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THE INFLUENCE OF LITHIUM COMPLEXING AGENTS ON THE REGIOSELECTIVITY OF REDUCTIONS OF SUBSTITUTED 2-CYCLOHEXENONES BY $LiAlH_4$ and $LiBH_4$

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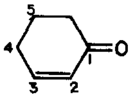
Abstract—A reversal of regioselectivity of $LiAlH_4$ or $LiBH_4$ reduction of 2-cyclohexenone induced by addition of [2.1.1]-cryptand to the reaction medium is accompanied by a rate decrease. In the absence of the cryptand, carbonyl attack predominates ($C_1:C_3 = 86:14$ with $LiAlH_4$ in THF). In the presence of the cryptand, double bond attack is favoured ($C_1:C_3 = 14:86$). This effect is larger with $LiAlH_4$ than with $LiBH_4$. This trend is general in the case of five substituted 2-cyclohexenones. Using 12-crown-4 as a Li^+ coordinator, a change in regioselectivity occurs but it is less pronounced than with the cryptand.

The electrophilic assistance of Li^+ cation in the reduction of carbonyl compounds by $LiAlH_4$ or $LiBH_4$ is quite well documented.[1-6] The addition of Li^+ complexing agents such as cryptands[1-4] crown ethers[5] or polyamines[6] to the reaction medium induces a notable rate decrease. However, the magnitude of this rate decrease depends upon the nature of the carbonyl compound.[3-5] More particularly, we have shown that although alicyclic ketone reduction is very markedly slowed, this is not the case for benzaldehyde or substituted acetophenones,[4] for which the rate decrease is less important.

For α, β-unsaturated carbonyl compounds such as 2-cyclohexenone **1a**, a theoretical approach[7] has indicated that the expected rate decrease of $LiAlH_4$ or $LiBH_4$ reduction when [2.1.1]cryptand[8] is added to the reaction mixture should be accompanied by a change in regioselectivity. When Li^+ participates in the reaction process, C_1 attack must predominate, while when the cation is cryptated, C_3 attack is favoured. In a preliminary communication[9] we have shown that this occurs.



1a

The present paper is devoted to a generalization of these results. Firstly, three specific Li^+ complexing agents [2.1.1]-cryptand **2**,[8] 12-crown-4 **3**,[10] and tetramethylethylenediamine **4** (TMEDA) are compared for their regioselectivity on $LiAlHI_4$ reduction **1a** as well as of 3-methyl 2-cyclohexenone **1b**.

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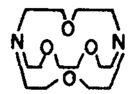

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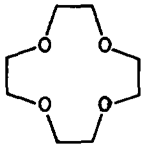

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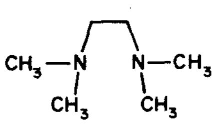
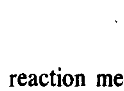


$CH_3—N(CH_3)—CH_2CH_2—N(CH_3)—CH_3$

Furthermore, the influence of 2-cyclohexenone substituents on the regioselectivities of $LiAlH_4$ and $LiBH_4$ reductions with or without added [2.1.1] are compared. The selected α-enones are the following: 3-methyl 2-cyclohexenone **1b**, 5,5-dimethyl 2-cyclohexenone **1c**, isophorone **1d**, 2-methyl 2-cyclohexenone **1e** and 4,4-dimethyl-2-cyclohexenone **1f**.

1b



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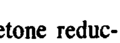
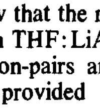
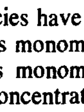


1d



1e



1f

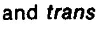
THF was used as reaction medium as ketone reductions are first order in [$LiAlH_4$] and [ketone] in this solvent, $LiAlH_4$ being monomeric.[5,6] Solution structural studies show that the reducing species have well defined structures in THF: $LiAlH_4$ exists as monomeric, solvent separated, ion-pairs and $LiBH_4$ as monomeric contact ion-pairs[12] provided that the concentration is low enough. In diethyl ether, aggregation causes a more complicated kinetic law for the same reduction;[11] however, for comparison with previous results,[2,9] we have also studied a few reactions in Et_2O.

RESULTS

The expected products are allylic alcohols **5**, deriving from C_1 attack, and saturated ketones **6** and alcohols **7**, resulting from C_3 attack.

5

6



7 (*cis* and *trans*)

The allylic alcohol **5** is not reduced to the saturated alcohol **7**, in accordance with the Dilling and Plepys reaction scheme.[13]

The various compounds **5**–**7** have been synthetized by literature methods (see Experimental) and were analysed by GLC with an internal standard.

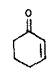
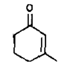
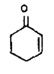
The reactions were run at room temperature, under nitrogen, by adding a THF solution of 0.0025 mole of 2-cyclohexenone **1** to a standardized solution of $LiAlH_4$[14] or $LiBH_4$ in this solvent; the final solutions were 0.08 M in each reactant (**1** and $LiAlH_4$ or $LiBH_4$). Occasionally, the complexing agent was added to the $LiAlH_4$ or $LiBH_4$ solution, which was then stirred for 30 min to 16 h before addition of **1**. The results are not dependent on the complexation time.

In Table 1 is shown the influence of the various coordinating agents **2**–**4** on $LiAlH_4$ reduction of **1a** and **1b** in THF and of **1a** in Et_2O.

In Table 2 are the results of $LiAlH_4$ reductions of **1a**–**f** in THF, with or without [2.1.1]; in Table 3 those of $LiBH_4$ reductions of **1a**, **b**, **d** under the same conditions.

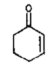
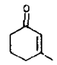
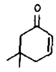
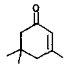
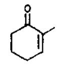
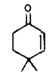
The addition of Li^+ coordinating agents to a THF or Et_2O solution of $LiAlH_4$ induces a sizeable rate decrease only in the case of [2.1.1] **2** (exp 1 and 2; 6 and 7; 9 and 10). The largest effect on C_1:C_3 attack ratio is also observed with this coordinating agent. With 12-crown-4

Table 1. Influence of Li^+ complexing agents on $LiAlH_4$ reduction of 2-cyclohexenones **1a** and **1b**

Exp. No.	α-enone	Coordinating agent	concent.	solvent	time (min)	yield%[a]	C_1 attack:C_3 attack
1	**1a** 	—	—	THF	1	>98	86:14
2	**1a**	[2.1.1] **2**	1.2 eq[b]	THF	1	85	14:86
3	**1a**	12-crown-4 **3**	1.2 eq[b]	THF	1	>98	75:25
4	**1a**	12-crown-4 **3**	5 eq[b]	THF	1	>98	62:38
5	**1a**	TMEDA **4**	10 eq	THF	1	>98	84:16
6	**1b** 	—	—	THF	1	>98	95:5
7	**1b**	[2.1.1] **2**	1.2 eq[b]	THF	15	50	24:76
8	**1b**	12-crown-4 **3**	2.5 eq[b]	THF	1	>98	88:12
9	**1a** 	—	—	Et_2O	1	>98	98:2
10	**1a**	[2.1.1] **2**	1.2 eq[b]	Et_2O	1	12	24:76
11	**1a**	[2.1.1] **2**	1.2 eq[b]	Et_2O	15	80	23:77
12	**1a**	12-crown-4 **3**	5 eq	Et_2O	1	90	54:46
13	**1a**	TMEDA **4**	10 eq	Et_2O	1	>98	96:4

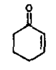
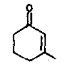
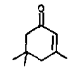
[a] Completion to 100% is starting **1**; total yield > 90% (relative to internal standard).
[b] The same result is obtained for either complexation time (30 min, 16 h).

Table 2. $LiAlH_4$ reduction of 2-cyclohexenones **1a**–**f** in THF 0.08 M at room temperature (molar ratio $LiAlH_4$:**1** ≃ 4)

Exp. No.	α-enone	Addend (1.2 eq)	Reaction time	Yield %[a]	%**5**	%**6**	%**7**	C_1 attack attack:C_3
1	**1a** 	—	1 min	>98	86	10	4	86:14[f]
2	**1a**	[2.1.1]	1 min[b]	85	14	50	36	14:86
6	**1b** 	—	1 min	>98	95	4	1[d]	95:5
7	**1b**	[2.1.1]	15 min	50	24	30	46[d]	24:76
14	**1b**	[2.1.1]	2 h	95	26	9	65[d]	26:74
15	**1c** 	—	1 min	90	58	5	37	58:42
16	**1c**	[2.1.1]	2 h	35	22	26	52	22:78
17	**1c**	[2.1.1]	8 h	90	20	8	72	20:80
18	**1d** 	—	1 h[c]	>98	84	16	—	84:16
19	**1d**	[2.1.1]	2 h	30	26	23	51[e]	26:74
20	**1d**	[2.1.1]	8 h	95	26	3	71[e]	26:74
21	**1e** 	—	1 min	>98	95	4	1	95:5
22	**1e**	[2.1.1]	5 min[b]	80	42	39	19	42:58
23	**1f** 	—	1 min	>98	>99	—	—	>99:1
24	**1f**	[2.1.1]	1 h	>98	45	10	45	45:55

[a] Completion to 100% is starting **1**; total yield >90% (relative to internal standard).
[b] When the reaction is run for 15 min, the yield is >98% and the C_1:C_3 attack ratio is the same.
[c] After 5 min, the yield is about 5–10%.
[d] *Trans*:*cis* ratio; 13:87 without [2.1.1] and 17:83 in the presence of [2.1.1].
[e] *Trans*:*cis* ratio; 70:30.
[f] Very close results are obtained in the literature (15).

Table 3. $LiBH_4$ reduction of 2-cyclohexenones **1a**, **b**, **d** in THF 0.08 M at room temperature (molar ratio $LiBH_4:1 \simeq 1$)

Exp. No.	α-enone		Addend (1.2 eq)	Reaction time	Yields %[a]	%5	%6	%7	C_1 attack : C_3 attack
25	1a		—	1 min	>98	52	—	48	52:48[b]
26	1a		[2.1.1]	15 min	5		undetermined		
27	1a		[2.1.1]	4 h	50[c]	12	49	39	12:88
28	1b		—	1 min	>98	63	13	24	63:37
29	1b		[2.1.1]	15 min	~2		undetermined		
30	1b		[2.1.1]	90 h	20	15	26	59	15:85
31	1d		—	30 min	55	61	—	39[d]	61:39
32	1d		—	1 h	80	62	—	38[d]	62:38
33	1d		[2.1.1]	120 h	10	13	22	65[e]	13:87

[a] Completion to 100% is starting **1**; total yield >90% (relative to internal standard).

[b] litt (15); same result.

[c] Enolization does not compete as CH_3I addition to the reaction mixture does not give rise to any other compound than **1**, **5**, **6** and **7**.

[d] *Trans*:*cis* alcohols ratio; 53:47.

[e] *Trans*:*cis* alcohols ratio; 75:25.

3, the $C_1:C_3$ attack ratio decrease depends on the nature of the solvent but, in no case, is any reversal in $C_1:C_3$ regioselectivity observed (exp 1,3 and 4; 6 and 8; 9 and 12). Furthermore this ratio varies with the ligand concentration in THF (exp 3 and 4). The addition of TMEDA **4** has a very weak influence, even in diethyl ether (exp 5 and 13).

All the $LiAlH_4$ reductions in THF without any Li^+ complexing agent are so fast, except with isophorone **1d**, that the rates cannot be compared. Although C_1 attack always predominates, the influence of substituents can be seen on the $C_1:C_3$ attack ratio which decreases in the following order: **1f** > **1b** ≃ **1e** > **1a** ≃ **1d** > **1c**. Therefore, relative to **1a**, two methyl groups on carbon 4 (**1f**, exp 23), as well as one CH_3 group on carbon 3 (**1b**) or on carbon 2 (**1e**, exp 6 and 21) decrease the amount of C_3 attack; two methyl groups on carbon 5 (**1c**, exp 15) decrease the amount of C_1 attack while, for **1d**, the two effects compensate each other so that the $C_1:C_3$ attack ratio is the same for **1a** and **1d** (exp 1 and 18).

In the presence of [2.1.1], C_3 attack always predominates. The reactions are slower, the relative rates being the following: **1a** > **1e** > **1f** > **1b** > **1c** ≥ **1d**. The $C_1:C_3$ attack ratio decreases according to the following sequence: **1f** ≃ **1e** > **1b** ≃ **1c** ≃ **1d** > **1a**. Relative to **1a** (exp 2), all the substituents decrease the amount of C_3 attack, the effect being larger when two methyl groups are on carbon 4 (**1f**) or one CH_3 on carbon 2 (**1e**, exp 22 and 24).

Some of the reactions with $LiBH_4$ have been described in the literature[2,15] and the authors have found that hydrolysis of the reaction medium induces some further reduction. We used experimental conditions where such a phenomenon does not occur as, when the reaction does not go to completion, we were able to identify the starting enones **1a**, **b**, **d** in the reaction mixture (exp 26, 27, 30 and 33).

The substituent effect is not very important. Without [2.1.1] the $C_1:C_3$ attack ratio is close to 60:40; in the presence of [2.1.1], the inversion of regioselectivity is observed as this ratio is about 15:85 for the three 2-cyclohexenones studied. The reactions are slower than with $LiAlH_4$ (exp 18 and 31), an effect most marked in the presence of [2.1.1] (exp 2 and 27; 7 and 30; 20 and 33). The fact that $LiAlH_4$ reductions are faster than $LiBH_4$ ones has some precedent in the literature.[16,17]

All our experimental results show that for $LiAlH_4$ or $LiBH_4$ reductions of 2-cyclohexenones **1**, $C_1:C_3$ attack ratio is strongly dependent upon the reaction medium. In diethyl ether, C_1 attack is essentially exclusive, as already pointed out in the literature,[2,9,18–21] and largely predominant with $LiAlH_4$ in THF. When the cation is cryptated, C_3 attack is preponderant with both reducing agent. Similar medium effects have been observed for $NaBH_4$ reduction of α-enones: Luche[22] has noticed an exclusive C_1 attack in methanol when adding lanthanide salts while, in pyridine, Jackson and Zurqiyah[23] observed only C_3 attack.

DISCUSSION

We have previously proposed an interpretation of the reduction of aliphatic or aromatic aldehydes and ketones in terms of Frontier Molecular Orbital treatment;[4,7] the closer the electrophile LUMO and nucleophile HOMO, the faster the reduction.

Kinetic effects

The influence of Li^+ is twofold: (a) by carbonyl complexation it lowers the electrophile LUMO level[4,7,24] to very close values whatever the carbonyl compound is; the kinetic effect is then rate enhancement. (b) By ionic association it also lowers the reducing agent HOMO level;[4] the kinetic effect is, on the opposite, a rate decrease.

The kinetic effect of [2.1.1] addition is a rate decrease[1,2,4] indicates that when Li^+ is cryptated the nucleophile and electrophile frontier orbitals levels are lying further apart than when Li^+ participates. LUMO lowering due to carbonyl complexation is thus larger than HOMO lowering due to ionic association.

The fast reactions we observed with 2-cyclohexenones **1** when the reduction takes place with the Li^+-complexed system are in line with this interpretation (see Tables 1–3). In the presence of [2.1.1], the behaviour of the α-enones is rather similar to that of aromatic ketones and aldehydes, the LUMO levels of which are quite close lying;[4,24,25] the reaction rate is not too strongly decreased, while we previously observed a greater influence of Li^+ complexation on aliphatic or alicyclic carbonyl compounds reactivity.[4]

Regioselectivity effects

Furthermore, in the case of carbonyl complexation of α-enones, another effect of lithium cation takes place. Calculations have shown that the regioselectivity of the reduction of these compounds depends upon the relative C_1 and C_3 atomic coefficients $|C|$ values in the LUMO. To the larger coefficient corresponds the predominating site of attack.[7,26] When Li^+ is complexed by the α-enone, $|C|_{C_1} > |C|_{C_3}$ and thus C_1 attack is favoured; according to the Li^+-carbonyl interaction strength, $|C|_{C_1} : |C|_{C_3}$ ratio changes and the stronger the interaction the larger the $C_1 : C_3$ attack ratio.[7] In the absence of such a complexation, as $|C|_{C_3} > |C|_{C_1}$,[7,26] predominating C_3 attack may be observed.

The strength of the carbonyl-Li^+ interaction will be strongly dependent upon the solvent, the nature of the complexing agent and upon the interaction between the Li^+ cation and the reducing agent.

Solvent effect

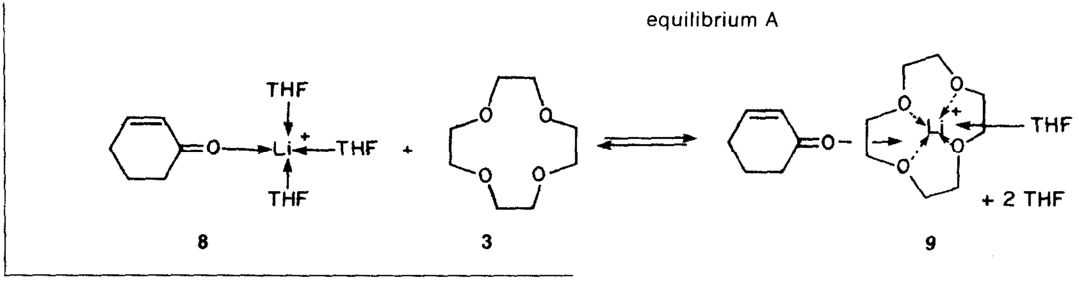
Everything being equal, the larger the solvent donicity[27] the weaker the Li^+-carbonyl interaction strength. In diethyl ether (D.N. = 19.2), Li^+ complexation interaction by the α-enone carbonyl group will be stronger than in THF (D.N. = 20.0) and significantly stronger than in pyridine (D.N. = 33.1). Thus, one can expect more C_1 attack in the less donating solvent. While **1a** reduction by $LiAlH_4$ or $LiBH_4$ in Et_2O gives practically only C_1 attack,[2] some C_3 attack takes place in THF; in pyridine, $NaBH_4$ reduction of **1b** only leads to the product of C_3 attack.[23] A similar trend, which can be interpreted on the same way, is observed for diisobutylaluminum hydride (DIBAH) reductions of **1a** in hexane, ether and THF.[28] The smaller solvent D.N., the larger the $C_1 : C_3$ attack ratio although, in this case, the carbonyl-aluminum interaction is involved.

We will not discuss the difference of rates observed in THF and Et_2O in the presence of [2.1.1], as, in Et_2O, the complex is poorly soluble.[5]

Complexing agent effect

As it is known that [2.1.1] is the most efficient complexing agent of Li^+,[8] the most significant results arise when the reactions are performed in its presence. Our previous results[9] are generalized. $C_1 : C_3$ attack ratio is inverted and the reaction rate is lowered when compared to the reduction without complexing agent.

12-Crown-4 **3** is less efficient than [2.1.1] **2** (Table 1); it induces a smaller change in the $C_1 : C_3$ attack ratio which is concentration-dependent. This indicates the intervention of at least two kinds of species; the 2-cyclohexenone-Li^+-THF solvated species **8** and the cyclohexenone-Li^+-12 crown-4 separated pair **9**† which are in equilibrium. Such an interpretation has some precedent in the literature, more especially for Na^+ and K^+ enolate–crown ether interactions.[29,30] However, in the case of lithium enolates, 12-crown-4 is unable to change the rate nor the regioselectivity of ethyl bromide alkylation of the acetoacetic ester lithium enolate in DEM.[31]



The regioselectivity changes are estimated in terms of transition states energy differences between C_1 and C_3 Attack $\Delta\Delta G^{\neq}$—in conditions where equilibrium A is strongly shifted to the right (5 eq of 12-crown-4) which means that **9** or Et_2O solvated analogous species is the only intervening one. The data are collected in Table 4.

It appears that $\Delta\Delta G^{\neq}_{[2.1.1]}$ is always larger than $\Delta\Delta G^{\neq}_{12\text{-}4}$, showing thus the greater efficiency of [2.1.1] as a ligand. Furthermore, 12-crown-4 and [2.1.1] efficiencies are larger in Et_2O than in THF, which is in agreement with a weaker Li^+–Et_2O interaction relative to Li^+–THF one.[12]

The regioselectivity change induced by TMEDA **4** addition is too close to experimental accuracy to be significant, indicative of a TMEDA-Li^+ interaction which is too weak in our cases (Et_2O or THF) to modify the relative LUMO coefficients. A different result merges from Corriu and Guerin's work[28] as TMEDA provokes a change in regioselectivity for **1a** reduction by DIBAH in hexane due to the low donicity of this solvent.

Reducing anion effect

The stronger the Li^+-anion association energy, the weaker the carbonyl-Li^+ complexation one. For tight or intimate ion pairs, complexation strength will be weaker than for loose or solvent separated ones; the $C_1 : C_3$ attack ratio will be smaller in the former case than in the latter. This is probably the reason why the reduction by $LiBH_4$ in THF (intimate ion pairs[12]) gives less C_1 attack than the reduction by $LiAlH_4$ (solvent separated ion pairs[12]).

Cyclohexenone substituents effects

Whatever the substituents on 2-cyclohexenone **1**, a net increase in C_3 attack is observed when Li^+ is cryptated, essentially due to a greater rate decrease of C_1 attack vs C_3 one.

The relative rates of reductions with AlH_4^-, which corresponds to reactions run in the presence of [2.1.1] (see Table 2), depend heavily on 2-cyclohexenone sub-

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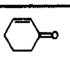
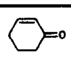
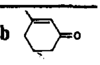
†According to Ref. 10*b*, we sketch the four oxygen atoms of the 12-crown-4 in a plane, leaving thus two free coordination sites, one for **1a**, one for a THF molecule.

Table 4. Energy differences $\Delta\Delta G^{\neq}$ (in kcal/mole) related to $LiAlH_4$ reductions—*solvent and coordinating agent effects*

α-enone solvent	**1a**  THF	**1a**  Et_2O	**1b**  THF
$LiAlH_4$			
$C_1:C_3$	86:14	98:2	95:5
$\Delta G^{\neq}{}_{Li}{}^{a}$	1.1	2.3	1.7
$LiAlH_4+[2.1.1]$			
$C_1:C_3$	14:86	23:77	26:74
$\Delta G^{\neq}{}_{[2.1.1]}{}^{a}$	−1.1	−0.7	−0.7
$LiAlH_4$ + 12-*crown*-4			
$C_1:C_3$	62:38	54:46	88:12
$\Delta G^{\neq}{}_{12-4}$	0.3	0.1	1.2
$\Delta\Delta G^{\neq}{}_{[2.1.1]}{}^{b}$	2.2	3.0	2.4
$\Delta\Delta G^{\neq}{}_{12-4}{}^{c}$	0.8	2.2	0.5

[a] Activation energy differences between C_1 and C_3 attack at 25°; $\Delta G^{\neq}{}_{Li}$ for $LiAlH_4$ reductions, $\Delta G^{\neq}{}_{2.1.1}$ for $LiAlH_4+[2.1.1]$ and $\Delta G^{\neq}{}_{12-4}$ for $LiAlH_4$ + 12-crown-4 ones.

[b] $\Delta\Delta G^{\neq}{}_{[2.1.1]} = \Delta G^{\neq}{}_{Li} - \Delta G^{\neq}{}_{[2.1.1]}$.

[c] $\Delta\Delta G^{\neq}{}_{12-4} = \Delta G^{\neq}{}_{Li} - \Delta G^{\neq}{}_{12-4}$.

stituents. Reaction times vary from 1 min (**1a**) to 8 h (**1c** and **1d**) so that a factor about 500 is involved. The same feature is observed for BH_4^- reduction (Table 3). The reaction is slower with **1b** and **1d** than with **1a**.

The changes in regioselectivity can be estimated in terms of transitions state energy differences $\Delta\Delta G_{211}{}^{\neq}$ when Li^+ participates or not in the reduction process. The data are in Table 5.

From this table, it appears that for $LiAlH_4$ reductions the $\Delta\Delta G_{211}{}^{\neq}$ values are rather different for the various α-enones; for instance, the influence of a methyl group on carbon 3 (**1b**) or of two methyl groups on carbon 4(**1f**) enhances $\Delta\Delta G^{\neq}{}_{211}$ relative to 2-cyclohexenone **1a** while two methyl groups on carbon 5 (**1c**) decrease it.

However, for $LiBH_4$ reductions the $\Delta\Delta G^{\neq}{}_{211}$ values are nearly the same (1.5 kcal/mole) for **1a**, **1b** and **1d** and are smaller than in the case of $LiAlH_4$. Such a weak effect of substituents has already been observed in similar cases.[32]

These remarkable substituents effects on rates and regioselectivity changes cannot be interpreted in terms of LUMO levels differences as these levels remain relatively close whatever the substituents are on 2-cyclohexenones.[33] Consequently, they imply some important differentiation in transition state structures which can be

Table 5. Energy differences $\Delta\Delta G^{\neq}$ (in kcal/mole) related to $LiAlH_4$ and $LiAlH_4+[2.1.1]$ reduction regioselectivities (solvent THF)

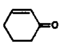
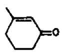
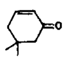
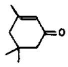
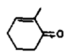
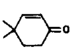
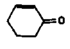
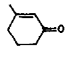
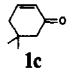
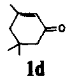
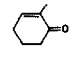
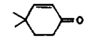
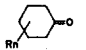
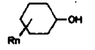
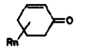
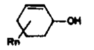
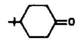
	1a 	**1b** 	**1c** 	**1d** 	**1e** 	**1f** 
$LiAlH_4$						
$C_1:C_3$	86:14	95:5	58:42	84:16	95:5	>99:1
$\Delta G^{\neq}{}_{Li}$	1.1	1.7	0.2	1.0	1.7	2.7
$LiAlH_4+[2.1.1]$						
$C_1:C_3$	14:86	26:74	20:80	26:74	42:58	45:55
$\Delta G^{\neq}{}_{[2.1.1]}$	−1.1	−0.7	−0.8	−0.7	−0.2	−0.1
$\Delta\Delta G^{\neq}{}_{[2.1.1]}$	2.2	2.4	1.0	1.7	1.9	2.8

Table 6. GLC conditions of the different products. Retention times (sec)

	 **1a**	 **1b**	 **1c**	 **1d**	 **1e**	 **1f**
Column	Carbowax 20 M 15%	Carbowax 20 M 15%	Carbowax 6000	Carbowax 20 M 15%	Carbowax 6000	Carbowax 6000
Conditions	2 m 1,8 b	3 m 1,3 b	2 m 1,3 b	2 m 1,3 b	2 m 1,3b	2 m 1,2 b
Temp. °C	100	130	110	140	100	100
 6	410	340	180	320	240	340
 7	670	*cis* 445 *trans* 480	320	*cis* 440 *trans* 520	330	540
 1	850	990	560	720	420	460
 5	970	700	700	650	610	600

Calibrating factors (1:r) relative to internal standard  are close to unity; 0.98–1.00 for ketones **6**; 1.01–1.04 for 2-cyclohexenones **1**; 1.09–1.11 for saturated alcohols **7**; 1.06–1.09 for allylic alcohols **5**.

attributed inter alia to the following factors; (a) the angle of carbonyl group or double bond attack by the nucleophile, which can differ when Li^+-complexation takes place or does not;[34] (b) the position of the transition state along the reaction coordinates, which can differ according to Li^+-α enone complexation or not and to the nucleophile.[35]

In relation to these factors, the "steric" effects of substituents will be more or less effective. This problem will be discussed in a forthcoming paper[33] in connection with other results on 2-cyclohexenones **1** reactions with some carbanionic nucleophiles obtained in our Laboratory.

EXPERIMENTAL

$LiAlH_4$ and $LiBH_4$ are Merck products. [2.1.1] is Merck Kryptofix; [12-crown-4] is Fluka and TMEDA is Merck commercial product. Solvents were purified by careful distillation over $LiAlH_4$ under N_2. The GLC analysis were performed on a Girdel 75 FF1 chromatograph (carrier gas N_2). The 2-cyclohexenones **1** were obtained as follows; **1a** commercial (Merck), **1b** prepared according to Ref. 36, **1c** kindly given by Dr. Geribaldi (Université de Nice), **1d** commercial (Merck), **1e** and **1f** kindly given by Dr. Roux-Schmitt of our Group.

The allylic alcohols **5** were either commercial; **5a** (Aldrich), or obtained by $LiAlH_4$ in ether reduction of the corresponding **1**, according to literature; **5b**,[20] **5c**,[19] and **5d**.[18]

The saturated ketones **6** were either commercial (**6a** (Prolabo), **6b** (Fluka), **6d** (KeK), **6e** (Fluka)) or obtained by catalytic hydrogenation of the corresponding enone [**6c** and **6f**].[37]

The saturated alcohols **7** were also obtained by $LiAlH_4$ reduction of ketones **6**.[21]

The gas chromatography parameters of the various compounds, as well as the determinations conditions are in Table 6.

$LiAlH_4$ reductions

(a) In a carefully dried rubber septum-stoppered vial containing a standardized (~0.12 M) $LiAlH_4$ solution[14] 2.5×10^{-3} mole 2-cyclohexenone **1** dissolved in the required volume of THF was added by a syringe so that the final concentration in each reagent is 0.08 M. After stirring under N_2 at room temperature, the reaction mixture is rapidly poured into a separating funnel containing 50 cm³ diethyl ether and 50 cm³ saturated NaCl solution, the organic layer is separated, washed twice with saturated NaCl solution. A part of Et_2O is distilled under normal pressure and the remaining solution is injected in the chromatograph.

(b) To the previous $LiAlH_4$ standardized solution, 1.2 equivalent [2.1.1] cryptand solution is added via a syringe. Stirring under N_2 is pursued for 30 min to 16 h according to the case. Then the 2-cyclohexenone **1** is added as previously. The reaction is then run as indicated in (a).

The same experimental method was followed using 12-crown-4 or TMEDA.

$LiBH_4$ reductions

To 55 mg $LiBH_4$ (2.5×10^{-3} mole) dissolved in 25 cm³ THF in a rubber septum-sealed, carefully dried vial was added. The 2-cyclohexenone and the complexing agents as for $LiAlH_4$ reductions. The reaction was run as indicated in (a).

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