hexanal 5f
IR : 1725 cm^{-1} (νC=O); NMR ^1H : 0.8-1.2 (m, 1 H); 0.9 (d, 3 H); 1.0 (s, 6 H); 2.15 (s, 3 H); 2.35 (d, 2 H); 9.5 (s, 1 H); NMR^{13}C : 14.85 (q); 18.1 (q); 18.9 (q); 30.35 (q); 32.65 (d); 45.9 (t); 48.4 (s); 205.7 (d); 207.2 (s).

2-n-pentyl-5-oxo hexanal 5g
IR ($CDCl_3$) : 1720 cm^{-1} (νC=O); NMR ^1H : 0.9 (m, 3 H); 1.0-1.95 (m, 8 H); 1.82 (q, 2 H); 2.15 (s, 3 H); 2.3-2.6 (m, 1 H); 2.95 (t, 2 H); 9.6 (d, 1 H); NMR ^{13}C : 14.0; 22.47 (2C); 26.7; 29.1; 29.95; 31.9; 40.75; 51.25; 204.7 (d); 207.75 (s).

2-Phenyl-5-oxo hexanal 5h
IR : 1725 cm^{-1} (νC=O); NMR ^1H : 2.02 (s, 3 H); 1.8-2.65 (m, 4 H); 3.35-3.7 (m, 1 H); 6.95-7.55 (m, 5 H); 9.7 (d, 1 H); NMR^{13}C : 23.56 (t); 29.9 (q); 40.5 (t); 57.9 (d); 127.85; 128.95; 129.25; 135.75 (s); 200.2 (d); 207.85 (s);
Anal.Calcd for $C_{12}H_{14}O_2$: C, 75.74; H, 7.4; Found : C, 75.4; H, 7.3.

3-Methyl-2-phenyl-5-oxo hexanal 5i
IR : 1715 cm^{-1} (νC=O)
2 diastereoisomers ratio 55/45
Major isomer : NMR ^1H : 1.05 (d, 3 H); 1.95 (s, 3 H); 2.25 (s, 2 H); 2.7-3.0 (m, 1 H); 3.45 (dd, 1 H); 7.15-7.55 (m, 5 H); 9.75 (d, 1 H); NMR^{13}C : 18.4 (q); 29.56 (q); 29.9 (d); 47.15 (t); 64.15 (d); 126.75; 127.8; 129.2; 129.65; 135.6 (s); 199.15 (d); 205.65 (s);
Minor isomer : NMR ^1H : 0.8 (d, 3 H); 2.1 (s, 3 H); 2.5 (d, 2 H); 2.7-3.0 (m, 1 H); 3.45 (dd, 1 H); 7.15-7.55 (m, 5 H); 9.72 (d, 1 H); NMR ^{13}C : 17.6 (q); 29.6 (q); 29.9 (d); 48.2 (t); 64.55 (d); 125.8; 127.4; 127.7; 129.9; 135.9 (s); 199.8 (d); 205.85 (s).

1,1-Dimethoxy-2-phenyl-5-hexanone 7h
IR : 1725 cm^{-1} (νC=O); NMR ^1H : 1.6-2.5 (m, 4 H); 2.05 (s, 3 H); 3.2 (s, 3 H); 3.4 (s, 3 H); 3.7 (d, 1 H); 4.5 (d, 1 H); 7.65-7.8 (m, 5 H); NMR ^{13}C (C_6D_6) : 24.75 (t); 28.95 (q); 40.5 (t); 47.9 (d); 53.4 (2 q); 107.55 (d); 126.2; 128.0; 128.45; 140.75 (s); 206.5 (s).

Cyclization in basic medium of the 1,5-diketones 4
To 6 mmol of 1,5-diketone 4 (table 3) was added 3.3 ml (0.65 ml/mmol) of KOH in EtOH (3 M). The solution was stirred 1 h at 20 °C and 10 ml of an aqueous saturated solution of NaCl was added. The mixture was then extracted with ether (7 x 20 ml). Organic layers were dried ($MgSO_4$) and evaporated. The cyclohexenones 8 were purified by flash chromatography[32] (Et_2O/petroleum ether : 10/100).
For spectral data and analysis of compounds 8a-e, h-k, see references in table 4.

10-Methyl-1-ethyl-2 octalone 8f
IR : 1610 cm^{-1} (νC=C); 1670 cm^{-1} (νC=O); NMR ^1H (CCl_4) : 0.8 (t, 3 H); 1.0 (q, 2 H); 1.2 (s, 3 H); 1.5-2.5 (m, 12 H); NMR ^{13}C : 14.2 (q); 18.3 (t); 21.65 (q); 22.65 (t); 27.4 (t); 29.8 (t); 34.15 (t); 36.25 (s); 37.9 (t); 42.3 (t); 134.95 (s); 162.6 (s); 198.55 (s).

7-Methoxy-1-methyl-1,2,3,9,10a-hexahydrophenanthrene-3-one 8m
IR : 1660 cm^{-1} (νC=O); 1590 cm^{-1} (νC=C); NMR ^1H : 1.15 (d, 3 H); 1.6-2.8 (m, 8 H); 3.7 (s, 3 H); 6.4-6.7 (m, 3 H); 7.6 (d, 1 H); NMR ^{13}C : 18.9 (q); 26.5 (t); 29.7 (t); 34.7 (d); 43.35 (d); 45.2 (t); 54.6 (q); 112.75 (2d, 2 c); 118.05 (d); 123.55 (s); 126.65 (d); 141.4 (s); 157.5 (s); 160.75 (s); 198.85 (s).

Cyclization of the 1,5-ketoaldehydes 5 in acidic medium
To 3 mmol of 1,5-ketoaldehyde 5 (table 4) was added 7.5 ml of an aqueous solution of HCl 3M. The vigourously stirred suspension was refluxed for 1 h and then cooled to room temperature. The mixture was then extracted with CH_2Cl_2 (5 x 15 ml). Organic layers were dried ($MgSO_4$) and evaporated. The cyclohexenones 9 were purified by flash chromatography.[32] Analysis and spectral data of the cyclohexenones 9a,c,f,j are in good agreement with the literature.[13,14, 29,30,31]

Cyclization of the 1,5-ketoaldehydes 5 in basic medium
To 12 mmol of MeONa in 5 ml of MeOH cooled at 0, - 5 °C was added a solution of 2 mmol (0.28 g) of ketoaldehyde 5c (table 4) in 2 ml of MeOH. The solution was stirred 1 h at 20 °C. 10 ml of a 10 % aqueous solution of HCl were then added. The mixture was then extracted with CH_2Cl_2 (4 x 10 ml). Organic layers were dried ($MgSO_4$) and evaporated. The cyclohexenone 9c was purified by flash chromatography.[32] Yield of cyclohexenone 9c : 54 %.

Spectral data of cyclohexenones 9 and 10 :

4,4-Dimethyl-2-ethyl-2-cyclohexen-1 one 9e
IR 1665 cm^{-1} (broad, νC=C; νC=O); NMR ^1H : 0.9 (t, 3 H); 1.05 (s, 6 H); 1.75 (t, 2 H); 2.1 (q, 2H); 2.35 (t, 2 H); 6.35 (s, 1 H); NMR ^{13}C : 12.95 (q); 22.45 (t); 28.15 (2 q); 32.8 (s); 34.8 (t); 36.35 (t); 138.2 (s); 153.3 (d); 198.98 (s).

4-n-pentyl-2-cyclohexen-1 one 9g
IR : 1675 cm^{-1} (broad, νC=C; νC=O); NMR ^1H (C_6D_6) : 0.4-1.6 (m, 13 H); 1.7-2.4 (m, 3 H); 5.88 (q, 1 H); 6.85 (d, 1 H); NMR ^{13}C : 14.2 (q); 22.85; 26.7; 28.65; 32.05; 34.65; 36.05; 37.05; 115.75 (d); 154.35 (d); 198.55 (s).

4-Phenyl-2-cyclohexen-1 one 9h
IR : 1690 cm^{-1} (νC=O; νC=C); NMR ^1H : 0.85 (t, 2 H); 3.05 (q, 2 H); 5.9 (q, 1 H); 6.5-7.3 (m, 6 H).

4-Phenyl-3-cyclohexen-1 one 10
IR : 1685 cm^{-1} (νC=C); 1720 cm^{-1} (νC=O); NMR ^1H : 0.7-1.45 (m, 2 H); 2.25 (m, 2 H); 2.7 (m, 2 H); 6.05 (t, 1 H); 7.35 (m, 5 H); NMR ^{13}C : 27.85 (t); 38.6 (t); 39.85 (t); 120.9 (d); 125.2; 127.35; 128.4; 137.7; 140.75 (s); 209.65 (s).

α-Cyperone 14 and 6-α-epi-cyperone 13[40]
The silyl enol ether 2p was prepared from dihydrocarvone (prepared by reduction with Li/NH_3 liquid of carvone[41]), using the process described before.
In the case of the silyl enol ether 2q, tertbutyldiphenyl silyl chloride was used instead of trimethyl silyl chloride, and commercially available dihydrocarvone (Aldrich).

2-Methyl-5-(1-methyl ethenyl)-1-trimethylsiloxycyclohexene 2p from carvone
Yield : 68 % ; bp : 59-60 °C/0.4 mmHg; IR : 1690 cm^{-1} (νC=C); NMR ^1H : 0.2 (s, 9 H); 1.55 (s, 3 H); 1.75 (s, 3 H); 1.6-2.5 (m, 7 H); 4.7 (s, 2 H).

2-Methyl-5-(1-methyl ethenyl)-1-tertbutyldiphenylsiloxycyclohexene 2q from dihydrocarvone
Yield : 80 %; IR : 1650-1695 cm^{-1} (νC=C); NMR ^1H (CCl_4) : 1.1 (s, 9 H); 1.25-2.0 (m, 10 H); 1.45 (s, 3 H); 4.5 (d, 2 H); 7.2-7.8 (m, 10 H); NMR ^{13}C : 16.2; 19.3; 20.45; 26.75; 27.55; 30.15; 35.55; 42.05; 108.45; 110.0; 127.35; 129.45; 134.4; 135.2; 142.95; 148.25.

Diketones 11 and 12
The 1,5-diketones 11 and 12 were prepared from the reaction of the hemiacetal vinylog 1b with the silyl enol ethers 2p or 2q using the process described above. When the reaction occured with the silyl enol ether 2p, the two diketones 11 and 12 were separated by flash chromatography (Et_2O/petroleum ether : 5/100). After three successive chromatographies, two fractions are obtained : 12 pure and 11 + 12.
2-Methyl-2-(3-oxo pentyl)-5-(1-methyl ethenyl) 11 and 12

Isomer 11 - IR : 1640 cm^{-1} (νC=C); 1705 cm^{-1} (νC=O); NMR ^1H : 1.0 (s, 3 H); 1.0 (t, 2 H); 1.5-2.7 (m, 15 H); 1.75 (s, 3 H); 4.75 (s, 2 H); NMR ^{13}C : 7.7; 20.55; 23.0; 25.7; 31.5; 35.7; 36.5; 37.2; 43.1; 45.55; 46.8; 109.95; 147.09; 211.3; 214.65.
$(\alpha)_D^{25°C}$ = + 30.41° (c = 1.8; dioxanne) (contaminated by a minor amount of 12, ratio 11/12 : 9/1).

Isomer 12 - IR : 1645 cm^{-1} (νC=C); 1705 cm^{-1} (νC=O); NMR ^1H : 1.05 (s, 3 H); 1.0 (t, 2 H); 1.5-2.7 (m, 15 H); 1.75 (s, 3 H); 4.75 (s, 2 H); NMR ^{13}C : 7;9; 20.55; 22.35; 26.3; 30.9; 35.7; 36.65; 38.7; 43.55; 46.3; 47.15; 109.9; 147.8; 208.65; 212.6.
$(\alpha)_D^{25°C}$ = + 77.02° (c = 1.98; dioxanne).

α-Cyperone 14 and 6-epi-α-cyperone 13 were obtained by cyclization in basic medium (as described above) of the corresponding 1,5-diketones 12 and 11.

α-Cyperone 14[40,43]
IR : 1610-1660 cm^{-1} (νC=C); NMR ^1H (CCl_4) : 1.25 (s, 3 H); 1.7 (s, 6 H); 1.3-2.75 (m, 11 H); 4.8 (s, 2 H); NMR ^{13}C : 10.9; 20.6; 22.58; 26.95; 32.95; 33.9; 35.9; 37.65; 42.0; 46.0; 109.3; 128.75; 148.85; 161.57; 198.3.
$(\alpha)_D^{20,5°C}$ = + 71.22° (c = 1.425; $CHCl_3$); (Lit.[43] $(\alpha)_D$ = 81° (c = 0,078, dioxanne)).

6-epi-α-cyperone 13 [40,43,44] (from mixture 13/14 : 9/1)

IR : 1610 cm^{-1} (νC=C), 1670 cm^{-1} (νC=O); NMR ^1H : 1.25 (s, 3 H); 1.75 (s, 3 H); 1.85 (s, 3 H); 1.3-2.75 (m, 11 H); 4.65 (s, 1 H); 4.85 (s, 1 H); NMR ^{13}C : 10.9; 22.6; 23.1 (2 c); 31.1; 33.9; 35.9 (2 c); 37.65; 41.0; 111.0; 129.05; 147.25; 161.6; 197.9.

$[\alpha]_D^{20.5°C}$ = -148.1° (C = 2.3; $CHCl_3$) (13 / 14 : 9/1); (Lit.[44] $[\alpha]_D^{20°C}$ = -192° (C = 1.7; $CHCl_3$; 13 pure).

REFERENCES

1) a - R. E. GAWLEY, Synthesis 1976, 777; b - M. E. JUNG, Tetrahedron 1976, 32, 3.
2) H. C. BROWN, U. S. RACHERLA and S. M. SINGH, Synthesis 1984, 922.
3) W. S. RAPSON and R. ROBINSON, J. Chem. Soc. 1935, 1285.
4) D. WICHTERLE, J. PROCHANKA and J. HOFFMAN, Coll. Czech. Chem. Comm. 1948, 13, 300.
5) W. L. MAYER, G. B. CLEMANS and R. A. MANNING, J. Org. Chem. 1975, 40, 3686.
6) J. A. MARSHALL and W. I. FANTA, J. Org. Chem. 1964, 29, 2501.
7) D. CAINE and F. N. TULLER, J. Org. Chem. 1969, 34, 222.
8) P. DUHAMEL, J. M. POIRIER and G. TAVEL, Tetrahedron Letters 1984, 25, 43.
9) a - M. T. REETZ, S. HÜTTENHAIN and F. HÜBNER, Synth. Comm. 1981, 11, 217;
b - S. DJURIC, T. SARKAR and P. MAGNUS, J. Am. Chem. Soc. 1980, 102, 6885.
10) The use of some other Lewis acids ($ZnCl_2$, $ZnBr_2$, $TiCl_4$, Montmorillonite K 10) did not increase the yield.
11) Reaction was monitored by TLC. No intermediate species have been detected for the compounds of tables 1 and 2.
12) Fluctuating yields in C-C bond formation with alkyl and silyl enol ethers may be due to on equilibrium reaction with alkyl enol ethers, that is not the case for the silyl derivatives because of irreversible desilylation. We acknowledge the referee for this valuable suggestion.
13) T. MIYAKOSHI, H. OMICHI and S. SAITO, Nippon Kagaku Kaishi 1979, 6, 748.
14) H. CHRISTOL, F. PLENAT and J. SALANCON, Bull. Soc. Chim. France 1970, 4468
15) I. FLEMING and M. H. KARGER, J. Chem. Soc. (C) 1967, 226.
16) K. L. COOK and A. J. WARING, J. Chem. Soc. Perkin, Trans I, 1973, 529.
17) M. PFAU, J. UGHETTO MONFRIN and M. JOULLAIN, Bull. Soc. Chim. France 1979, II-627.
18) J. COLONGE, J. DREUX and M. THIERS, Bull. Soc. Chim. France 1959, 370.
19) S. W. BALDWIN, R. E. GAWLEY, R. J. DOLL and K. H. LEUNG, J. Org. Chem. 1975, 40, 1865.
20) J. A. MARSHALL and D. J. SCHAEFFER, J. Org. Chem. 1965, 30, 3642.
21) M. LARCHEVEQUE, G. VALETTE and T. CUVIGNY, Synthesis 1977, 424.
22) F. E. ZIEGLER and K. J. HWANG, J. Org. Chem. 1983, 48, 3349.
23) M. JULIA and B. MALASSINE, Tetrahedron 1974, 30, 695.
24) H. L. BROWN, G. L. BUCHANON, A. C. W. CURRAN and G. W. Mc LAY, Tetrahedron 1968, 24, 4565.
25) E. BROWN, J. TOUET and M. RAGAULT, Bull. Soc. Chim. France 1972, 212.
26) K. NARASAKA, K. SOAI, Y. AIKAWA and T. MUKAIYAMA, Bull. Chem. Soc. Japan 1976, 49, 779.
27) A. PONS, J. C. MILHAVET and J. P. CHAPAT, Bull. Soc. Chim. France 1979, 381.
28) B. MAURER, M. FRACHEBOUD, A. GRIEDER and G. OHLOFF, Helvetica Chim. Act. 1972, 55, 2371.
29) H. RIVIERE and T. TOSTAIN, Bull. Soc. Chim. France 1969, 568.
30) H. O. KRABBENHOFT, J. Org. Chem. 1979, 44, 4050.
31) M. E. FLAUGH, T. A. CROWELL and D. S. FARLOW, J. Org. Chem. 1980, 45, 5399.
32) W. C. STILL, M. KAHN and A. MITRA, J. Org. Chem. 1978, 43, 2923.
33) E. SMISSMANN and A. NELSON-VOLDENG, J. Org. Chem. 1964, 29, 3161.
34) R. MOLLER, N. ENGEL and W. STEGLICH, Synthesis 1978, 620.
35) R. E. IRELAND, S. THAISRIVONGS, N. VANIER and C. S. WILCOX, J. Org. Chem. 1980, 45, 48.
36) For a recent review, see P. BROWNBRIDGE, Synthesis 1983, 1.
37) P. CAZEAU, F. MOULINES, O. LAPORTE and F. DUBOUDIN, J. Organometal. Chem. 1980, 201, C9.
38) H. EMDE, A. GÖTZ, K. HOFMANN and G. SIMCHEN, Liebigs Ann. Chem. 1981, 1643.
39) H. O. HOUSE, L. J. CZUBA, M. GALL and H. D. OLMSTEAD, J. Org. Chem. 1969, 2324.
40) J. W. HUFFMAN, W. E. SWAIN, J. JACOBUS and A. T. Mc PHAIL, J. Org. Chem. 1980, 45, 3088.
41) Purchased from ALDRICH $[\alpha]_D^{20}$ = - 58° (neat) (Lit.[42] : $[\alpha]_D^{25}$ = - 62.21°).
42) M. H. SHASTRI, D. G. PATIL, V. D. PATIL and D. SUKH, Tetrahedron 1985, 41, 3083.
43) C. DJERASSI, R. RINIKER and B. RINIKER, J. Am. Chem. Soc. 1956, 78, 6362.
44) T. G. MALSALL, D. W. THEOBALD and K. B. WALSHAW, J. Chem. Soc. 1964, 1029.