Pergamon

Tetrahedron 58 (2002) 5163–5172

TETRAHEDRON

Six- and five-membered 3-alkoxy-2-lithiocycloalkenes: new stable non-anionic β-functionalised organolithium compounds

Miguel Yus,*,† Diego J. Ramón and Inmaculada Gómez

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, E-03080 Alicante, Spain

Received 10 January 2002; accepted 19 April 2002

Abstract—Naphthalene-catalysed reductive lithiation of various functionalised chlorocycloalkenes **18** leads to the corresponding non-anionic β-alkoxyfunctionalised organolithium reagents **14**. Their reaction with different electrophiles, such as water, aldehydes, ketones and imines, gave the expected products **19** and **24**. The diastereoselection in the reaction with aldehydes can be modified by the use of different additives. In the case of using 3-methoxy-2-chlorocyclopentene (**18a**) as starting material, and depending on reaction time, unexpected bicyclopentadiene derivatives **25** were isolated, together with the expected compounds **24**.

1. Introduction

Functionalised non-stabilised organolithium compounds are interesting intermediates for the construction of organic structures due to the fact that their reactions with electrophiles usually lead directly to polyfunctionalised molecules. Therefore, in the last years, a great effort has been done in the development of highly functionalised organolithium reagents.[1] Their stability depends strongly on three factors. (a) The type of functionality, so for example, the stability of different organolithium compounds decreases when the functionality has a good leaving-group character, the organolithium intermediate with anionic functionalities being more stable than the corresponding ones having a neutral functionality (compare structures **1** and **2**). (b) The relative position between the functional group and the carbon–lithium bond, so the proximity between both moieties (n=0, 1, 2, 3, … in structures **1** and **2**) makes easier the corresponding α, β, γ, δ elimination reaction to give the corresponding carbene, alkene or cycloalkanes, respectively. (c) The hybridisation of the carbanionic atom: it is generally known that the stability of a carbanionic intermediate follows the series $sp>sp^2>sp^3$.

1 [X = Hal, OR, NR_2,...] **2** [Y = O, NR,...]

Due to the former considerations, organolithium compounds possessing a non-anionic leaving group in β position to the anionic carbon atom remain notoriously elusive[2] due to their great tendency to undergo β-elimination reactions to yield alkenes.[3] In the literature, there are only a few examples of this kind of organolithium species which are relatively stable. In the case of an amino-leaving group, the structures are of type **3**,[4] **4**,[5] **5**[5] and **6**,[6] while in the case of alkoxy-leaving group there are more different types of structures, such as **7**,[7] **8**,[8] **9**,[9] **10**,[10] **11**,[11] **12**[12] and **13**.[13] In spite of these examples, the different factors that prevent the elimination reactions in the aforementioned remarkable stable intermediates have not been definitely established. Thus, for example, in the case of intermediates **3** and **5**, the stability may arise from the presence of other chelating functionalities. In other cases, the cyclic nature of some of them, such as **4**, **5**, **7**–**9**, **11** and **13** may prevent the appropriate conformation for the β-elimination reaction. Finally, it must be pointed out that in other cases, the stability may be due to the hybridisation either of the anionic carbon atom (see reagents **6**, **8**–**12**), or of the carbon atom which bears the functionality (see intermediate **13**).

With this in mind, and due to the lack in the preparation of most simple organolithium intermediates of type **14**, we anticipated that the preparation of this kind of intermediates could be carried out using a chlorine–lithium exchange catalysed by an arene[14] and they could be useful in organic synthesis. Furthermore, the presence of an extra allylic ether group introduces the opportunity of further reductive cleavage of this functionality to yield a new allyllithium intermediate.[15]

2. Results and discussion

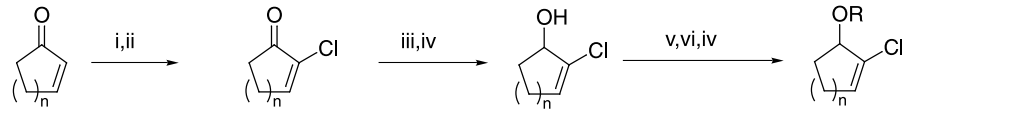
The starting chlorinated cycloalkenes compounds **18** were

Keywords: lithiation; elimination reactions; lithium and compounds; cycloalkenes.

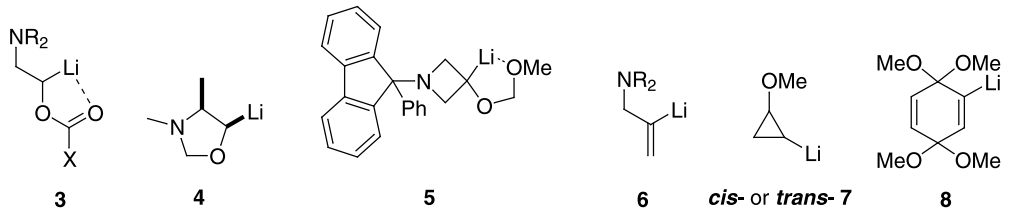
* Corresponding author. Tel.: +34-9-6590-3548; fax: +34-9-6590-3549; e-mail: yus@ua.es

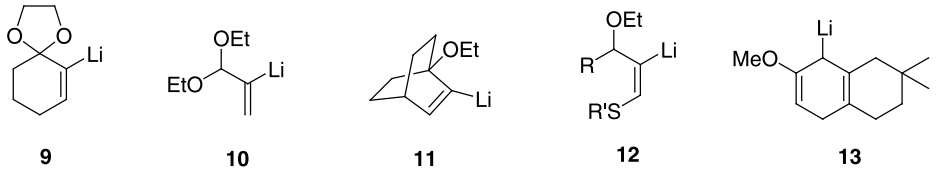
† www.ua.es/dept.quimorg

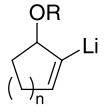
0040–4020/02/$ - see front matter
PII: S0040-4020(02)00454-4



Scheme 1. *Reagents and conditions*: (i) $HCl_{(g)}$/DMF, *m*CPBA, 0 to 25°C; (ii) $NaHCO_3$ (sat); (iii) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, 0°C; (iv) H_2O; (v) NaH, DMF, 0°C, (vi) RX, 0 to 25°C.

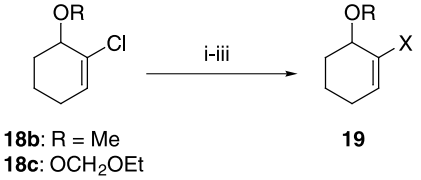






prepared as shown in Scheme 1. The oxidative chlorination[16] of cycloalkenones **15** gave the corresponding α-chloroenones **16**, which were reduced with sodium borohydride in the presence of $CeCl_3{\cdot}7H_2O$[17] to give the expected allylic alcohols **17**. Finally, these alcohols were transformed into the corresponding ethers **18** by deprotonation followed by alkylation[18] with iodomethane (for compounds **18a**,**b**) or with chloromethyl ethyl ether (for compound **18c**).

The lithiation of the starting chlorinated cyclohexenes **18b**,**c**, using lithium powder and a substoichiometric amount of naphthalene[14] (4% molar ratio) gave the expected β-alkoxydofunctionalised organolithium intermediates of type **14**, which were trapped by reaction with different electrophiles affording, after hydrolysis with water, the expected products **19** (Scheme 2 and Table 1).



Scheme 2. *Reagents and conditions*: (i) Li, $C_{10}H_8$ (4 mol%), THF, −78°C; (ii) E=H_2O, Bu^tCHO, PhCHO, Et_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, PhCOMe, PhCH=NPh; (iii) H_2O, −78 to 25°C.

The first conclusion which arouse from the data included in Table 1 is that the intermediates of type **14** (n=1) are stable at low temperature, independently of the presence of an extra coordinating atom, such as it occurs in the starting

Table 1. Preparation of compounds **19**

Entry	Starting material		E	Product		
	No.	R		No.	X	Yield (%)[a]
1	**18b**	Me	H_2O	**19a**	H	93
2	**18b**	Me	Bu^tCHO	**19b**	Bu^tCHOH	81[b]
3	**18b**	Me	PhCHO	**19c**	PhCHOH	56[c]
4	**18b**	Me	Et_2CO	**19d**	Et_2COH	78
5	**18b**	Me	$(CH_2)_5CO$	**19e**	$(CH_2)_5COH$	65
6	**18b**	Me	PhCOMe	**19f**	PhC(OH)Me	66[d]
7	**18b**	Me	PhCHNPh	**19g**	PhCHNHPh	70[e]
8	**18c**	CH_2OEt	H_2O	**19h**	H	91
9	**18c**	CH_2OEt	Bu^tCHO	**19i**	Bu^tCHOH	87[f]
10	**18c**	CH_2OEt	Et_2CO	**19j**	Et_2COH	75
11	**18c**	CH_2OEt	$(CH_2)_4CO$	**19k**	$(CH_2)_4COH$	50
12	**18c**	CH_2OEt	$(CH_2)_5CO$	**19l**	$(CH_2)_5COH$	80

[a] Isolated yield (>95% from GLC and/or 300 MHz ^1H NMR) after flash chromatography (silica gel, hexane/ethyl acetate) based on the starting material **18**.

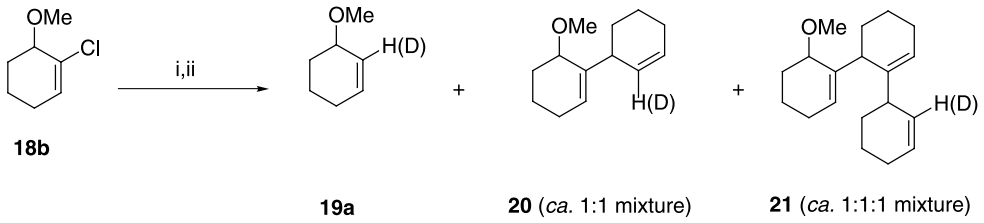
[b] 1.1:1 (R^*,R^*)/(R^*,S^*) diastereomeric ratio (300 MHz ^1H NMR of crude mixture).

[c] 1.8:1 (R^*,R^*)/(R^*,S^*) diastereomeric ratio (300 MHz ^1H NMR of crude mixture).

[d] 4:1 (R^*,R^*)/(R^*,S^*) diastereomeric ratio (300 MHz ^1H NMR of crude mixture).

[e] 9:1 (R^*,S^*)/(R^*,R^*) diastereomeric ratio (300 MHz ^1H NMR of crude mixture).

[f] 1.4:1 (R^*,R^*)/(R^*,S^*) diastereomeric ratio (300 MHz ^1H NMR of crude mixture).



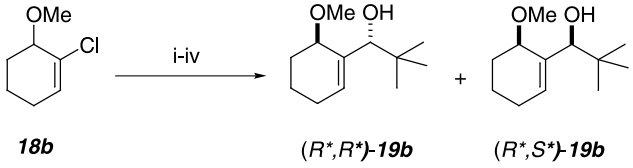
Scheme 3. *Reagents and conditions*: (i) Li, $C_{10}H_8$ (4 mol%), THF, −78 to 25°C, 2 days; (ii) D_2O.

compound **18b**. When carbonylic compounds were used as electrophile, the only by-product found was either **19a** or **19b**, probably due to the abstraction of a proton from the reaction media by the organolithium intermediate.[19] Furthermore, when the temperature was allowed to rise to room temperature, after lithiation of compound **18b**, and the mixture was quenched after 2 days with D_2O, the only products detected by ^1H NMR and CG-MS analysis of the crude mixture were the compound **19a** (ca. 80% yield) as well as different amounts of dimers (**20**) and trimers (**21**) as a ca. 1:1 and 1:1:1 mixture of diastereomers, respectively (Scheme 3), in all cases the incorporation of deuterium being never higher than 60% (according to GC–MS spectrum analysis). This result contrasts with some previous reports which showed the easy preparation of 1,2-cyclohexadienes by β-elimination reaction on β-functionalised cabanions.[20] When the reaction gives a mixture of diastereoisomers (Table 1, entries 2, 3, 6 and 9), their separation was accomplished by flash chromatography and their relative configuration determined by NOESY experiments (see Section 4).

Another interesting result appeared when the chlorinated starting compound **18c** was lithiated and the intermediate of type **14** was reacted with chlorotrimethylsilane as electrophile (Scheme 4). In this case, the only isolated product **22** (41% yield) came from a sequential (a) chloro–lithium exchange, (b) reaction with the electrophile to give a compound of type **19** (with R=CH_2OEt and X=$SiMe_3$) followed by (c) reductive lithiation of the resulting allylic ether with the excess of lithium and a substoichiometric amount of naphthalene, to give the corresponding allylic lithium derivative[21] **23** and (d) final quenching with water.

On the other hand, it is well known that the presence of different additives, such as cosolvents or/and some metallic salts may change the diastereomeric ratio in the addition of organometallic intermediates to aldehydes.[22] For studying the influence of some additives, the sequential lithiation of chlorinated system **18b** followed by filtering-off the excess of lithium at low temperature, addition of corresponding additive and final reaction with pivaldehyde to give compound **19b**, were carried out as standard processes (Scheme 5 and Table 2). It must be pointed out that the addition of toluene (THF/toluene: 1:1 v/v) did not have a strong influence in the diastereomeric ratio (Table 1, compare entry 2 with Table 2, entry 1). Similar results were obtained using ether as cosolvent. However, the addition of different amounts of CuI[22] had some influence on the diastereomeric ratio (Table 2, entries 2 and 3).

Surprisingly, when 3-methoxy-2-chlorocyclopentene (**18a**) was used as starting material (Scheme 6 and Table 3), a mixture of two products was obtained, the ratio of these products being strongly dependent on the reaction time for the reaction of the corresponding organolithium intermediate with the electrophile. Thus, short reaction times gave the expected cyclopentene derivative **24** as the major product with a small amount of the bicyclopentadiene

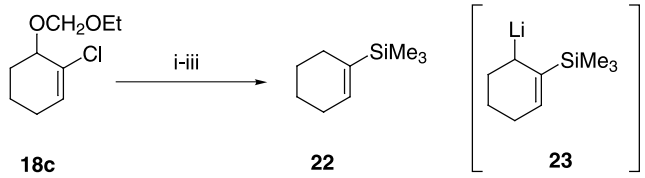


Scheme 5. *Reagents and conditions*: (i) Li, $C_{10}H_8$ (4 mol%), THF, −78°C; (ii) additive; (iii) Bu^{t}CHO; (iv) H_2O −78 to 25°C.

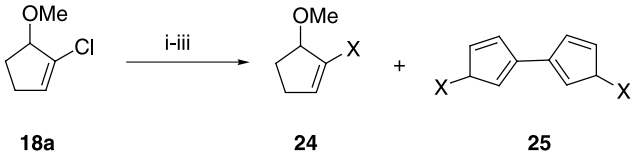
Table 2. Influence of additive on the diastereomeric ratio

Entry	Additive	Product **19b**	
		Yield (%)[a]	(R^*,R^*)/(R^*,S^*) diastereomeric ratio[b]
1	PhMe	73	1:1
2	PhMe/CuI (0.5 equiv.)	79	1:2.7
3	PhMe/CuI (1 equiv.)	82	1:2

[a] Yield determined by GLC of crude mixture.
[b] Determined by integration in the 300 MHz ^1H NMR spectra of crude mixture.



Scheme 4. *Reagents and conditions*: (i) Li, $C_{10}H_8$ (4 mol%), THF, −78°C; (ii) Me_3SiCl; (iii) H_2O −78 to 25°C.

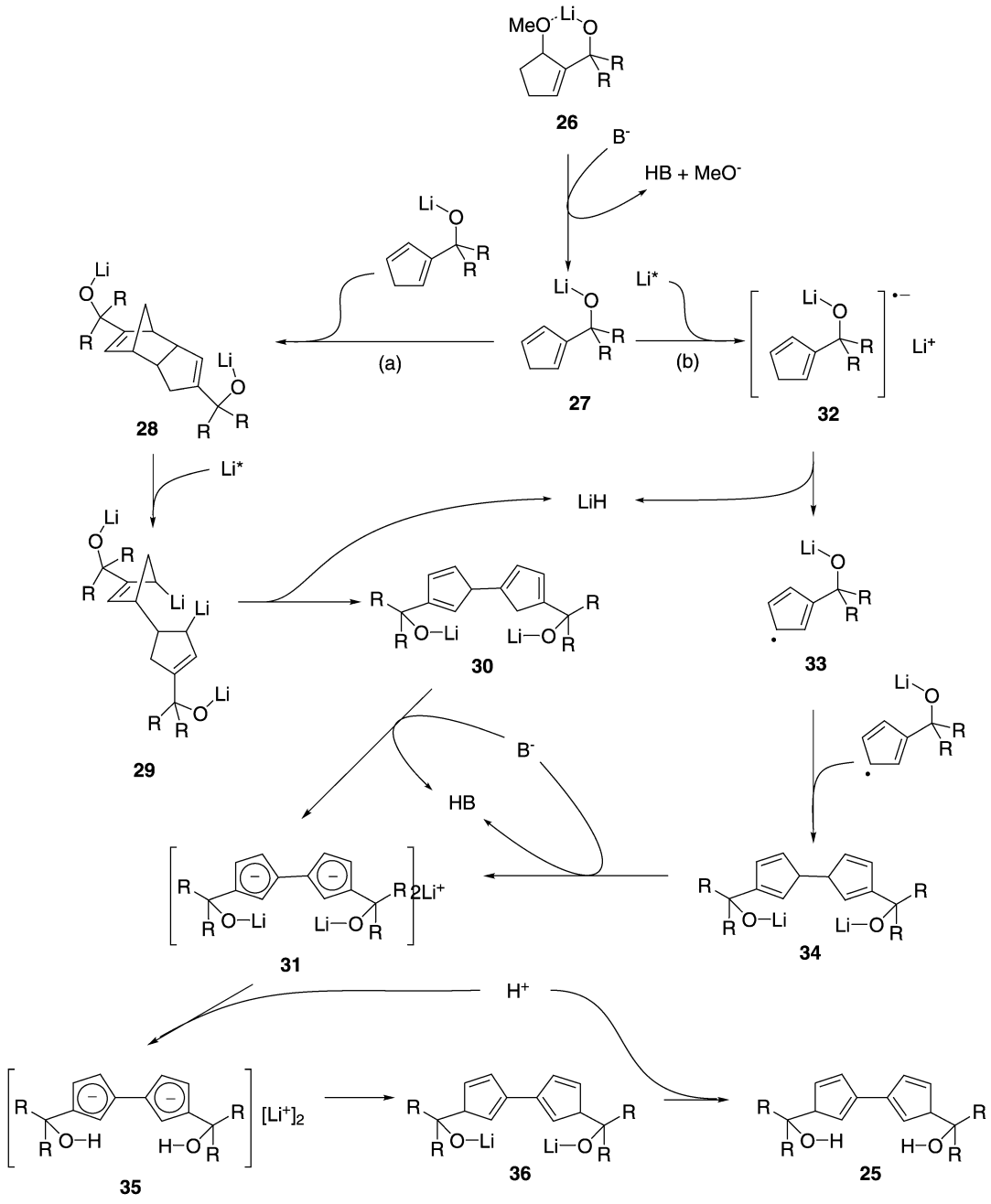


Scheme 6. *Reagents and conditions*: (i) Li, $C_{10}H_8$ (4 mol%), THF, −78°C; (ii) E=Et_2CO, $(CH_2)_5CO$; (iii) H_2O −78 to 25°C.

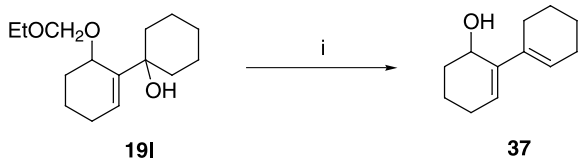
Table 3. Lithiation of compound **18a** and reaction with ketones

Entry	E	t (h)[a]	Products				
			X	Cyclopentene		Bicyclopentadiene	
				No.	Yield (%)	No.	Yield (%)
1	Et_2CO	1	Et_2COH	**24a**	59[b]	**25a**	8[c]
2	$(CH_2)_5CO$	1	$(CH_2)_5COH$	**24b**	77[b]	**25b**	4[c]
3	Et_2CO	4	Et_2COH	**24a**	8[c]	**25a**	42[b]
4	$(CH_2)_5CO$	4	$(CH_2)_5COH$	**24b**	5[c]	**25b**	58[b]

[a] Reaction time of organolithium intermediate with ketones.
[b] Isolated yield of compound (>95% from GLC and/or 300 MHz ^1H NMR) after flash column chromatography (silica gel, hexane/ethyl acetate).
[c] Yield determined by GLC of crude mixture.



Scheme 7.



Scheme 8. *Reagents and conditions*: (i) 2 M HCl, Me_2CO, 25°C.

derivative **25**. However, longer reaction times yielded the unexpected bicyclopentadiene **25** as the main product, the cyclopentene **24** being a minor component in the crude mixture. The determination of structure **25** was performed in base of different NOESY, HMBC and HMQC experiments.

From a mechanistic point of view, the above formation of dicyclopentadiene **25** may be explained by two different pathways. Both pathways start from the alcoholate **26**, which arises in its turn from the addition of organolithium intermediate of type **14** (with n=1 and R=Me) to the corresponding symmetrical ketone. Its deprotonation followed by a β-elimination reaction gives the cyclopentadiene derivative **27**. Now, two alternative sequences of reaction might occur. (a) A Diels–Alder reaction gave the adduct **28** which, in its turn, might suffer a reductive cleavage lithiation[23,24] to give the most stable diallylic organodilithium intermediate **29**. The elimination of lithium hydride[24] on intermediate **29** gives the dialcoholate **30**, the driven force of this unusual elimination being the further formation of the more stable bicyclopentadienyllithium derivative **31**. (b) Another alternative approach implies the addition of lithium to the aforementioned alcoholate **27** to yield the anion radical **32**, elimination of lithium hydride gives the radical **33** which, through a radical dimerization reaction, may be transformed into the dialcoholate **34**. Then, either lithium hydride or other bases present in the reaction media may deprotonate the system to give the symmetric intermediate **31**. Finally, the quenching with water protonates in first term the tertiary alcoholate moiety to give the corresponding alcohol **35** ($pK_a \approx 17$).[25] This alcohol moiety is now the proton source to lead to a new protonation of lithium cyclopentadienyl system ($pK_a \approx 16$),[26] yielding the alcoholate–cyclopentadiene intermediate **36**, in which the protonated carbon atom is the closest to the hydroxy group. The aforementioned intramolecular transfer of protons may explain the regiochemistry found. In all tested cases, 5,5′-disubstituted-2,2′-bicyclopenta-1,3-dienes **25** were isolated after a further protonation of the alcoholate moieties (Scheme 7). An indirect proof that the mechanism can go throughout the Diels–Alder adduct **28**, followed by a reductive cleavage lithiation is that the lithiation of dicyclopentadiene using lithium powder and a substoichiometric amount of naphthalene at low temperature in the presence of cyclohexenone gives the expected product **25b** in ca. 10% yield.[27]

Finally, it must be pointed out that the aforementioned cycloalkenes derivatives **19h–l** can be easy transformed into the corresponding alcohol derivatives, just by aqueous acid treatment. As an example, the compound **19l** was treated with a solution of 2 M hydrochloric acid in acetone to give after work-up the corresponding allylic alcohol **37** with 84% yield (Scheme 8), in which the tertiary alcohol has suffered a dehydration process and the ketal was hydrolysed, under the assayed reaction conditions, to give the corresponding dienic system.[28]

3. Conclusion

In conclusion, we have described here a simple method for the preparation of lithiated β-functionalised cycloalkenes by a naphthalene-catalysed chlorine–lithium reductive exchange. These organolithium derivatives are stable under the conditions assayed and allow the preparation of various functionalised cyclic derivatives. In the case of cyclopentene derivatives, besides the expected modified cyclopentene derivatives, symmetrical functionalised dicyclopentadiene derivatives were also obtained. This methodology allowed the further in situ lithiation of allylic ether to yield a new allyllithium derivative.

4. Experimental

4.1. General

For general information, see Ref. 29.

4.2. Isolation of compounds 16: general procedure[16]

Oxidative chlorination of cycloalkenones. To an efficiently stirred solution of the corresponding enone **15** (80 mmol) in DMF (100 mL) was added a solution of $HCl_{(g)}$–DMF (20 mL, 6.6 M) at 0°C. To the above solution was added *m*CPBA (100 mmol) in several portions. After 1 h, the reaction mixture was quenched with $NaHCO_3$ (1 M) until pH>7. The resulting mixture was stirred at room temperature for 2 h and extracted with ether (3×75 mL). The combined organic layers were washed with water (4×100 mL) and dried over anhydrous Na_2SO_4. The solvents were evaporated (15 Torr) to give a residue, which was purified by column chromatography, affording the pure title compounds **16**. Yields are included in Scheme 1. Physical and spectroscopic data, as well as the literature reference, follow.

4.2.1. 2-Chloro-2-cyclopentenone (16a).[16] Pale yellow oil, t_r 6.0; R_f 0.59 (hexane/ethyl acetate: 1:1); ν (film) 3071, 1597 (HC=C), 1726 cm^{-1} (C=O); δ_H ($CDCl_3$) 2.50–2.55 (2H, m, CH_2CH), 2.70–2.75 (2H, m, CH_2CO), 7.61 (1H, t, J=2.7 Hz, $CHCH_2$); δ_C ($CDCl_3$) 25.7, 32.9, 130.0, 157.45, 201.3; m/z 118 (M^++2, 14%), 116 (M^+, 45), 88 (24), 53 (100), 52 (19), 51 (24), 50 (15), 43 (10).

4.2.2. 2-Chloro-2-cyclohexenone (16b).[16] White solid, mp 72–74°C, t_r 6.8; R_f 0.55 (hexane/ethyl acetate: 1:1); ν (film) 3044, 1606 (HC=C), 1683 cm^{-1} (C=O); δ_H ($CDCl_3$) 2.05–2.10, 2.45–2.55, 2.55–2.60 (2, 2 and 2H, respectively, 3m, 3×CH_2), 7.16 (1H, t, J=4.6 Hz, CH); δ_C ($CDCl_3$) 22.4, 26.9, 38.3, 131.9, 146.65, 191.3; m/z 132 (M^++2, 20%), 130 (M^+, 64), 104 (25), 102 (70), 91 (14), 89 (42), 88 (20), 76 (16), 74 (51), 73 (12), 67 (85), 65 (21), 63 (11), 61 (18), 55 (100), 53 (22), 51 (20), 50 (15), 42 (27), 41 (40), 40 (18).

4.3. Isolation of compounds 17: general procedure[17]

Reduction of chlorocycloalkenones. To a stirred solution of the corresponding ketone **16** (35 mmol) in methanol (95 mL) was added $CeCl_3{\cdot}7H_2O$ (36 mmol) at 25°C. Once the salt was dissolved, the solution was cooled at 0°C and $NaBH_4$ (36 mmol) was added in several portions. After 1 h, methanol was removed under low pressure (15 Torr) and the corresponding residue was solved in water (150 mL) and ether (100 mL) and extracted with ether (2×75 mL). The organic layers were dried over anhydrous Na_2SO_4 and the solvents were evaporated (15 Torr) to give a residue, which was purified by column chromatography, affording the pure title compounds **17**. Yields are included in Scheme 1. Physical and spectroscopic, as well as analytical data, follow.

4.3.1. 2-Chloro-2-cyclopentenol (17a). Yellow oil, t_r 5.34; R_f 0.59 (hexane/ethyl acetate: 7:3); ν (film) 3394 (OH), 3071, 1599 (HC=C), 1090, 1020 cm^{-1} (CO); δ_H ($CDCl_3$) 1.80–1.90, 2.25–2.55 (1 and 4H, respectively, 2m, 2×CH_2 and OH), 4.60–4.65 (1H, m, CHO), 5.85–5.90 (1H, m, HC=C); δ_C ($CDCl_3$) 28.5, 31.85, 77.6, 129.5, 134.85; *m/z* 120 (M^++2, 2%), 118 (M^+, 7), 83 (100), 65 (16), 55 (61), 53 (36), 43 (11); HRMS: M^+, found 118.0178 C_5H_7ClO requires 118.0185.

4.3.2. 2-Chloro-2-cyclohexenol (17b). Colourless oil, t_r 5.5; R_f 0.51 (hexane/ethyl acetate: 7:3); ν (film) 3383 (OH), 3037, 1650 (HC=C), 1080, 1057 cm^{-1} (CO); δ_H ($CDCl_3$) 1.50–2.20 (6H, m, 3×CH_2), 3.10 (1H, s, OH), 4.10–4.15 (1H, m, CHO), 5.95 (1H, t, *J*=4.1 Hz, HC=C); δ_C ($CDCl_3$) 17.35, 26.2, 31.7, 68.2, 128.0, 133.6; *m/z* 134 (M^++2, 1%), 132 (M^+, 3), 104 (26), 97 (100), 88 (10), 79 (42), 77 (17), 70 (10), 69 (15), 67 (21), 55 (34), 53 (17), 51 (17), 43 (22), 41 (55), 40 (13); HRMS: M^+, found 132.0346 C_6H_9ClO requires 132.0342.

4.4. Isolation of compounds 18: general procedure

Alkylation of alcohols. To a stirred suspension of NaH (7.5 mmol) in dry DMF (40 mL) at 0°C was added a solution of the corresponding alcohol **17** (6.5 mmol) in dry DMF (10 mL) under nitrogen atmosphere. After 30 min at this temperature, the alkylating reagent (MeI or $ClCH_2OEt$, 7.5 mmol) was added allowing the temperature to rise to room temperature during 1 h. The reaction was quenched by addition of water (20 mL) and the resulting mixture was extracted with ether (3×30 mL). The combined organic layers were washed with water (4×50 mL) and dried over anhydrous Na_2SO_4. The solvents were evaporated (15 Torr) to give a residue, which was purified by column chromatography, affording the pure title compounds **18**. Yields are included in Scheme 1. Physical and spectroscopic data, as well as analytical data, follow.

4.4.1. 2-Chloro-3-methoxycyclopentene (18a). Yellow oil, t_r 5.4; R_f 0.61 (hexane/ethyl acetate: 7:3); ν (film) 3070, 1598 (HC=C), 2853 (OMe), 1102 cm^{-1} (CO); δ_H ($CDCl_3$) 1.90–2.00, 2.20–2.50 (1 and 3H, respectively, 2m, 2×CH_2), 3.39 (3H, s, Me), 4.34 (1H, t, *J*=3.3 Hz, CHO), 5.90–5.95 (1H, m, HC=C); δ_C ($CDCl_3$) 28.6, 28.95, 55.85, 85.9, 131.0, 133.0; *m/z* 134 (M^++2, 1%), 132 (M^+, 3), 101 (27), 97 (100), 67 (22), 65 (69), 53 (45), 51 (13), 43 (10), 41 (23); HRMS: M^+, found 132.0356 C_6H_9ClO requires 132.0342.

4.4.2. 2-Chloro-3-methoxycyclohexene (18b). Yellow oil, t_r 6.0; R_f 0.66 (hexane/ethyl acetate: 7:3); ν (film) 3010, 1643 (HC=C), 2855 (OMe), 1093, 1021 cm^{-1} (CO); δ_H ($CDCl_3$) 1.55–1.70, 1.95–2.20 (3 and 3H, respectively, 2m, 3×CH_2), 3.45 (3H, s, Me), 3.68 (1H, m, CHO), 5.95–6.00 (1H, m, HC=C); δ_C ($CDCl_3$) 16.85, 26.3, 28.0, 55.25, 77.3, 129.0, 131.8; *m/z* 148 (M^++2, <1%), 146 (M^+, 1), 118 (22), 114 (30), 111 (75), 79 (100), 77 (49), 75 (22), 58 (22), 53 (23), 51 (36), 50 (17), 45 (35), 43 (15), 41 (44); HRMS: M^+, found 146.0509 $C_7H_{11}ClO$ requires 146.0498.

4.4.3. 2-Chloro-3-(ethoxymethoxy)cyclohexene (18c). Colourless oil, t_r 4.92; R_f 0.74 (hexane/ethyl acetate: 7:3); ν (film) 3041, 1650 (HC=C), 1098, 1031 cm^{-1} (CO); δ_H ($CDCl_3$) 1.23 (3H, t, *J*=7.0 Hz, Me), 1.60–1.75, 1.85–2.20 [3 and 3H, respectively, 2m, $(CH_2)_3$], 3.60–3.80 (2H, m, CH_2CH_3), 4.10–4.15 (1H, m, CHO), 4.80 (2H, s, OCH_2O), 6.02 (1H, t, *J*=4.0 Hz, HC=C); δ_C ($CDCl_3$) 14.9, 17.0, 26.25, 29.6, 63.25, 73.25, 94.0, 129.3, 131.85; *m/z* 160 (M^+−30, 3%), 144 (17), 116 (18), 115 (25), 114 (35), 97 (11), 81 (11), 80 (13), 79 (73), 77 (29), 68 (12), 59 (100), 51 (14), 41 (28); HRMS: M^+, found 190.0778 $C_9H_{15}ClO_2$ requires 190.0760.

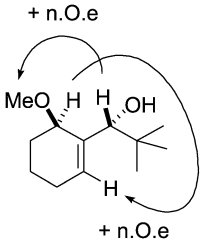
4.5. Isolation of compounds 19, 22, 23 and 24: general procedure

*Naphthalene-catalysed lithiation of chloro alkoxycycloalkenes **18** and reaction with electrophiles*. To a green suspension of lithium powder (50 mg, 7 mmol) and naphthalene (20 mg, 0.16 mmol) in THF (10 mL) was slowly added (ca. 10 min) the corresponding cycloalkene **18** (2 mmol) at −78°C under nitrogen atmosphere. After 3 h under these conditions, the electrophile (2.5 mmol) was added [for the results in Table 2, after this time, the excess of lithium was filtered off and toluene (30 mL) together CuI were added, see Table 2]. Stirring was continued at the same temperature during 1 h (for other reaction times see Table 3). The resulting mixture was then hydrolysed by subsequential addition of water (1 mL) and NH_4Cl (sat, 20 mL). The resulting mixture was extracted with ethyl acetate (2×30 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvents were evaporated (15 Torr) to give a residue, which was purified by flash column, affording the pure title compounds. Yields are included in Tables 1–3 and text. Physical, spectroscopic and analytical data follow.

4.5.1. 3-Methoxycyclohexene (19a). Yellow oil, t_r 3.7; R_f 0.68 (hexane/ethyl acetate: 9:1); ν (film) 1600 (HC=C), 2853 (OMe), 1025 cm^{-1} (CO); δ_H ($CDCl_3$) 1.50–2.05 (6H, m, 3×CH_2), 3.36 (3H, s, Me), 3.70–3.75 (1H, m, CHO), 5.75–5.90 (2H, m, HC=CH); δ_C ($CDCl_3$) 19.10, 25.15, 29.65, 55.60, 74.05, 127.40, 130.70; *m/z* 112 (M^+, 30%), 11 (28), 97 (34), 84 (55), 81 (27), 79 (43), 77 (16), 69 (43), 55 (16), 54 (17), 53 (28), 51 (15), 45 (17), 43 (68), 42 (11), 41 (100); HRMS: M^+, found 112.0881 $C_7H_{12}O$ requires 112.0888.

4.5.2. (*R,*R**)-1-(3-Methoxy-1-cyclohexen-2-yl)-2,2-dimethyl-1-propanol [(*R**,*R**)-19b].** Colourless oil, t_r 9.7;

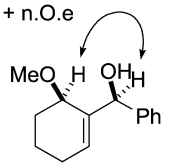
R_f 0.51 (hexane/ethyl acetate: 7:3); ν (film) 3415 (OH), 2867 (OMe), 1650 (HC═C), 1090, 1066, 1050 cm^{-1} (CO); δ_H ($CDCl_3$) 0.92 (9H, s, CMe_3), 1.15–2.20 (6H, m, 3×CH_2), 3.35 (3H, s, OMe), 3.75–3.80 (2H, m, C*H*OMe and OH), 4.00–4.05 (1H, m, C*H*OH), 5.73 (1H, t, J=3.8 Hz, HC═C); δ_C ($CDCl_3$) 17.25, 25.0, 25.45, 26.65 (3C), 35.9, 55.5, 75.55, 85.25, 131.10, 136.15; *m/z* 166 (M^+-32, <1%), 141 (28), 110 (16), 109 (100), 91 (13), 81 (54), 79 (48), 77 (11), 57 (48), 55 (13), 53 (17), 43 (23) 41 (70); HRMS: M^+-H_2O, found 180.1512. $C_{12}H_{20}O$ requires 180.1514.



4.5.3. (*R,*S**)-1-(3-Methoxy-1-cyclohexen-2-yl)-2,2-dimethyl-1-propanol [(*R**,*S**)-19b].** Colourless oil, t_r 9.8; R_f 0.28 (hexane/ethyl acetate: 7:3); ν (film) 3450 (OH), 2868 (OMe), 1659 (HC═C), 1090, 1070 cm^{-1} (CO); δ_H ($CDCl_3$) 0.93 (9H, s, CMe_3), 1.45–1.70, 1.90–2.20 (4 and 3H respectively, 2m, 3×CH_2 and OH), 3.36 (3H, s, OMe), 3.50–3.55 (1H, m, C*H*OMe), 3.89 (1H, s, C*H*OH), 5.98 (1H, t, J=3.8 Hz, HC═C); δ_C ($CDCl_3$) 16.85, 24.95, 25.55, 26.10 (3C), 35.95, 56.75, 76.10, 78.75, 128.20, 140.80; *m/z* 180 (M^+-H_2O, <1%), 141 (11), 110 (28), 109 (100), 105 (14), 92 (12), 91 (27), 81 (81), 79 (67), 77 (16), 73 (16), 67 (13), 65 (11), 57 (61), 55 (24), 53 (24), 43 (30) 41 (95); HRMS: M^+-H_2O, found 180.1499. $C_{12}H_{20}O$ requires 180.1514.

4.5.4. (*R,*R**)-1-(3-Methoxy-1-cyclohexen-2-yl)-1-phenylmethanol [(*R**,*R**)-19c].** Colourless oil, t_r 12.3; R_f 0.29 (hexane/ethyl acetate: 8:2); ν (film) 3470 (OH), 3084, 3059, 3026, 1600, 1482, 1449 (HC═C), 2863 (OMe), 1089, 1077, 1062, 1017 cm^{-1} (CO); δ_H ($CDCl_3$) 1.45–2.20 (6H, m, 3×CH_2), 3.22 (3H, s, OMe), 3.55–3.60 (1H, m, C*H*OMe), 4.12 (1H, d, J=7.3 Hz, OH), 5.20 (1H, d, J=7.3 Hz, C*H*OH), 6.01 (1H, t, J=3.7 Hz, CH_2CH═C), 7.20–7.40 (5H, m, ArH); δ_C ($CDCl_3$) 18.1, 25.25, 26.20, 55.8, 74.6, 78.9, 125.45, 126.55, 127.95 (2C), 130.8 (2C), 138.4, 143.5; *m/z* 218 (M^+, <1%), 187 (14), 186 (95), 185, (42), 168 (31), 167 (30), 158 (14), 157 (39), 141 (15), 129 (23), 128 (20), 115 (24), 111 (81), 109 (14), 105 (100), 91 (41), 81 (24), 79 (79), 78 (16), 77 (73), 55 (20), 53 (21), 52 (39), 45 (27), 43 (17), 41 (48); HRMS: M^+, found 218.1309. $C_{14}H_{18}O_2$ requires 218.1307.

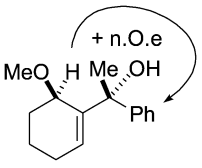
4.5.5. (*R,*S**)-1-(3-Methoxy-1-cyclohenen-2-yl)-1-phenylmethanol [(*R**,*S**)-19c].** Colourless oil, t_r 12.5; R_f 0.18 (hexane/ethyl acetate: 8:2); ν (film) 3415 (OH), 3084, 3059, 3027, 1493, 1453 (HC═C), 2862 (OMe), 1089, 1071 cm^{-1} (CO); δ_H ($CDCl_3$) 1.50–1.70, 1.85–2.10 (3 and 3H, respectively, 2m, 3×CH_2), 3.26 (1H, s, OH), 3.34 (3H, s, OMe), 3.65–3.70 (1H, m, C*H*OMe), 5.32 (1H, s, C*H*OH), 5.65–5.70 (1H, m, CH_2CH═C), 7.25–7.35 (5H, m, ArH); δ_C ($CDCl_3$) 17.7, 25.1, 26.1, 56.2, 75.8, 76.2, 127.2, 127.3, 127.5, 128.0, 128.1 (2C), 139.6, 142.25; *m/z* 218 (M^+, <1%), 186 (71), 185, (33), 168 (21), 167 (23), 158 (13), 157 (29), 141 (13), 129 (23), 128 (16), 115 (22), 111 (67), 109 (11), 105 (100), 91 (32), 81 (19), 79 (55), 78 (19), 77 (81), 55 (15), 53 (17), 52 (12), 51 (32), 45 (24), 43 (13), 41 (34); HRMS: M^+, found 218.1308. $C_{14}H_{18}O_2$ requires 218.1307.



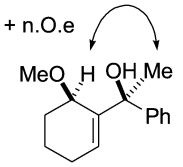
4.5.6. 3-(3-Methoxy-1-cyclohexen-2-yl)pentan-3-ol (19d). Pale yellow oil, t_r 7.2; R_f 0.18 (hexane/ethyl acetate: 8:2); ν (film) 3500 (OH), 3044 (HC═C), 2832 (OMe), 1190, 1159, 1076, 1058 cm^{-1} (CO); δ_H ($CDCl_3$) 0.78, 0.85 (3 and 3H, respectively, 2t, J=7.3 Hz, CMe), 1.35–1.65, 1.95–2.20 (8 and 3H, respectively, 2m, 5×CH_2 and OH), 3.34 (3H, s, OMe), 3.80–3.85 (1H, m, CHO), 5.68 (1H, t, J=3.7 Hz, HC═C); δ_C ($CDCl_3$) 7.55, 8.35, 16.65, 25.3, 25.45, 31.75, 33.3, 55.4, 73.55, 77.6, 126.8, 139.2; *m/z* 180 (M^+-H_2O, <1%), 169 (22), 137 (88), 109 (15), 91 (15), 79 (14), 67 (15), 59 (10), 57 (100), 55 (12), 45 (12), 43 (17), 41 (34).; HRMS: M^+-H_2O, found 180.1518. $C_{12}H_{20}O$ requires 180.1514.

4.5.7. 1-(3-Methoxy-1-cyclohexen-2-yl)cyclohexanol (19e). Pale yellow oil, t_r 9.4; R_f 0.31 (hexane/ethyl acetate: 8:2); ν (film) 3471 (OH), 2860 (OMe), 1189, 1090, 1066 cm^{-1} (CO); δ_H ($CDCl_3$) 1.25–2.20 (17H, m, 8×CH_2 and OH), 3.36 (3H, s, OMe), 3.95–4.00 (1H, s, CHO), 5.88 (1H, t, J=4.0 Hz, HC═C); δ_C ($CDCl_3$) 17.1, 22.2, 22.3, 25.35, 25.85 (2C), 36.7, 37.8, 55.4, 73.1, 73.75, 126.05, 141.8; *m/z* 210 (M^+, 2%), 178 (24), 161 (11), 160 (64), 149 (17), 145 (23), 136 (17), 135 (37), 132 (15), 131 (27), 121 (11), 119 (11), 118 (13), 117 (44), 115 (12), 109 (19), 108 (55), 107 (25), 105 (17), 104 (25), 94 (16), 93 (16), 92 (16), 91 (55), 81 (33), 80 (24), 79 (63), 78 (14), 77 (33), 67 (26), 65 (15), 55 (40), 53 (25), 51 (17), 45 (15), 43 (31), 42 (11), 41 (100), 40 (11); HRMS: M^+ found 210.1621. $C_{13}H_{22}O_2$ requires 210.1620.

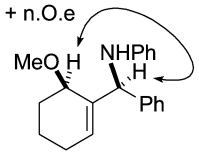
4.5.8. (*R,*R**)-1-(3-Methoxy-1-cyclohexen-2-yl)-1-phenylethanol [(*R**,*R**)-19f].** Colourless oil, t_r 13.1; R_f 0.59 (hexane/ethyl acetate: 8:2); ν (film) 3450 (OH), 3056, 3022, 1599 (HC═C), 2831 (OMe), 1091, 1068, 1058 cm^{-1} (CO); δ_H ($CDCl_3$) 1.30–2.20 (9H, m, 3×CH_2 and CMe), 3.05 (3H, s, OMe), 3.35–3.40 (1H, m, CHO), 4.80 (1H, s, OH), 6.14 (1H, t, J=7.9 Hz, CH_2CH═C), 7.10–7.35 (5H, m, ArH); δ_C ($CDCl_3$) 17.55, 25.45, 26.0, 29.5, 55.65, 75.65, 77.6, 125.0 (2C), 126.1, 127.2, 127.95 (2C), 140.2, 148.6; *m/z* 217 (M^+−Me, 11%), 185 (18), 182 (30), 167 (42), 165 (15), 157 (14), 141 (13), 129 (13), 128 (13), 123 (12), 115 (14), 111 (19), 105 (35), 91 (28), 83 (14), 79 (23), 77 (37), 51 (18), 45 (13), 43 (100), 41 (20); HRMS: M^+-CH_3 found 217.1221. $C_{14}H_{17}O_2$ requires 217.1228.



4.5.9. (R^*,S^*)-1-(3-Methoxy-1-cyclohexen-2-yl)-1-phenylethanol [(R^*,S^*)-19f]. Colourless oil, t_r 13.3; R_f 0.36 (hexane/ethyl acetate: 8:2); ν (film) 3376 (OH), 3010, 1601 (HC=C), 1095 cm^{-1} (CO); δ_H ($CDCl_3$) 1.40–2.10 (9H, m, 3×CH_2 and CMe), 3.29 (3H, s, OMe), 3.95–4.00 (1H, m, CHO), 4.08 (1H, s, OH), 5.32 (1H, t, J=4.0 Hz, CH_2CH=C), 7.10–7.40 (5H, m, ArH); δ_C ($CDCl_3$) 17.15, 25.3, 26.05, 28.9, 55.65, 74.35, 77.6, 124.35, 126.35 (2C), 126.45, 127.7 (2C), 142.0, 147.0; m/z 217 (M^+–Me, 14%), 185 (19), 182 (31), 167 (45), 165 (17), 152 (10), 141 (16), 129 (14), 128 (13), 115 (16), 111 (17), 105 (36), 103 (12), 91 (26), 89 (11), 82 (12), 79 (21), 78 (11), 77 (46), 51 (21), 45 (14), 43 (100), 41 (21); HRMS: M^+-CH_3 found 217.1229. $C_{14}H_{17}O_2$ requires 217.1228.

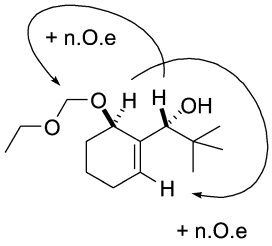


4.5.10. (R^*,S^*)-*N*-Phenyl-*N*-[1-(3-methoxy-1-cyclohexen-2-yl)-1-phenyl]methylamine [(R^*,S^*)-19g]. Yellow oil, t_r 17.05; R_f 0.71 (hexane/ethyl acetate: 8:2); ν (film) 3403 (NH), 3055, 3024, 1600, 1502, 1450 (HC=C), 2863 (OMe), 1076 cm^{-1} (CO); δ_H ($CDCl_3$) 1.30–2.20 (6H, m, 3×CH_2), 3.31 (3H, s, OMe), 3.50–3.55 (1H, m, CHO), 5.03 (1H, s, CHN), 4.95 (1H, s, NH), 5.89 (1H, t, J=3.9 Hz, CH_2CH=C), 6.90–7.50 (10H, m, ArH); δ_C ($CDCl_3$) 17.3, 25.4, 26.1, 56.20, 63.90, 73.55, 112.95 (2C), 113.7 (2C), 117.75, 120.85, 127.5, 128.2 (2C), 128.75 (2C), 129.0, 141.85, 147.45; m/z 293 (M^+, 28%), 261 (21), 260 (27), 201 (11), 200 (15), 182 (18), 171 (18), 170 (18), 169 (100), 168 (40), 167 (31), 154 (13), 153 (13), 152 (10), 142 (11), 141 (59), 129 (21), 128 (23), 115 (29), 109 (11), 104 (16), 93 (38), 92 (14), 91 (87), 78 (10), 77 (69), 71 (14), 67 (18), 66 (16), 65 (24), 51 (25), 45 (17), 41 (39); HRMS: M^+ found 293.1779. $C_{20}H_{23}NO$ requires 293.1780.



4.5.11. 3-(Ethoxymethoxy)cyclohexene (19h). Yellow oil, t_r 7.1; R_f 0.58 (hexane/ethyl acetate: 7:3); ν (film) 3028, 1651 (HC=C), 1108, 1065, 1038 cm^{-1} (CO); δ_H ($CDCl_3$) 1.13 (3H, t, J=7.0 Hz, Me), 1.50–1.95 [6H, m, $(CH_2)_3$], 3.50–3.60 (2H, m, CH_2Me), 4.00–4.05 (1H, m, CHO), 4.65–4.75 (2H, m, OCH_2O), 5.65–5.80 (2H, m, CH=CH); δ_C ($CDCl_3$) 14.9, 18.95, 24.9, 28.85, 62.8, 70.25, 93.3, 127.85, 130.55; m/z 127 (M^+−Et, <1%), 110 (10), 97 (13), 84 (15), 81 (52), 80 (11), 79 (30), 73 (34), 70 (10), 59 (100), 55 (11), 53 (13), 41 (52); HRMS: M^+ found 156.1145. $C_9H_{16}O_2$ requires 156.1150.

4.5.12. (R^*,R^*)-1-(3-Ethoxymethoxy-1-cyclohexen-2-yl)-2,2-dimethyl-1-propanol [(R^*,R^*)-19i]. Pale yellow oil, t_r 11.94; R_f 0.76 (hexane/ethyl acetate: 7:3); ν (film) 3504 (OH), 2869 (OCH_2), 1650 (HC=C), 1180, 1105, 1091, 1012 cm^{-1} (CO); δ_H ($CDCl_3$) 0.92 (9H, s, CMe_3), 1.22 (3H, t, J=7.0 Hz, $MeCH_2$), 1.55–1.80, 2.00–2.20 [3 and 3H, respectively, 2m, $(CH_2)_3$], 3.35 (1H, s, OH), 3.60–3.70 (2H, m, CH_2Me), 3.83 (1H, s, CHOH), 4.35–4.40 (1H, m, $CHOCH_2$), 4.76, 4.82 (1 and 1H, respectively, 2d, J=6.7 Hz, OCH_2O), 5.75–5.80 (1H, m, CH=C); δ_C ($CDCl_3$) 15.05, 16.8, 24.9, 26.65 (3C), 27.65, 36.0, 64.15, 72.3, 84.85, 94.15, 131.6, 136.05; m/z 185 (M^+−Bu^t, 1%), 139 (63), 111 (31), 110 (22), 109 (100), 91 (11), 81 (53), 79 (42), 67 (17), 59 (41), 57 (43), 55 (13), 43 (27), 41 (60); HRMS: $M^+-C(CH_3)_3$ found 185.1170. $C_{10}H_{17}O_3$ requires 185.1178.



4.5.13. (R^*,S^*)-1-(3-Ethoxymethoxy-1-cyclohexen-2-yl)-2,2-dimethyl-1-propanol [(R^*,S^*)-19i]. Pale yellow oil, t_r 12.01; R_f 0.55 (hexane/ethyl acetate: 7:3); ν (film) 3470 (OH), 2862 (OCH_2), 1650 (HC=C), 1181, 1101, 1028 cm^{-1} (CO); δ_H ($CDCl_3$) 0.93 (9H, s, CMe_3), 1.24 (3H, t, J=7.0 Hz, $MeCH_2$), 1.55–1.70, 1.95–2.15 [4 and 3H, respectively, 2m, $(CH_2)_3$ and OH], 3.60–3.80 (2H, m, CH_2Me), 3.88 (1H, s, CHOH), 3.90–3.95 (1H, m, $CHOCH_2$), 4.68, 4.79 (1 and 1H, respectively, 2d, J=7.3 Hz, OCH_2O), 6.00–6.05 (1H, m, CH=C); δ_C ($CDCl_3$) 15.05, 16.7, 24.8, 26.05 (3C), 27.4, 36.0, 63.4, 72.5, 78.25, 93.85, 128.65, 140.60; m/z 185 (M^+−Bu^t, 3%), 139 (77), 110 (18), 109 (100), 81 (40), 79 (38), 67 (10), 59 (40), 57 (43), 43 (21), 41 (55); HRMS: $M^+-C(CH_3)_3$ found 185.1169. $C_{10}H_{17}O_3$ requires 185.1178.

4.5.14. 3-(3-Ethoxymethoxy-1-cyclohexen-2-yl)pentan-3-ol (19j). Pale yellow oil, t_r 13.05; R_f 0.19 (hexane/ethyl acetate: 8:2); ν (film) 3506 (OH), 2878 (OCH_2), 1650 (HC=C), 1180, 1159, 1103, 1027 cm^{-1} (CO); δ_H ($CDCl_3$) 0.78, 0.85 (3 and 3H, respectively, 2t, J=7.6 Hz, 2×$MeCH_2$C), 1.22 (3H, t, J=6.9 Hz, $MeCH_2O$), 1.25–1.70, 2.00–2.15 [7 and 3H, respectively, 2m, $(CH_2)_3$ and CH_2CCH_2], 3.02 (1H, s, OH), 3.64 (2H, q, J=6.9 Hz, OCH_2Me), 4.25–4.30 (1H, m, CHO), 4.73, 4.79 (1 and 1H, respectively, 2d, J=7.0 Hz, OCH_2O), 5.70–5.75 (1H, m, CH=C); δ_C ($CDCl_3$) 7.65, 8.15, 14.95, 16.4, 25.2, 28.1, 32.5, 33.0, 64.1, 71.0, 77.6, 94.2, 127.05, 139.25; m/z 213 (M^+−Et, 2%), 167 (48), 138 (11), 137 (100), 109 (20), 79 (15), 67 (13), 59 (29), 57 (84), 55 (11), 43 (17), 41 (26); HRMS: $M^+-CH_2CH_3$ found 213.1479. $C_{12}H_{21}O_3$ requires 213.1491.

4.5.15. 1-(3-Ethoxymethoxy-1-cyclohexen-2-yl)cyclopentan-1-ol (19k). Colourless oil, t_r 9.3; R_f 0.40 (hexane/ethyl acetate: 8:2); ν (film) 3463 (OH), 2868 (OCH_2), 1650 (HC=C), 1181, 1101, 1032 cm^{-1} (CO); δ_H ($CDCl_3$) 1.22 (3H, t, J=6.8 Hz, Me), 1.50–2.20 [14H, m, $(CH_2)_3$ and $(CH_2)_4$], 3.20 (1H, s, OH), 3.65 (2H, q, J=6.8 Hz, CH_2Me), 4.35–4.40 (1H, m, CHO), 4.75, 4.84 (1 and 1H, respectively, 2d, J=7.0 Hz, OCH_2O), 5.95–6.00 (1H, m,

CH═C); δ_C (d_6-DMSO) 14.4, 15.9, 22.05, 24.8, 27.4, 31.8, 32.25, 62.4, 69.45, 82.85, 93.15, 127.2, 142.05; *m/z* 193 [$M^+-(Et+H_2O)$, <1%], 149 (12), 148 (92), 147 (37), 146 (100), 145 (15), 133 (32), 131 (57), 120 (21), 119 (32), 118 (24), 117 (53), 115 (15), 107 (19), 106 (17), 105 (42), 104 (23), 93 (16), 92 (23), 91 (83), 81 (19), 80 (30), 79 (53), 78 (18), 77 (28), 67 (39), 65 (16), 59 (27), 55 (12), 53 (11), 51 (11), 41 (52); HRMS: M^+ found $M^+-(OCH_2CH_3+H_2O)$ 117.1258. $C_{12}H_{17}O$ requires 177.1279.

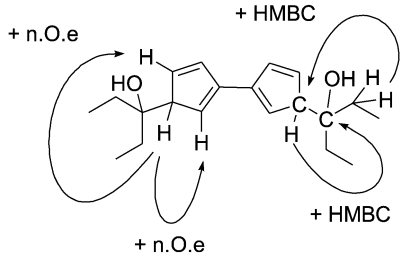
4.5.16. 1-(3-Ethoxymethoxy-1-cyclohexen-2-yl)cyclohexan-1-ol (19l). Pale yellow oil, t_r 9.7; R_f 0.43 (hexane/ethyl acetate: 8:2); ν (film) 3487 (OH), 3047, 1645 (HC═C), 2861 (OCH_2), 1180, 1102, 1026 cm^{-1} (CO); δ_H ($CDCl_3$) 1.22 (3H, t, *J*=7.0 Hz, Me), 1.45–1.70, 1.85–2.50 [13 and 3H, respectively, 2m, $(CH_2)_3$ and $(CH_2)_5$], 3.15 (1H, s, OH), 3.60–3.70 (2H, m, CH_2Me), 4.40–4.45 (1H, m, CHO), 4.73, 4.83 (1 and 1H, respectively, 2d, *J*=7.3 Hz, OCH_2O), 5.92 (1H, t, *J*=3.7 Hz, CH═C); δ_C ($CDCl_3$) 14.9, 16.9, 22.2, 25.3, 25.8 (2C), 28.3, 37.2, 37.3, 64.15, 71.05, 73.2, 94.0, 126.55, 141.85; *m/z* 254 (M^+, 1%), 208 (14), 179 (12), 178 (86), 162 (13), 161 (30), 160 (34), 150 (18), 149 (44), 145 (10), 136 (35), 135 (66), 133 (11), 131 (18), 122 (17), 121 (19), 120 (14), 119 (11), 117 (23), 109 (34), 108 (97), 107 (45), 105 (15), 104 (18), 97 (16), 95 (30), 94 (44), 93 (25), 92 (15), 91 (42), 82 (10), 81 (62), 80 (37), 79 (92), 78 (15), 77 (33), 69 (15), 67 (42), 65 (14), 59 (49), 55 (66), 53 (22), 43 (45), 42 (12), 41 (100); HRMS: M^+ found 254.1878. $C_{15}H_{26}O_3$ requires 254.1882.

4.5.17. 1-Trimetilsilylcyclohenene (22). Colourless, t_r 9.1; R_f 0.84 (hexane); ν (film) 1600 (HC═C), 1247, 833, 750 cm^{-1} [$Si(CH_3)_3$]; δ_H ($CDCl_3$) 0.05 (9H, d, *J*=4.9 Hz, 3×Me), 1.25–2.05, (8H, m, $(CH_2)_4$], 5.90–5.95 (1H, m, CH═C); δ_C ($CDCl_3$) −0.40 (2C), −0.25, 20.75, 25.70, 26.25, 27.95, 134.65, 141.25; *m/z* 154 (M^+, 5%), 80 (15), 73 (100); HRMS: M^+ found 154.1183. $C_9H_{18}Si$ requires 154.1178.

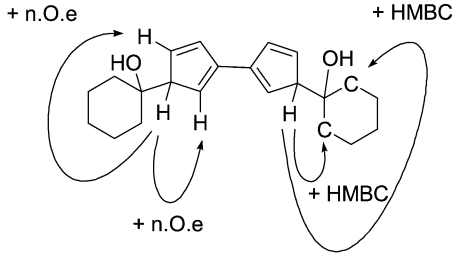
4.5.18. 3-(3-Methoxy-1-cyclopenten-2-yl)pentan-3-ol (24a). Colourless oil, t_r 11.1; R_f 0.67 (hexane/ethyl acetate: 7:3); ν (film) 3439 (OH), 3057 (HC═C), 2854 (OMe), 1080, 1024 cm^{-1} (CO); δ_H ($CDCl_3$) 0.77, 0.89 (3 and 3H, respectively, 2t, *J*=7.3 Hz, CMe), 1.55–1.70 (4H, m, 2×CH_2Me), 1.80–1.90, 2.10–2.30, 2.45–2.55 (1, 2 and 1H, respectively, 3m, $(CH_2)_2$), 3.33 (3H, s, OMe), 3.61 (1H, s, OH), 3.80–3.85 (1H, m, CHO), 5.65–5.70 (1H, m, HC═C); δ_C ($CDCl_3$) 7.60, 8.40, 29.0, 29.9, 31.25, 32.55, 56.0, 75.57, 87.3, 129.40, 146.35; *m/z* 166 (M^+-H_2O, <1%), 155 (11), 123 (37), 95 (20), 57 (100), 41 (16); HRMS: M^+, found 184.1486. $C_{11}H_{20}O_2$ requires 184.1463.

4.5.19. 1-(3-Methoxy-1-cyclopenten-2-yl)cyclohexan-1-ol (24b). Colourless oil, t_r 11.05; R_f 0.56 (hexane/ethyl acetate: 7:3); ν (film) 3506 (OH), 3058 (HC═C), 2853 (OMe), 1085 cm^{-1} (CO); δ_H ($CDCl_3$) 1.35–1.90, 2.15–2.45 (11 and 3H, respectively, 2m, 7×CH_2), 3.33 (3H, s, Me), 3.47 (1H, s, OH), 4.55–4.60 (1H, m, CHO), 5.75–5.80 (1H, m, HC═C); δ_C ($CDCl_3$) 22.25, 22.3, 25.9, 29.2, 29.9, 36.65, 37.7, 56.05, 70.85, 86.7, 128.7, 148.2; *m/z* 196 (M^+, 2%), 164 (35), 146 (32), 131 (25), 121 (25), 118 (11), 117 (29), 109 (11), 108 (14), 107 (13), 105 (14), 97 (20), 95 (26), 94 (89), 93 (53), 92 (15), 91 (41), 81 (30), 80 (52), 79 (53), 78 (15), 77 (31), 67 (45), 66 (46), 65 (39), 55 (64), 53 (26), 51 (18), 43 (31), 42 (13), 41 (100), 40 (23); HRMS: M^+, found 196.1464. $C_{12}H_{20}O_2$ requires 196.1463.

4.5.20. 5,5′-Di(1-ethyl-1-hidroxypropyl)-2,2′-bicyclopenta-1,3-diene (25a). Colourless oil, t_r 20.7; R_f 0.55 (hexane/ethyl acetate: 7:3); ν (film) 3371 (OH), 3058, 3031, 1633 (HC═C), 1128 cm^{-1} (CO); δ_H ($CDCl_3$) 0.90–1.00 (14H, m, 4×Me and 2×OH), 1.55–1.85 (8H, m, 4×CH_2), 3.60–3.65 (2H, m, 2×CHCO), 6.15–6.20, 7.15–7.20 (2 and 4H, respectively, 2m, 6×HC═C); δ_C ($CDCl_3$) 8.15 (2C), 8.6 (2C), 29.15 (2C), 29.7 (2C), 46.95 (2C), 77.0 (2C), 125.35 (2C), 128.9 (2C), 131.0 (2C), 137.45 (2C); *m/z* 266 ($M^+-2\times H_2O$, 1%), 198 (20), 170 (15), 169 (100), 141 (25), 129 (15), 128 (34), 87 (45), 69 (11), 57 (93), 45 (65), 43 (15), 41 (47); HRMS: $M^+-2\times H_2O$, found 266.2035. $C_{20}H_{26}$ requires 266.2034.



4.5.21. 5,5′-Di(1-hidroxycyclohex-1-yl)-2,2′-bicyclopenta-1,3-diene (25b). Colourless oil, t_r 19.5; R_f 0.41 (hexane/ethyl acetate: 7:3); ν (film) 3382 (OH), 3028 (HC═C), 1147 cm^{-1} (CO); δ_H ($CDCl_3$) 1.25–1.95 (22H, m, 10×CH_2 and 2×OH), 3.50–3.55 (2H, m, 2×CHCO), 6.15–6.20, 7.15–7.20 (2 and 4H, respectively, 2m, 6×HC═C); δ_C ($CDCl_3$) 22.25 (2C), 22.4 (2C), 25.7 (2C), 37.7 (2C), 38.0 (2C), 50.65 (2C), 73.4 (2C), 125.39 (2C), 128.6 (2C), 131.1 (2C), 136.8 (2C); *m/z* 210 {$M^+-[(CH_2)_5COH+OH]$, 100%}, 168 (10), 167 (48), 154 (14), 153 (10), 142 (30), 141 (24), 129 (17), 128 (74), 99 (38), 81 (41), 55 (12); HRMS: $M^+-2\times H_2O$, found 290.2042. $C_{22}H_{26}$ requires 290.2034.



4.5.22. Isolation of 2-(1-cyclohexen-1-yl)-2-cyclohexen-1-ol (37). *Acid deprotection of compound **19l**.* To a solution of compound **19l** (0.25 mmol) in acetone (5 mL) was slowly added HCl (2 M, 5 mL) at room temperature. After 1 h, a solution of $NaHCO_3$ (sat) until pH>7. The resulting mixture was extracted with ethyl acetate (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvents were evaporated (15 Torr) to give the pure title compound **37**. Yield is included in the text. Physical, spectroscopic and analytical data, follow: Yellow oil, t_r 7.38; R_f 0.30 (hexane/ethyl acetate: 8:2); ν (film) 3381 (OH), 3036 (HC═C), 1056 cm^{-1} (CO); δ_H ($CDCl_3$) 1.50–2.20 (15H, m, 7×CH_2

and OH), 4.50–4.55 (1H, m, CHO), 5.83, 6.00–6.05 (1 and 1H, respectively, t and m, respectively, J=4.0 Hz, 2×HC=C); δ_C ($CDCl_3$) 16.85, 22.3, 22.9, 25.75, 25.8, 25.85, 31.15, 63.25, 122.85, 124.55, 134.9, 139.05; *m/z* 178 (M^+, 28%), 149 (100), 135 (20), 131 (10), 121 (13), 108 (13), 107 (20), 94 (22), 93 (25), 92 (31), 91 (54), 81 (58), 80 (30), 79 (78), 78 (25), 77 (38), 67 (56), 65 (23), 55 (32), 53 (28), 52 (18), 42 (20), 41 (75), 40 (22); HRMS: M^+, found 178.1350 $C_{12}H_{18}O$ requires 178.1358.

Acknowledgements

This work was financially supported by the DGICYT (Project PB97-0133) from the Spanish Ministerio de Educación, Cultura y Deporte. I. G. thanks Spanish Ministerio de Ciencia y Tecnología for a predoctoral fellowship. We thank Dr E. Lorenzo for nOe, NOESY, HMBC and HMQC measurements.

References

1. For reviews on functionalised organolithium compounds, see: (a) Nájera, C.; Yus, M. *Trends Org. Chem.* **1991**, *2*, 155–181. (b) Gray, M.; Tinkl, M.; Snieckus, V. *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 11, pp 1–92; *Comprehensive Organometallic Chemistry II*, Pergamon: Oxford, 1995; Vol. 11, pp 1–92. (c) Nájera, C.; Yus, M. *Recent Res. Dev. Org. Chem.* **1997**, *1*, 67–96. (d) Boudier, A.; Bromm, L. O.; Lozt, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 4414–4435.
2. For recent examples of β-anionic functionalised organolithium intermediates, see: (a) Yus, M.; Ramón, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 398–400. (b) Yus, M.; Foubelo, F. *Rev. Heteroatom. Chem.* **1997**, *17*, 73–107. (c) Ramón, D. J.; Yus, M. *Tetrahedron* **1998**, *54*, 5651–5666. (d) Foubelo, F.; Gutiérrez, A.; Yus, M. *Synthesis* **1999**, 503–514.
3. (a) Barluenga, J.; Yus, M.; Bernad, P. *J. Chem. Soc., Chem. Commun.* **1978**, 847. (b) Maguire, A. R. *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon: Oxford, 1995; Vol. 1, pp 589–671.
4. (a) Beak, P.; Carter, L. G. *J. Org. Chem.* **1981**, *46*, 2363–2373. (b) Schwerdtfeger, J.; Hoppe, D. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1505–1507. (c) Schwerdtfeger, J.; Kolczewski, S.; Weber, B.; Fröhlich, R.; Hoppe, D. *Synthesis* **1999**, 1573–1592. (d) Weber, B.; Schwerdtfeger, J.; Kolczewski, S.; Fröhlich, R.; Hoppe, D. *Synthesis* **1999**, 1593–1606. (e) Weber, B.; Schwerdtfeger, J.; Fröhlich, R.; Göhrt, A.; Hoppe, D. *Synthesis* **1999**, 1915–1924.
5. Calaza, M. I.; Paleo, M. R.; Sardina, F. J. *J. Am. Chem. Soc.* **2001**, *123*, 2095–2096.
6. (a) Corey, E. J.; Cane, D. E.; Libit, L. *J. Am. Chem. Soc.* **1971**, *93*, 7016–7021. (b) Barluenga, J.; Cantelli, R. M.; Flórez, J. *J. Org. Chem.* **1994**, *59*, 1586–1588. (c) Huerta, F. F.; Gómez, C.; Guijarro, A.; Yus, M. *Tetrahedron* **1995**, *51*, 3375–3388.
7. Corey, E. J.; Ulrich, P. *Tetrahedron Lett.* **1975**, 3685–3688.
8. Manning, M. J.; Raynolds, P. W.; Swenton, J. S. *J. Am. Chem. Soc.* **1976**, *98*, 5008–5009.
9. (a) Bachki, A.; Foubelo, F.; Yus, M. *Tetrahedron Lett.* **1994**, *35*, 7643–7646. (b) Bachki, A.; Foubelo, F.; Yus, M. *Tetrahedron* **1997**, *53*, 4921–4934.
10. Ficini, J.; Depezay, J.-C. *Tetrahedron Lett.* **1969**, 4797–4799.
11. (a) Kruithof, K. J. H.; Schmitz, R. F.; Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 3–6. (b) Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 1–21.
12. Ekogha, C. B. B.; Ruel, O.; Julia, S. A. *Tetrahedron Lett.* **1983**, *24*, 4825–4828.
13. Corey, E. J.; Lee, J. *J. Am. Chem. Soc.* **1993**, *115*, 8873–8874.
14. For reviews on arene-catalysed reductive lithiation, see: (a) Yus, M. *Chem. Soc. Rev.* **1996**, 155–161. (b) Ramón, D. J.; Yus, M. *Eur. J. Org. Chem.* **2000**, 225–237. (c) Yus, M. *Synlett* **2001**, 1197–1205.
15. For examples on reductive cleavage of allylic ketals, see: (a) Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1994**, *50*, 3437–3446. (b) Shin, J.; Qualls, M. M.; Boomer, J. A.; Robarge, J.; Thompson, D. H. *J. Am. Chem. Soc.* **2001**, *123*, 508–509.
16. Kim, K. M.; Chung, K. H.; Kim, J. N.; Ryu, E. K. *Synthesis* **1993**, 283–284.
17. Imamoto, T. In *Lanthanides in Organic Synthesis*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Academic: London, 1994; pp 67–74.
18. Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1999; pp 17–200.
19. Bates, R. B.; Kroposki, L. M.; Potter, D. E. *J. Org. Chem.* **1972**, *4*, 560–562.
20. (a) Johnson, R. P. *Chem. Rev.* **1989**, *89*, 1111–1124. (b) Johnson, R. P.; Shakespeare, W. C. *J. Am. Chem. Soc.* **1990**, *112*, 8578–8579.
21. (a) Alonso, F.; Lorenzo, E.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 3303–3306. (b) Lorenzo, E.; Alonso, F.; Yus, M. *Tetrahedron* **2000**, *56*, 1745–1757. (c) Lorenzo, E.; Alonso, F.; Yus, M. *Tetrahedron Lett.* **2000**, *41*, 1661–1665.
22. (a) Matsuzawa, S.; Isaka, M.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1989**, *30*, 1975–1978. (b) Reetz, M. T.; Wang, F.; Harms, K. *J. Chem. Soc., Chem. Commun.* **1991**, 1309–1311. (c) Arai, M.; Nemoto, T.; Ohashi, Y.; Nakamura, E. *Synlett* **1992**, 309–310.
23. (a) Rawal, V. H.; Dufor, C. *J. Am. Chem. Soc.* **1994**, *116*, 2613–2614. (b) Rawal, V. H.; Fabré, A.; Iwasa, S. *Tetrahedron Lett.* **1995**, *36*, 6851–6854.
24. Maerker, A. In *Lithium Chemistry. A Theoretical and Experimental Overview*; Sapse, A.-M., von Ragué Schleyer, P., Eds.; Wiley: New York, 1995; pp 477–577 and literature quoted therein.
25. Reeve, W.; Erikson, C. M.; Aluotto, P. F. *Can. J. Chem.* **1979**, *57*, 2747–2754.
26. Streitwieser, A.; Nebenzahl, L. L. *J. Am. Chem. Soc.* **1976**, *98*, 2188–2190.
27. Work is in progress in order to make synthetically useful this reductive cleavage lithiation of dicyclopendiene derivatives.
28. For an example on regioselectivity dehydration of tertiary alcohols in the presence of secondary alcohols, see: Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1994**, *24*, 7307–7314.
29. Prieto, O.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2000**, *11*, 1629–1644.