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CYCLOPENTANOIDS FROM PHENOL—9[1]

3-ALKYL- AND 3-ALKENYL-5-HYDROXYCYCLOPENT-2-ENONES

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Abstract—An efficient and versatile synthesis of 3-alkyl- and 3-alkenyl-5-hydroxycyclopent-2-enones is described. The key intermediate, 4-(t-butyldimethylsilyloxy)-3-methoxycyclopent-2-enone (**5**), is prepared in five steps from phenol. 1,2-Addition of various organolithium and Grignard reagents yields tertiary alcohol intermediates which afford the title compounds after solvolysis and desilylation.

4-Hydroxycyclopent-2-enone[2] and various 2-alkyl- and 3-alkyl-substituted 4-hydroxycyclopent-2-enones[1,3-7] have been efficiently synthesised in racemic and enantiomerically pure forms from the t-butyldimethylsilyl ether (**1**) of 3-chloro-4-hydroxycyclopent-2-enone. This chloro-enone intermediate **1** is readily available from ring contraction of phenol, via the resolvable[1,3,7] acid **4**[8], the trichloro-enone **2**[9] and the monochloro-enone **3**,[4] and reacts with organic[4,5] and stannyl[6] cuprate reagents by 1,4-addition-elimination processes. In this paper we describe the preparation from the trichloro-enone **2** of the t-butyldimethylsilyl ether (**5**) of 4-hydroxy-3-methoxycyclopent-2-enone, which reacts with various Grignard and organolithium reagents exclusively by 1,2-addition. Solvolysis of the resulting tertiary alcohol intermediates followed by desilylation then leads under mild conditions to 3-alkyl- and 3-alkenyl-substituted 5-hydroxycyclopent-2-enones (e.g. **14b–21b**). The route is efficient and versatile, and by use of the resolved acid **4**[1,3,7] can be applied to chiral materials if required. 3-Alkyl-5-hydroxycyclopent-2-enones have been prepared previously by acetoxylation[10,11] of 3-substituted cyclopentenones[12] followed by ester hydrolysis,[11] an approach which affords only racemic products and in which the nature of the 3-substituent is limited by the vigorous reaction conditions involved.

Synthesis of 4-(*t-butyldimethylsilyloxy*)-3-*methoxycyclopent-2-enone* (**5**)

Treatment of the trichloro-enone **2** with Zn (2 equiv) in methanol[13] at 0° for 7 h afforded 5,5-dichloro-4-hydroxy-3-methoxy-cyclopent-2-enone (**6**) in 88% yield. The reaction does not proceed in the absence of Zn, and may be due to the formation of zinc methoxide.[14] t-Butyldimethylsilylation[15] (97%) followed by dechlorination (96%) of the resulting silyl ether **7** with chromous chloride gave the methoxy-enone **5** efficiently in 84% overall yield from the acid **4**.

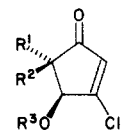
We examined the possibility of a direct conversion of the trichloro-enone **2** to the methoxy-enone **8**, since Zn in methanol is known[9] to be capable of reducing the *gem*-dichloro group in addition to displacing the vinylic halogen. However, reaction at room temperature over 2.5 h produced a mixture of four cyclopentenones from which the desired methoxy-enone **8** could only be separated as a minor component (5%), the major product (44%) being its *trans*-monochloro derivative **9**. All four products were unstable as the free alcohols, and their separation and characterization were facilitated by t-butyldimethylsilylation of the mixture. Chromatography then yielded the methoxy-enone **5** (6%), its *trans*- and *cis*-monochloro derivatives **10** (40%) and **11** (3%), and the imidazolyl-enone **13** (11%). These ethers arise from the alcohols **8**, **9**, **12** and **3**, respectively, the chloro-enone **3** being known[4] to suffer displacement of halogen by imidazole under silylation conditions.

The relative configuration of the isomeric enones **10** and **11** follows from their ^{1}H NMR spectra, the *trans*-related protons in **10** being more weakly coupled (J = 2.7 Hz) than the *cis* protons in **11** (J = 6.0 Hz).[16] Dechlorination with chromous chloride afforded in each case the same methoxy-enone **5** (98%). Formation of the *trans*-enone **9** predominated over that of the *cis*-enone **12** in all experiments, and their combined yields could be increased to 71% by strict control of the Zn-methanol treatment of the trichloro-enone **2**. However, all attempts to increase the yield of the desired fully dechlorinated methoxy-enone **8**, by use of additional Zn, elevated temperature or extended reaction times were unsuccessful, and only diminished the recovery of material.

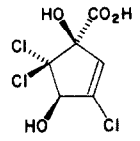
The distribution of products in these Zn-methanol reactions reflects the relative rates of conjugate addition to C-3 and reduction at C-5 in the starting trichloro-enone **2** and in the various intermediates which are formed. At 0°, reduction of **2** is slow and conjugate addition predominates, affording in high yield the vinylogous ester **6** which is reduced even more slowly. At room temperature, reduction of **2** competes with conjugate addition; subsequent addition or reduction is then electronically retarded, and the observed product mixture results.

Reaction of the methoxy-enone **5** *with organometallic reagents*

4-(t-Butyldimethylsilyloxy)-3-methoxycyclopent-2-enone (**5**) reacted with a variety of saturated and unsaturated organolithium and Grignard reagents[17] to give after work-up under mildly acidic conditions the 3-substituted 5-(t-butyldimethylsilyloxy)cyclopent-2-enones **14a–21a** in high yields (Table 1). Treatment of the silyl ethers with dilute acetic acid afforded the free 3-substituted 5-hydroxycyclopent-2-enones **14b–21b**. The route permits ready synthetic access to such compounds, including representatives with labile substituents (e.g.



	R¹	R²	R³
1:	H	H	Bu^tMe_2Si
2:	Cl	Cl	H
3:	H	H	H



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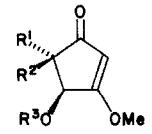
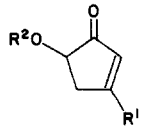
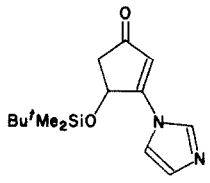


	R¹	R²	R³
5:	H	H	Bu^tMe_2Si
6:	Cl	Cl	H
7:	Cl	Cl	Bu^tMe_2Si
8:	H	H	H
9:	Cl	H	H
10:	Cl	H	Bu^tMe_2Si
11:	H	Cl	Bu^tMe_2Si
12:	H	Cl	H



	R¹
14:	CH_2=CH
15:	Me
16:	*n*-Bu
17:	*i*-Pr
18:	*t*-Bu
19:	$PhCH_2$
20:	CH_2=$CHCH_2$
21:	*n*-Pr
22:	H

	R²
a:	Bu^tMe_2Si
b:	H



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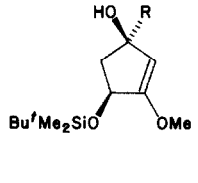

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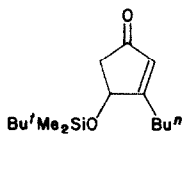

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14a, **20a**) which would be inacceseible by the previous acetoxylation route.[10,11]

The initial products of the organometallic addition reaction are probably labile tertiary alcohols[18] of the type **23**, which undergo subsequent solvolysis assisted by the OMe group. Only in the reaction with 1-lithio-3-(trimethylsilyl)prop-2-yne was this species **23** ($R=Me_3SiC{\equiv}C{-}CH_2$) isolated (70%). In this case the expected cyclopentenone solvolysis product could not be detected in the ^1H NMR spectrum of the crude mixture, while more severe acidic treatment of the alcohol resulted in decomposition. The alcohol **23** ($R=Me_3SiC{\equiv}C{-}CH_2$) was a single diastereoisomer, which was assigned the *cis*-diol configuration by analogy with the direction of 1,2-addition to 4-(t-butyldimethylsilyloxy)-3-chlorocyclopent-2-enones.[3-7]

The methoxy-enone **5** was recovered (*ca* 80%) after exposure to lithium dibutylcuprate or to butylmagnesium bromide in the presence of a stoichiometric amount of cuprous iodide, and no 3-butyl-4-(t-butyldimethylsilyloxy)cyclopent-2-enone[4] or 3,3-dibutyl-4-(t-butyldimethylsilyloxy)cyclopentanone[4] was formed. These results support the prediction[19] and evidence[19,20] that the reduction potential of β-alkoxy-enones is not appropriate for the conjugate addition of cuprate species. Reports to the contrary[21,22] probably reflect the presence of *free* alkyl-Li reagents[23] which react via 1,2-addition followed by solvolysis, as in the present work.

Reduction of the methoxy-enone **5**

Reduction of the methoxy-enone **5** with sodium di-(2-methoxyethoxy)aluminium hydride[24] gave a single relatively stable secondary alcohol, shown by ^1H NMR to be the expected[3-7] *cis*-diastereoisomer **23** (R=H). Subsequent treatment with oxalic acid-sodium oxalate in chloroform (to avoid cleavage of the silyl ether) afforded 5-(t-butyl-dimethylsilyloxy)cyclopent-2-enone (**22a**) in 74% yield overall. 5-Hydroxycyclopent-2-enone itself

Table 1. Yields, IR and analytical data for 5-hydroxycyclopent-2-enones **14–21** prepared from methoxy-enone **5** with organometallic reagents

R' in 14-21	Reagent Type	Product Ether	Yield[a] %	$\nu_{C=O}$[b] cm^{-1}	ANALYTICAL DATA Found % C	Found % H	Calculated % C	Calculated % H	Product Alcohol	Yield[a] %	$\nu_{C=O}$[b] cm^{-1}	ANALYTICAL DATA Found % C	Found % H	Calculated % C	Calculated % H
$CH=CH_2$	Li	14a	96	1710	65.7	9.3	65.5	9.3	14b	16	1705	[d]			
Me	Li	15a	99	1720	63.9	9.75	63.65	9.8	15b	52	1715	[e]			
n-Bu	Li or Mg	16a	90	1720	67.25	10.3	67.1	10.5	16b	84	1710	69.9	8.9	70.1	9.15
i-Pr	Li	17a	40[c]	1720	66.4	10.25	66.1	10.3	17b	43	1705	68.25	8.45	68.55	8.65
t-Bu	Li	18a	88	1715	67.0	10.25	67.1	10.5	18b	68	1695	70.3	9.05	70.1	9.15
CH_2Ph	Mg	19a	88	1720	71.25	8.65	71.45	8.65	19b	83	1700	76.4	6.2	76.55	6.45
$CH_2CH=CH_2$	Mg	20a	74	1720	66.85	9.6	66.6	9.6	20b	71	1700	69.65	7.15	69.55	7.3
n-Pr	Mg	21a	79	1720	66.15	10.05	66.1	10.3	21b	68	1700	68.75	8.55	68.55	8.65

[a] Refers to yield of purified material.

[b] I.r. data refer to liquid films, except for 18b which was run as a KBr disc.

[c] The product 17a was accompanied by a substantial amount of 3-(2,3-dimethylbutyl)-5-(t-butyldimethylsilyloxy)cyclopent-2-enone. The commercial isopropyl-lithium reagent was shown by independent experiment to contain quantities of 2,3-dimethylbutyl-lithium, formed presumably by generation of propene and subsequent reaction with isopropyl-lithium.

[d] Found M^+ m/z 124.0522. $C_7H_8O_2$ requires m/z 124.0524.

[e] Prepared previously by Gowda and McMurry.[11]

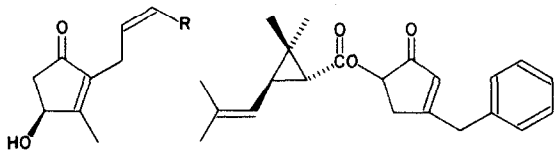
(**22b**) has previously been prepared in only 6% yield *via* acetoxylation of cyclopent-2-enone and subsequent hydrolysis.[10,11]

NMR spectra of 5-hydroxycyclopent-2-enones

^{1}H NMR data (Table 2) for the 5-hydroxy cyclopent-2-enones **14a–22a** are in full accord[16] with the assigned substitution pattern.† Thus the spectrum of the 3-methylcyclopentenone **15a** shows the olefinic proton at δ 5.89 as a six line signal, identified by decoupling as a triplet of quartets ($J_t = J_q = 1.5$ Hz) due to interaction with the protons of both the Me substituent and the 4-methylene group. The methylene protons themselves, centered at δ 2.88 and 2.44, form the AB portion of an ABX system with the 5-methine proton at δ 4.25 ($J_{trans} = ca$ 3 Hz, $J_{cis} = ca$ 6 Hz), and each is further coupled not only with the olefinic proton ($J = 1.5$ Hz) but also through four bonds ($J = 1.5$ Hz) to the Me protons.

^{1}H NMR is the only convenient spectroscopic method for unambiguously distinguishing 3-substituted 5-hydroxycyclopent-2-enones from their 4-OH isomers.[4] The shift and multiplicity of the alcoholic methine proton resonance is particularly diagnostic. For example, this proton (H-5) in the 3-butyl-5-hydroxycyclopentenone derivative **16a** appears at δ 4.23 as a sharp doublet of doublets. The corresponding proton (H-4) in the 3-butyl-4-hydroxycyclopentenone derivative **24**, however, resonates at lower field, δ 4.78, and the fourline pattern resulting from its coupling with the adjacent methylene group is broadened by unresolved long range coupling to the olefinic and butyl methylene protons.

^{13}C NMR spectra of these 3-alkyl-5-hydroxycyclopent-2-enones, assigned on the basis of chemical shifts and signal multiplicity (Table 3), are very similar to spectra of their 4-OH isomers.[4] Thus even the C-4 (41.3, t) and C-5 (73.0, d) resonances of the 3-butyl-5-hydroxycyclopentenone derivative **16a** resemble the C-5 (45.8, t) and C-4 (72.1, d) signals of its isomer **24**,[4] while the other ring and side chain resonances show the expected similarities.



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3-Benzyl-5-hydrocyclopent-2-enone (+)-chrysanthemate (**26**)

The pyrethrins, insecticidal constituents of pyrethrum flowers, are (+)-chrysanthemate or (+)-pyrethrate esters of 4-hydroxycyclopent-2-enones of type **25** (R=Me, Et, CH=CH$_2$).[26] Extensive structure-activity relationship studies of natural and synthetic pyrethroids[27] indicated that (+)-chrysanthemate esters of hitherto unavailable 5-hydroxycyclopent-2-enones such as **19b** and **20b** might show significant insecticidal activity.[28] Accordingly, in collaboration with Dr. M. Elliott of Rothamsted Experimental Station, Harpenden, U.K., the (±)-3-benzyl-5-hydroxycyclopent-2-enone (**19b**) was esterified with (+)-*trans*-chrysanthemoyl chloride and the resulting mixture of two diastereoisomeric chrysanthemates **26** was tested for insecticidal activity. Surprisingly, the product **26** proved to be non-toxic to houseflies and mustard beetles.

†The structure **18b** has previously been tentively assigned to an impure ring contraction product of 5-t-butylpyrogallol.[25] However, the published melting point (115–119°) and ^{1}H NMR data do not agree with those of material (m.p. 68.5–69.5°) prepared by the present route, and the earlier assignment[25] must be incorrect.

EXPERIMENTAL

General details are as given in Part IV,[4] except for GLC analysis which was performed on a Perkin–Elmer 900 chromatograph with a 72 × 1/16 in. internal diameter glass column containing 2% OV-17.

Materials. These are described in Part IV,[4] in addition to the following. Ethereal solvents were distilled from sodium benzophenone ketyl prior to use. MeOH was dried over molecular sieves (3 Å), distilled, and stored over sieves (3 Å). Mg turnings and Zn powder were used as purchased. Organolithiums were commercial solns in hexane (n-BuLi), hexane/pentane (t-BuLi), pentane (i-PrLi) and ether (MeLi, vinyl-Li). The preparation of **2** has been described previously.[9]

5,5-Dichloro-4-hydroxy-3-methoxycyclopent-2-enone (**6**)

Zn power (0.65 g, 10 mmol) was added with stirring to **2** (1 g, 5 mmol) in MeOH (75 ml) at 0°. After 7 h at this temp. the mixture was filtered and the residue washed with chilled MeOH (4 × 75 ml). Upon evaporation of the filtrate, the residue was extracted with CH_2Cl_2 (6 × 200 ml) and the extracts were dried ($MgSO_4$) and evaporated. Distillation of the residual oil (b.p. 80°/0.01 mmHg) gave **6** (870 mg, 88% yield), m.p. 85–88° (Found: C, 36.8; H, 2.9; Cl, 35.9. $C_6H_6Cl_2O_3$ requires: C, 36.6; H, 3.05; Cl, 36.0%); IR ν_{max}(KBr) 3400, 1720 cm^{-1}; NMR δ(CDCl$_3$) 5.40 (s, 1H, H-2), 4.98 (s, 1H, H-4), 3.96 (s, 3H, OMe), 3.22 (br.s, 1H, OH).

4-(t-Butyldimethylsilyloxy)-5,5-dichloro-3-methoxycyclopent-2-enone (**7**)

To **6** (3.5 g, 17.5 mmol) in dry DMF (6.9 ml) at 0° under N_2 was added t-butyldimethylchlorosilane (3.2 g, 1.2 equiv) and imidazole (3 g, 2.5 equiv). After 16 h ice (120 g) was added and the product was isolated with Et_2O. Column chromatography on silica gel using CH_2Cl_2–MeOH (50 : 1) gave **7** (5.3 g, 97%) as needles, m.p. 69–70°, from MeOH-H_2O-acetone (Found: C, 46.6; H, 6.45; Cl, 22.95. $C_{12}H_{20}Cl_2O_3Si$ requires: C, 46.3; H, 6.5; Cl, 22.8%); IR ν_{max}(KBr) 1715 cm^{-1}; NMR δ(CDCl$_3$) 5.32 (s, 1H, H-2), 4.90 (s, 1H, H-4), 3.90 (s, 3H, OMe), 0.94 (s, 9H, t-Bu), 0.21 and 0.19 (each s, 3H, SiMe$_2$).

4-(t-Butyldimethylsilyloxy)-3-methoxycyclopent-2-enone (**5**)

To **7** (360 mg, 1.16 mmol) in acetone (25 ml) under CO_2 was added an aqueous soln (40 ml) of chromous chloride.[29] After 15 min the soln was diluted with water and the product was extracted into Et_2O. Removal of the dried ($MgSO_4$) solvent gave **5** (270 mg, 96%) as plates, m.p. 47–49°, from MeOH–H_2O-acetone (Found: C, 59.4; H, 9.35. $C_{12}H_{22}O_3Si$ requires: C, 59.45; H, 9.15%); IR ν_{max}(KBr) 1705, 1685 (sh.) cm^{-1}; NMR δ_H (CDCl$_3$) 5.29 (s, 1H, H-2), 4.76 (dd, $J = 6.4$ Hz, 2.7 Hz, 1H, H-4), 3.82 (s, 3H, OMe), 2.75 (dd, $J = 18.0$ Hz, 6.4 Hz, 1H, H-5 *cis* to H-4), 2.33 (dd, $J = 18.0$ Hz, 2.7 Hz, 1H, H-5 *trans* to H-4), 0.87 (s, 9H, t-Bu), 0.10 (s, 6h, SiMe$_2$), δ_C 201.5 (s), 104.8 (d), 188.3 (s), 69.5 (d) and 45.3 (t) (C-1 to C-5, respectively, of cyclopentenone ring), 58.8 (q) (OMe).

Zinc-methanol reduction of the trichloro-enone **2**

(a) *Isolation of 4-hydroxycyclopentenones* **8** *and* **9**. To **2** (2 g, 10 mmol) in MeOH (40 ml) at room temp. was added Zn powder (1.3 g, 20 mmol) with stirring. After 2.5 h the mixing was filtered and the filtrate was diluted with H_2O (70 ml) and extracted with Et_2O. Removal of the dried ($MgSO_4$) solvent and column chromatography on silica gel in CH_2Cl_2-MeOH (20 : 1) of the residual oil (1.1 g) gave two bands: the faster moving band (900 mg) was a mixure, estimated by NMR to contain **3**[4] (*ca*

Table 2. ^{1}H NMR data for 5-silyloxycyclopent-2-enones **14a–22a**[a,b]

COMPOUND	R'	CHEMICAL SHIFT, δ_H(multiplicity)					COUPLING CONSTANT, Hz					
		H-2	H-4 cis	H-4 trans	H-5	Protons of 3-substituent R'	$J_{2,4}$	$J^{cis}_{4,5}$	$J^{trans}_{4,5}$	$J_{4,4}$	$J_{2,R'}$	$J_{4,R'}$
14a	$CH=CH_2$	6.02(m)	3.13(ddm)	2.54(dm)	4.33(dd)	5.56(1H,d,J 10.5 Hz), 5.77(1H,d, J 17.0 Hz), 6.80(1H,dd,J 10.5 Hz, 17.0 Hz).	-	7.0	3.5	17.5	-	-
15a	Me	5.89(tq)	2.88(dddm)	2.44(dddm)	4.25(dd)	2.09(3H,dt,J 1.5, 1.5 Hz).	1.5	6.0	3.0	18.0	1.5	1.5
16a	n-Bu	5.89(tt)	2.88(ddm)	2.43(ddm)	4.23(dd)	0.95(3H,t,J 7 Hz), 1.2-1.8(4H,m), 2.36(2H,t,J 6.5 Hz).	1.5	7.0	3.5	18.0	1.5	-
17a	i-Pr	5.87(dt)	2.93(dddd)	2.43(dddd)	4.24(dd)	1.16(6H,d,J 7 Hz), 2.52(1H, heptet, J 7 Hz).	1.5	6.5	3.0	18.0	1.5	1.0
18a	t-Bu	5.90(t)	3.01(ddd)	2.44(ddd)	4.26(dd)	1.17(9H,s).	1.5	7.0	3.5	17.5	0	0
19a	CH_2Ph	5.82(tt)	2.85(dddt)	2.39(dddt)	4.20(dd)	3.63(2H,bs), 7.06-7.40(5H,m).	1.5	6.5	3.2	18.0	1.5	1.0
20a	$CH_2CH=CH_2$	5.92(tt)	2.98(dddt)	2.44(dddt)	4.23(dd)	3.11(2H,dm,J 6.5 Hz), 5.15(1H,dm J 17.0 Hz), 5.18(1H,dm,J 9.0 Hz), 5.84(1H,ddt,J 17.0, 9.0, 6.5 Hz).	1.5	6.5	3.5	18.0	1.5	1.0
21a	n-Pr	5.90(tt)	2.88(dddt)	2.43(dddt)	4.24(dd)	0.97(3H,t,J 7.5 Hz), 1.61(2H, sextet, J 7.5 Hz), 2.35(2H,tm, J 7.5 Hz).	1.5	7.0	3.5	17.5	1.5	1.0
22a	H	6.15(dt)	3.00(dddd)	2.51(dddd)	4.19(dd)	7.54(1H,ddd,J 6.5, 3.0, 2.5 Hz).	2.5	6.5	3.0	18.5	6.5	3.0 2.5

[a] The protons of the t-butyldimethylsilyloxy substituent appear consistently at δ0.08 (6H, s, Me) and 0.91 ± 0.04 (9H, s, t-Bu).

[b] The chemical shifts of the cyclopentenone ring protons in the free alcohols **14b** - **21b** appear 0.0-0.1 p.p.m. to lower field than those in the corresponding silyl ether.

Table 3. ^{13}C NMR data for 5-silyloxycyclopent-2-enones

COMPOUND	R'	^{13}C CHEMICAL SHIFTS, δ from Me_4Si (multiplicity)					
		C-1 (s)	C-2 (d)	C-3 (s)	C-4 (t)	C-5 (d)	Side Chain
15a	Me	207.3	128.2	174.3	42.7	73.2	19.74 (q).
16a	n-Bu	207.1	126.9	178.4	41.3	73.0	33.5 (t), 28.8 (t), 22.5 (t), 13.8 (q).
16b	n-Bu	209.3	126.3	180.7	40.0	72.4	33.6 (t), 28.9 (t), 22.4 (t), 13.7 (q).
19b	$PhCH_2$	209.0	127.1[a]	178.4	40.4	72.5	38.6 (t), 136.1 (s), 129.0 (d), 127.4 (d)[a].
21b	n-Pr	209.3	126.4	180.4	40.0	72.4	35.9 (t), 20.1 (t), 13.8 (q).

[a] These values could be interchanged.

180 mg, 13%) and **9** (*ca* 720 mg, 44%). Further chromatography (PLC) yielded pure **9** as plates, m.p. 121–123°, from CCl_4 (Found: C, 44.2; H, 4.3; Cl, 21.6. $C_6H_7ClO_3$ requires: C, 44.3; H, 4.35; Cl, 21.8%); IR ν_{max}(Nujol) 3255, 1677 cm^{-1}; NMR δ(acetone[D_6]) 5.47 (s, 1H, H-2), 5.44 (br. s, 1H, OH), 4.72 (d, J = 2.8 Hz, 1H, H-4), 4.23 (d, J = 2.8 Hz, 1H, H-5), 3.95 (s, 3H, OMe). The slower moving band gave pure **8** (64 mg, 5%) as prisms, m.p. 82–83°, from CCl_4 (Found: C, 56.0; H, 6.2. $C_6H_8O_3$ requires: C, 56.25; H, 6.3%); IR ν_{max}(Nujol) 3300, 1680 cm^{-1}; NMR δ(acetone[D_6] + D_2O, *cf* ref.[9]) 5.36 (s, 1H, H-2), 4.76 (dd, J = 6.7 Hz, 2.7 Hz, 1H, H-4), 3.89 (s, 3H, OMe), 2.74 (dd, J = 17.8 Hz, 6.7 Hz, 1H, H-5 *cis* to H-4), 2.19 (dd, J = 17.8 Hz, 2.7 Hz, 1H, H-5 *trans* to H-4).

Compound **8** (40 mg) as described for **9** (below) gave **5** (55 mg, 73%).

Treatment of **2** (2 g) with Zn powder (1.3 g) in MeOH (150 ml) for 1.3 h at 23 ± 1° gave after chromatography a mixture (71%) of **9** and **12**.

(b) *Isolation of* 4-(*t-butyldimethylsilyloxy*)*cyclopentenones* **5**, **7**, **10**, **11** *and* **13**. To **2** (4 g, 20 mmol) in MeOH (75 ml) at room temp was added Zn powder (2.6 g, 40 mmol). After 2.5 h, filtration and extraction with Et_2O gave an oil (2 g) which was silylated (t-$BuMe_2SiCl$, imidazole, DMF as described above) without prior purification. Column chromatography on silica gel using CH_2Cl_2–MeOH (50 : 1) gave, in order of elution, **10** (2.2 g, 40%), *cis*-4-(*t-butyldimethylsilyloxy*)-5-*chloro*-3-*methoxycyclopent*-2-*enone* (**11**) (170 mg, 3%) as needles, m.p. 60–62°, from MeOH–H_2O-acetone (Found: C, 52.35; H, 7.7; Cl, 12.95. $C_{12}H_{21}ClO_3Si$ requires: C, 52.05; H, 7.65; Cl, 12.8%); IR ν_{max} (KBr) 1705 cm^{-1}; NMR δ($CDCl_3$) 5.34 (s, 1H, H-2), 4.79 (d, J = 6 Hz, 1H, H-4), 4.36 (d, J = 6 Hz, 1H, H-5), 3.90 (s, 3H, OMe), 0.94 (s, 9H, t-Bu), 0.19 (s, 6H, $SiMe_2$), **5** (290 mg, 6%), and **13**[4] (610 mg, 11%).

A similar reaction between **2** (1.5 g, 7.5 mmol) and Zn powder (970 mg, 15 mmol) in MeOH (30 ml) at room temp for 15 min followed by silylation and chromatography as described above, gave **10** + **11** (472 mg, 23%), **5** (0%), **13** (396 mg, 19%) and **7** (380 mg, 16%).

trans-4-(*t-Butyldimethylsilyloxy*)-5-*chloro*-3-*methoxycyclopent*-2-*enone* (**10**)

Treatment of **9** (65 mg, 0.4 mmol) in DMF (0.5 ml) with t-butyldimethylchlorosilane (75 mg) and imidazole (68 mg) at 0° overnight followed by dilution with water and extraction with Et_2O gave pure **10** (114 mg, 93%) as needles, m.p. 40–43°, from MeOH–H_2O (Found: C, 52.0; H, 7.75; Cl, 12.9. $C_{12}H_{21}ClO_3Si$ requires: C, 52.05; H, 7.65; Cl, 12.8%); IR ν_{max}(KBr) 1720 cm^{-1} NMR δ($CDCl_3$) 5.35 (s, 1H, H-2), 4.74 (d, J = 2.7 Hz, 1H, H-4), 4.18 (d, J = 2.7 Hz, 1H, H-5), 3.86 (s, 3H, OMe), 0.90 (s, 9H, t-Bu), 0.18 (s, 6H, $SiMe_2$).

Treatment of **10** (222 mg) with chromous chloride in the manner described for **7** above gave **5** (191 mg, 98%).

3-*Alkyl- and* 3-*alkenyl*-5-(*t-butyldimethylsilyloxy*)*cyclopent*-2-*enones* **14a–21a**.

Via Grignard reagents. **5** (121 mg, 0.5 mmol) in Et_2O (1 ml) was added over 5 min to the appropriate Grignard reagent [prepared in Et_2O (2 ml) from the corresponding alkyl halide (2.5 equiv) and Mg turnings (2.7 equiv); with allylmagnesium chloride 5 equiv were employed; n-BuMgBr was prepared in THF] at 0°. After a further 30 min at room temp 10% aq NH_4Cl (5 ml) was added and the product was isolated with Et_2O. PLC [CH_2Cl_2–MeOH (50 : 1)] and distillation (Kugelrohr, bath temp *ca* 80°/0.01 mm except for **19a** which required 172°/0.03 mm) gave pure product.

Via organolithium reagents. The appropriate Li reagent (1.2 equiv; with vinyl-Li 2.5 equiv were used) was added dropwise to **5** (121 mg, 0.5 mmol) in Et_2O (2 ml) at −78°. The mixture was allowed to approach -20° over 1 h before work-up as described for the Grignard reaction products.

Yields of **14a–21a** are given in Table 1.

(*1R**, 4*S**) - 4 - (*t-Butyldimethylsilyloxy*) - 3 - *methoxy* - 1 - [3 - (*trimethylsilyl*)*prop* - 2 - *yn* - 1 - *yl*] *cyclopent* - 2 - *en* - 1 - *ol* (**23**, R = $CH_2C \equiv CSiMe_3$)

1-Lithio-3-(trimethylsilyl)prop-2-yne was generated at −5° in Et_2O (0.2 ml) containing tetramethylethylenediamine (TMEDA) (38 μl, 0.25 mmol) from 1-(trimethylsilyl)prop-1-yne[30] (38 μl, 0.25 mmol) and n-BuLi (151 μl, 1.66 M, 0.25 mmol) over 15 min. After chilling (−78°) this soln, **5** (50 mg, 0.21 mmol) in Et_2O (0.1 ml) was added and the mixture was maintained at −78° for 1 h before warming to −20°. At this temp, sat NH_4Cl aq was added and the product was isolated by extraction with Et_2O. Flash chromatography[31] using petrol–EtOAc (4 : 1) gave recovered **5** (15 mg, 30%) and **23** (R=$CH_2C \equiv CSiMe_3$) (35 mg, 69% based on consumed **5**) as an oil; NMR δ($CDCl_3$) 4.70 (s, 1H, H-2), 4.55 (dd, J = 7.0 Hz, 4.0 Hz, 1H, H-4), 3.64 (s, 3H, OMe), 2.58 (dd, J = 13.5 Hz, 7.0 Hz, 1H, H-5 *cis* to H-4), 2.54 (s, 2H, $CH_2C \equiv C$), 2.17 (s, 1H, OH), 1.83 (dd, J = 13.5 Hz, 4.0 Hz, 1H, H-5 *trans* to H-4), 0.90 (s, 9H, t-Bu), 0.15 (s, 9H, $SiMe_3$), 0.11 (s, 6H, $SiMe_2$); mass spectrum m/z 336 (M^+–H_2O), 297 (M^+–Bu), 279 (M^+–H_2O–Bu), 265 (M^+–H_2O–Bu–CH_2), 243 (M^+–$CH_2C \equiv CSiMe_3$).

Treatment of methoxy-enone **5** *with cuprate reagents*

Lithium di-n-butylcuprate. **5** (121 mg, 0.5 mmol) was added to lithium di-n-butylcuprate [1.35 mmol; prepared at −45° in THF from n-BuLi (1.8 ml, 1.54 M, 2.7 mmol) and CuI (285 mg, 1.5 mmol)] in THF at −78° and the mixture was maintained at −78° for 2.5 h. Addition of 10% NH_4Cl aq and extraction with Et_2O (*cf.* ref.[4]) gave **5** (95 mg, 80%) as the only isolable product by PLC.

n-Butylmagnesium bromide-CuI. n-BuMgBr in THF (1 ml, 0.72 M, 0.72 mmol) was added with stirring to a suspension of CuI (68 mg, 0.36 mmol) in THF (1 ml) containing **5** (87 mg, 0.36 mmol) at −10°. After 2.5 h, TLC [SiO_2, CH_2Cl_2–MeOH (50 : 1)] and GLC analysis of the mixture revealed only the presence of **5** (76% by GLC).

3-*Alkyl- and* 3-*alkenyl*-5-*hydroxycyclopent*-2-*enones* **14b–21b**

The corresponding t-butyldimethylsilyl ether in HAc–H_2O–THF (3 : 1 : 1) was stirred at room temp overnight. (**20b** was hydrolysed over 4 days at 4°.) The mixture was diluted with H_2O, extracted with Et_2O and the extracts were washed with $NaHCO_3$ aq, dried ($MgSO_4$), and evaporated. **14b–21b** (Table 1) were purified by PLC [CH_2Cl_2–MeOH (20 : 1)] and distillation (Kugel-

rohr, bath temp 70–80°/0.05 mm except for **19b** which required 105°/0.01 mm).

Compound **15b** has been prepared previously by Gowda and McMurry.[11]

5-(t-Butyldimethylsilyloxy)cyclopent-2-enone (**22a**)

To **5** (242 mg, 1 mmol) in THF (5 ml) at −78° was added Red-Al (Aldrich Chemical Co.) (1.2 ml, 3.46 M, 4 mmol). After 2 h at this temp H_2O was added carefully and the mixture was allowed to warm to room temp. Extractive work-up (Et_2O) gave a residue (290 mg) which was dissolved in $CHCl_3$ (5 ml) and stirred over oxalic acid dihydrate (150 mg) and sodium oxalate (300 mg). Filtration, evaporation of solvent and chromatography (PLC) on silica gel using CH_2Cl_2–MeOH (50 : 1) gave two principal bands: the slower moving band yielded **5** (23 mg, 9.5%); the faster moving band contained **22a** (170 mg, 88% based on consumed **5**) as a liquid, b.p. (Kugelrohr) 50° at 0.05 mmHg (Found: C, 62.25; H, 9.3. $C_{11}H_{20}O_2Si$ requires: C, 62.2; H, 9.5%); IR ν_{max}(film) 1720 cm^{-1}; NMR data in Table 2.

In a second reaction, the use of a larger excess of Red-Al (16 equiv) gave the unstable intermediate (R=H) in quantitative yield after PLC on silica in CH_2Cl_2; NMR $\delta(CDCl_3)$ 4.82 (d, $J = 2$ Hz, 1H, H-2), 4.39–4.66 (m, 2H, H-1 and H-4), 3.66 (s, 3H, OMe), 2.68 (dt, $J = 8$ and 14 Hz, 1H, H-5 *cis* to H-1 and H-4), 2.21 (bs, 1H, OH), 1.73 (dt, $J = 3$ and 14 Hz, 1H, H-5 *trans to* H-1 and H-4), 0.91 (s, 9H, t-Bu), 0.09 (s, 6H, $SiME_2$).

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