Reduction of Aliphatic and Aromatic Cyclic Ketones to *sec*-Alcohols by Aqueous Titanium Trichloride/Ammonia System. Steric Course and Mechanistic Implications

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In contrast to the dissolved metal and metal hydride reductions, the reduction of cyclic ketones by the aqueous $TiCl_3$/NH_3 system favours the formation of the less thermodynamically stable axial alcohol. The ammonium ion formed in situ is essential for the reduction to proceed because it behaves as a mild Brønsted acid in basic medium and favours the protonation of the intermediate ketyl. The corresponding α-hydroxy radical is then rapidly reduced under conditions where the first electron transfer to the substrate takes place. We suggest that the stereoselectivity is determined by the second reduction step, which occurs through the less hindered transition state, regardless of whether the radical to be reduced is thermodynamically favoured or not.

Introduction

A variety of metal reagents have been used to effect the reduction of ketones to *sec*-alcohols,[1] in particular, the use of dissolved alkali metals in the reduction of aliphatic cyclic ketones has been extensively studied[2] in order to understand the mechanism in detail and the stereochemical control.[3]

Over the past decade we have found that: a) an aqueous $TiCl_3$ solution efficiently couples carbonyl compounds (Ar−CO−X) activated toward reduction by an electron-withdrawing group (X = CN, COOR, COR, etc.) in acidic medium (pH = 1−2);[4] b) simple aromatic aldehyde and ketones dimerise smoothly in aqueous $TiCl_3$ solution in basic media (pH =11−12) with moderate stereoselectivity,[5] owing to an increase in the reducing power of $TiCl_3$ with increasing pH;[6] c) an anhydrous $TiCl_3/CH_2Cl_2$ solution stereo and chemoselectively couples aromatic aldehydes, but not aromatic ketones, to *dl*-hydrobenzoins.[7] The increased reactivity of aromatic aldehydes to Ti^{III} reduction in CH_2Cl_2 was attributed to a strong carbonyl-Lewis acid complexation, which would favour an inner-sphere ET.

From these results it clearly emerges that Ti^{III} salts, even in basic media[5,6] or in aprotic solvents,[7] do not have sufficient reduction potential to reduce a covalently metal-bonded ketyl [Ar−C$^{\cdot}$−OTi^{IV}] which, instead, dimerises. Thus, it might be argued that Ti^{III} salts are primarily of interest as reagents for reductive coupling of aromatic carbonyls, but of no utility in the reduction to form alcohols.

To our surprise we observed that cyclic aliphatic and aromatic ketones were reduced to alcohols in moderate to good yield in less than 5 min, at 0 °C, by the addition of an aqueous NH_3 solution (30% w/v) until pH 10−11 to a methanolic solution containing the ketone and 2 equivalents of an aqueous acidic $TiCl_3$ solution (15% w/v). In addition, the reduction favours the formation of the less thermodynamically stable axial alcohol, in contrast to the dissolved metal[2] or the metal hydride reductions,[8] the latter reactions give a mixture in which the equatorial isomer strongly predominates.

In the present study, it became clear that the reduction of ketones to alcohols by the aqueous Ti^{III}/NH_3 system is successful only because the NH_4^+, formed in situ, is the strongest acid available in aqueous-methanolic basic medium and favours the protonation of the intermediate metal-bonded ketyl **A** to the corresponding α-hydroxy radical **B**, this radical is then further reduced by Ti^{III}. In the absence of NH_4^+, the reaction loses its synthetic potential.

Results and Discussion

The ketones used in this study (Table 1) reflect different degrees of steric hindrance at the carbonyl group, ranging from unhindered (3- or 4-equatorial substituted, **2**, **3**, **5** and **7**) to hindered (2-equatorial or 3-axial substituted, **4**, **6**, **8**, **9**, **14** and **20**) cyclic ketones[9] and from relatively flexible (α-heterosubstituted, **10** and **11**) to conformationally locked (**5**, **8** and **19**) cyclic ketones.[8c−10]

In order to evaluate the applicability of the method and to gain some useful mechanistic information on the stereochemistry observed, selected aromatic cyclic ketones (α-tetralone **12**, and indan-1-ones **16**−**18**), acyclic ketones (**21**−**23**) and 2,2,6-trimethylcyclohexane-1,4-dione **9** were studied.

The yield of alcohols and the ratio of isomers obtained from the reduction of these ketones with the aqueous $TiCl_3$/NH_3 system (Table 1) have been determined by GC analysis with an internal standard and were confirmed by ^{1}H NMR by direct comparison with authentic samples. Two runs at least were made for each ketone investigated and, within experimental errors, the results were entirely reproducible.

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The material balance was always ≥ 95% and the only by-product was the corresponding acetal[11] [$R_1R_2C(OCH_3)_2$], which was formed in higher yield with unhindered (10−12%) than with hindered ketones (traces).

From the yield of alcohols (Table 1), it can be shown that the tendency of a ketone to be reduced is determined by its reduction potential[12] and/or its capability to form a coordination complex with the metal, and this would favour an inner-sphere ET. Aromatic cyclic ketones (**12**, **16**, **17**, and **18)** were cleanly reduced in almost quantitative yields even in the presence of an equimolar amount of **5** (see Exp. Section). *Thus, this protocol may well be chosen to chemoselectively reduce an aromatic ketone in the presence of an aliphatic one.*

The reduction of **10** was followed by chloride ion elimination,[13] and afforded cyclohexanone in quantitative

Table 1. Reduction of ketones to alcohols by aqueous $TiCl_3/NH_3$ system

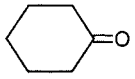
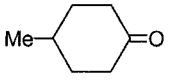
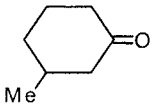
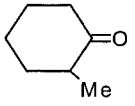
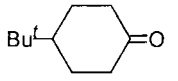
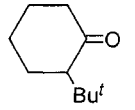
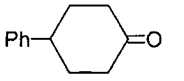
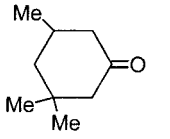
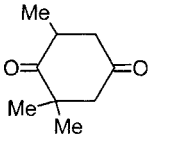
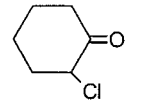
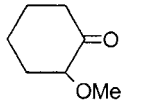
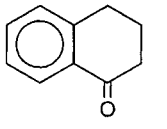
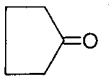
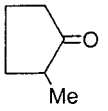
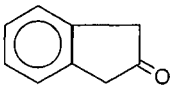
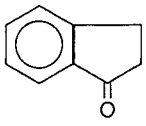
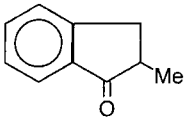
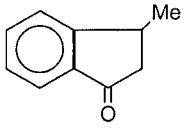
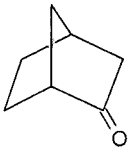
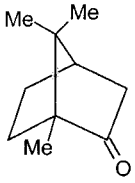
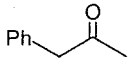
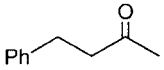
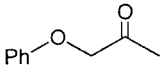
Ketone	N°	Alcohol Yield (%)[a]	OH_{ax} Yield (%)[a]	OH_{eq} Yield (%)[a]	OH_{ax}/OH_{eq} Ratio (%)[a]	OH_{ax}/OH_{eq} Ratio (%) at equilibrium
	**1**	68				
	**2**	65	42 (*cis*)	23 (*trans*)	65/35	
	**3**	64	44 (*trans*)	20 (*cis*)	69/31	23/87[b]
	**4**	32	13 (*cis*)	19 (*trans*)	40/60	10/90[b]
	**5**	71	47 (*cis*)	24 (*trans*)	66/34	12/88[b]
	**6**	no reaction				
	**7**	58	37 (*cis*)	22 (*trans*)	63/37	
	**8**	40	37 (*trans*)	3.0 (*cis*)	93/7	1/99[b]
	**9**	63[c]	27 (*trans*)	36 (*cis*)	43/57	
	**10**	quantit. ($cyC_6H_{10}O$)				
	**11**	66	33 (*cis*)	33 (*trans*)	50/50	
	**12**	quantit.				

Table 1 *(Continued)*

Ketone	N°	Alcohol Yield (%)[a]	OH_{ax} Yield (%)[a]	OH_{eq} Yield (%)[a]	OH_{ax}/OH_{eq} Ratio (%)[a]	OH_{ax}/OH_{eq} Ratio (%) at equilibrium
	**13**	78				
	**14**	45	36 (*cis*)	8.5 (*trans*)	82/18	10/90[d]
	**15**	76				
	**16**	quantit.				
	**17**	91	57 (*cis*)	34 (*trans*)	63/37	
	**18**	96	74 (*cis*)	22 (*trans*)	77/23	
	**19**	37	33 (*endo*)	3.7 (*exo*)	90/10	9/91[e]
	**20**	no reaction				
	**21**	36				
	**22**	31				
	**23**	15+(70% PhOH)				

[a] Determined by ^1H NMR and/or GC analysis with a suitable internal standard. – [b] Ref.[18] – [c] It is only reduced at the less hindered 4-position. – [d] Ref.[25] – [e] Ref.[2b], p.153.

yield.[12c] The same type of reductive cleavage was observed with **23**, which gave phenol in 70% yield. However, with **11** reductive cleavage was not observed and this can be ascribed to the poorer leaving group methoxide compared with chloride and phenoxy ions.

The steric hindrance at the carbonyl moiety severely inhibits the reduction; compounds **4** and **14** are less prone to reduction than the corresponding unsubstituted cycloalkanones **1** and **13** or than the corresponding 3- or 4-substituted isomers (**2**, **3** and **15**).

Table 2. Reduction of 4-*t*Bu-cyclohexanone under different experimental conditions and comparison of stereoselectivity with other reducing agents

Entry	Solvent	Additive (eq.)	Base	Yield (%)[a] Alcohols	Yield (%)[a] OH_{ax}	Yield (%)[a] OH_{ax}	OH_{ax}/OH_{eq} (*cis*)/(*trans*)
1	MeOH[b]		NH_3	44	27	17	61/39
2	MeOH		NH_3	71	47	24	66/34
3	MeOH[c]		NH_3	72	47	25	65/35
4	*i*ProOH		NH_3	35	27	8	77/23
5	*t*BuOH		NH_3	13	10	3	77/23
6	MeOH		NaOH	23	8	15	35/65
7	MeOH	NH_4Cl (2)	NaOH	38	23	15	60/40
8	MeOH	NH_4Cl (6)	NaOH	70	47	23	67/33
9	MeOH	NH_4Cl (2)	NH_3	75	49	26	65/35
10	MeOH	NH_4Cl (6)	NH_3	75	53	22	70/30
11	Li, NH_3/*t*BuOH[d]						2/98
12	$LiAlH_4/Et_2O$[e]						10/90
13	$NaBH_4$/MeOH[f]						20/80
14	BH_3/THF[g]						10/90
15	Cp_2TiBH_4/THF[h]						3/97
16	$(i\text{Pro})_2TiBH_4/CH_2Cl_2$ [i]						3/97
17	PMHS/ZnH[j]						13/87

[a] Determined by ^1H NMR analysis with an internal standard. – [b] Molar ratio 4-*t*Bu-cyclohexanone/$TiCl_3$ was 1:1 in this case and 1:2 in all other reductions. – [c] In this case the reaction was quenched after 1.5 h. – [d] Ref.[2e] – [e] Ref.[8c] – [f] Ref.[28] – [g] Ref.[29] – [h] Ref.[8e] – [i] Ref.[8d] – [j] Ref.[30]

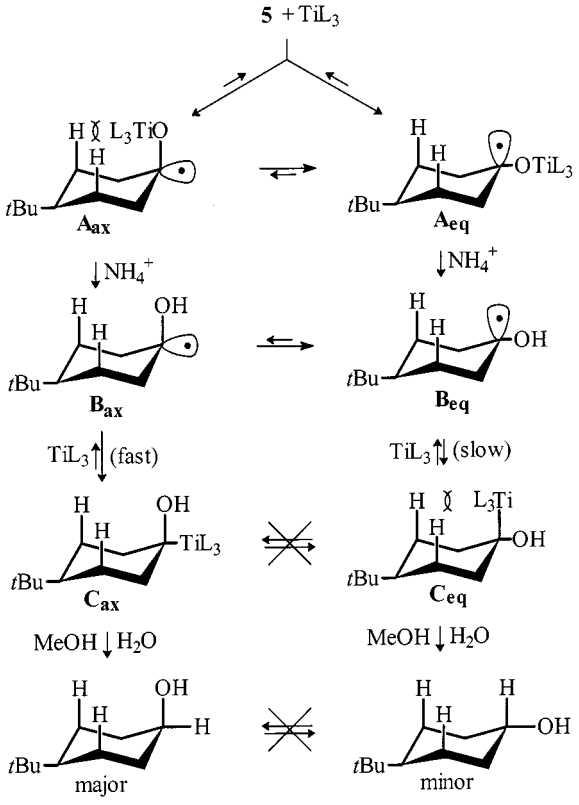
Ketones with greater steric congestion near the reaction centre, such as **6** and **20** were reduced only by a trace amount (<5%). In agreement with this sensitivity to steric congestion, **9** was regioselectively reduced at the less hindered 4-position. However, the reactivity of α-oxygenated ketones, which can form a stable five-membered Ti^{III}-chelate intermediate (see later), is strongly enhanced; for example, **11** and **23** are more reactive than **4** and **22**, respectively.

All of the cycloalkanones in Table 1 gave the less stable axial alcohol in greater yield[14] compared with that present at equilibrium and compared with the experimentally determined yields found with dissolved metal[2] or metal hydride reductions,[8] with the exception of **19** (see later). Thus, we directed our attention to the stereochemical course of these reductions to gain more information on the stereodetermining step. For this study the conformationally chair-locked 4-*t*Bu-cyclohexanone **5** served as a model compound.

Since the *t*Bu group is "frozen" in an equatorial position and is remote from the reaction centre, its inductive and steric effect should be minimal.[8c] Thus, the data in Table 2 (the yields of the isomeric 4-*t*Bu-cyclohexanols formed in the reduction of **5** under different conditions), should accurately represent the ratio of axial to equatorial alcohol on the chair conformation of the ketone.

From these data it emerges that: a) the stoichiometry of Ti^{III}/ketone is 2:1 (entries 1 and 2); b) the reduction is very fast and the isomeric alcohols do not interconvert during the reaction, since with longer reaction time (1.5 hours instead of 5 minutes, entries 3 and 2) neither the overall yield nor the isomer ratio changed; c) methanol is the solvent of choice.

In aqueous NH_3/MeOH solution, the effective reductant is no longer $TiCl_3$ but some other monomeric or polymeric species (the notation TiL_3 is used in Scheme 1, with L=



Scheme 1

OR, Cl). Therefore, with a change in the solvent from methanol to *iso*-propanol and to *tert*-butyl alcohol (entries 2, 4 and 5), the ligands (OR) at the metal become bulkier, the size of the effective reductant increases and, consequently, steric interactions between the reagents becomes more demanding, and the yield of alcohols decreases.

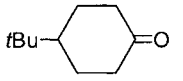
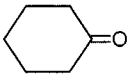
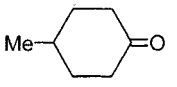
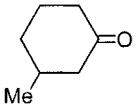
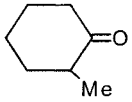
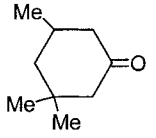
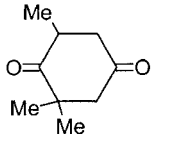
The lower yield of *4-t*Bu-cyclohexanol isomers found in entry 4 excludes any mechanistic interpretation based upon hydride-transfer from alkoxide ion to ketone (similar to the Meerwein−Pondorf−Verley reduction).

The more interesting results from a mechanistic point of view come from entries 6−10. In entry 6, an aqueous 30% NaOH solution, instead of an aqueous 30% NH_3 solution, was added to the reaction mixture until pH 10−11; under these conditions the yield of alcohol was much lower (23 vs. 71%) and the stereoselectivity was reversed (35:65 vs. 66:34) with respect to entry 2. However, with addition of two or six equivalents of NH_4Cl before the NaOH addition to the reaction mixture (entries 7 and 8), a proportional increase of the axial alcohol was observed (from 8% to 23 and 47%, respectively) whereas the yield of equatorial isomer was essentially the same as in the absence of NH_4Cl. Conversely, addition of NH_4Cl before NH_3 [15] (entries 9 and 10) did not substantially change either the overall yield of alcohols or the isomers ratio. Thus, in the presence of ammonium chloride (added or formed in situ)[15] the overall yield of the isomeric 4-*t*Bu-cyclohexanols only increased because more of the less stable axial alcohol was formed.

The mechanism we propose in Scheme 1 to account for the stereochemistry observed with the model compound **5** is based on the following considerations: a) the Ti^{III} ion, even in a basic medium, does not have a sufficient reduction potential[5,6] to add an electron to an aliphatic ketone,[12] unless prior or synchronous synergetic carbonyl-Ti^{III} Lewis acid complexation intervenes leading to the metal-bonded ketyls **A**, via an inner-sphere ET; b) when, ammonium ion (pK_a = 9.24) is present in the reaction medium, protonolysis of **A** to **B** (pK_a = 12.1)[16] is expected to be fast and thermodynamically feasible;[17] c) evidence derived from EPR studies[18] and ab initio calculations[3,19] indicates that the geometries of $\mathbf{A_{eq}}$ and $\mathbf{B_{eq}}$,with the unpaired electron in an axial and the large group in an equatorial position, are the more stable conformations.

As a consequence, the observed stereochemistry cannot be established by the most favourable conformation adopted by the radical but will be, instead, governed by the

Table 3. Relative reactivities of ketones towards $TiCl_3/NH_3$ system[a]

[a] ketone	N°	K_{rel} [b]	K_{ax} [b]	K_{eq} [b]
	**5**	1.00	1.00	1.00
	**1**	0.56		
	**2**	0.60	0.58	0.65
	**3**	0.58	0.59	0.60
	**4**	0.10	0.05	0.18
	**8**	0.66	0.88	0.22
	**9**	1.44	1.09	2.04

[a] Competition experiments vs. 4-*t*Bu-cyclohexanone (**5**). − [b] Determined by ^1H NMR and/or GC analysis.

relative rates at which $\mathbf{B_{eq}}$ and $\mathbf{B_{ax}}$ are further reduced within the coordination sphere of TiL_3.

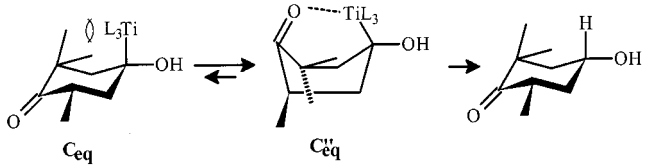
Since the approach of TiL_3 to the α-hydroxy radicals **B** would have a lower transition state energy when it occurs from the least hindered equatorial side, formation of the transient intermediate $\mathbf{C_{ax}}$ would prevail over $\mathbf{C_{eq}}$. The kinetically controlled population of $\mathbf{C_{ax}}$ and $\mathbf{C_{eq}}$ would then be irreversibly trapped by fast protonation before inversion can occur,[20] and leads to the observed final alcohols, which do not interconvert under the reaction conditions.

In the absence of any ammonium ion, radicals **B** may not even form,[19] since they are much stronger acids than the alcoholic solvents ($pK_a \approx 16$) or water ($pK_a = 15.74$). Thus, equilibria $\mathbf{A_{eq}} \leftrightarrow \mathbf{B_{eq}}$ and $\mathbf{A_{ax}} \leftrightarrow \mathbf{B_{ax}}$ are shifted to the left[17,19] and the steric course of the reduction would be essentially controlled by the more demanding steric interference involved in the reduction of the species present in such equilibria. The combined yields of alcohol in the absence of any ammonium ions dropped to 23% (entry 6, Table 2) and the reaction loses its synthetic interest.

The mechanism postulated in Scheme 1 for **5** correctly predicts the OH_{ax}/OH_{eq} ratio from the other ketones (Table 1) and the relative rates found in competitive experiments (Table 3).

In particular, the comparison of the opposite stereochemical outcome found in the reduction of ketones **8** and **9** is worthy of note, since it strongly supports a transient C−Ti bond formation during the second stereodetermining reduction step. Both ketones **8** and **9** have an axial Me group in the β-position with respect to the carbonyl, which is going to be reduced. The greater steric control exerted by a Me group compared with an H atom would raise the TS energy for an axial TiL_3 approach to $\mathbf{B_{eq}}$, and the amount of equatorial alcohol would be lowered.

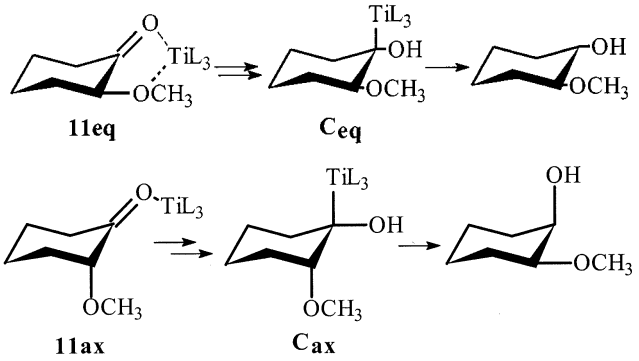
Accordingly, the OH_{ax}/OH_{eq} ratio found in the reduction of **8**, which is frozen in a chair conformation, is much higher (93:7, Table 1) than for other cyclohexanones examined, and a competitive rate experiment versus **5** (Table 3) confirms that the rate of equatorial alcohol formation (K_{eq}) is greatly retarded (0.22:1). Conversely, reduction of **9** gave an exceptionally greater amount of equatorial alcohol (43:57) and K_{eq} is two fold higher than for **5** (2.04:1) and nine fold higher than for **8** (2.04:0.22).



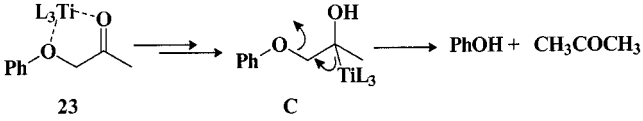
If $\mathbf{C_{eq}}$ [see Equation (1)] were involved in the reduction of **9**, the amount of OH_{eq} would be close to that from **8** (3%). However, this value is much higher (36%), therefore, $\mathbf{C_{eq}}$ may be assumed to adopt, at the time of its formation, the more stable six-membered-Ti^{IV}-chelate-boat conformation $\mathbf{C''_{eq}}$ [see Equation (1)] in which the steric hindrance due to the axial β-Me group is no longer present, and the more stable equatorial alcohol is formed.

With the α-oxygenated ketones **11** and **23**, intermolecular Ti^{III}-bridging precedes or is synchronous with the first inner-sphere ET, and the reactivity of these ketones is enhanced with respect to their nonoxygenated analogues **4** and **22**.

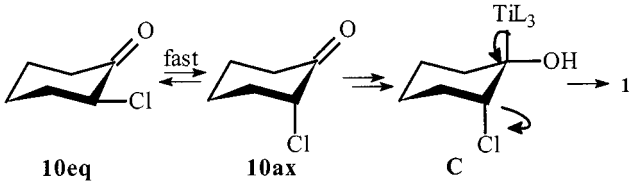
Moreover, chelation control would render conformer $\mathbf{11_{eq}}$ [see Equation (2)] more easily reducible[21] than $\mathbf{11_{ax}}$ [see Equation (3)] and this accounts for the larger amount of equatorial alcohol with respect to ketones **2**−**8**.



Ketone **23** undergoes, via the postulated intermediate **C**, *anti*-elimination of the good leaving group phenoxy (70% yield of phenol) in competition with protonolysis to the corresponding alcohol (15%) [Equation (4)].

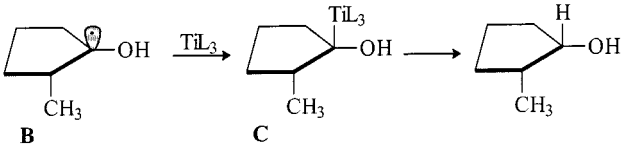


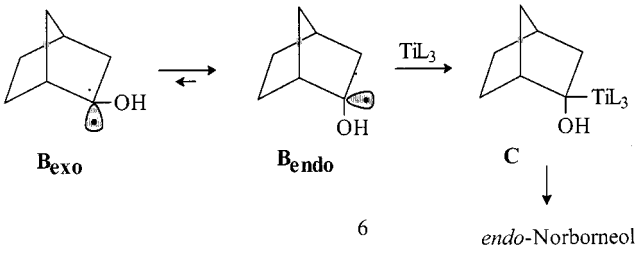
As discussed above, the quantitative reduction of 2-Cl-cyclohexanone **10**[21] to cyclohexanone is believed to occur by the preferred *anti*-elimination[22] of the chloride ion from the intermediate **C** [Equation (5)].



Finally, the stereochemistry observed in the reduction of cyclopentanones **14**, **17**, **18** and 2-norbornanone **19** confirms satisfactorily that the second reduction step invariably occurs through the less hindered TS regardless of whether the intermediate α-hydroxy radical, which is going to be reduced faster, is thermodynamically stable or not.

In fact, for these ketones, the TS would be lower in energy when TiL_3 approaches the more stable radical B[23] *trans* to the Me group [Equation (6)] and the more stable B_{endo} [24] from the *exo* side [Equation (7)]. In agreement with this, the less stable *cis*-cyclopentanols[25] and the less stable *endo*-norborneol[2b] are obtained as the major products.





It should be emphasised that the kinetically favoured intermediate **C** invariably places the larger TiL_3 substituent[26] in the position taken up by the OH group in the thermodynamically more stable alcohol. Hence, under our conditions, the same mechanism explains the preferential formation of the less stable alcohol from cyclohexanones, cyclopentanones and 2-norbornanone. Conversely, both dissolved metal[2,27] and metal hydride[28] reductions afford the more stable alcohol from cyclopentanones and cyclohexanones, but the less stable *endo*-alcohol from 2-norbornanone, and these anomalous results have been extensively debated.[2,8]

Conclusions

The present study extends the use of aqueous $TiCl_3$ as a reducing agent to produce alcohols from carbonyls. The reducing properties of aqueous $TiCl_3$ can be easily manipulated by changing the reaction medium. Aqueous $TiCl_3$ is shown to be an exceptionally powerful and highly selective reductant provided that a mild Brønsted acid is present in basic medium. The reported procedure here is a valid alternative to the many literature methods to obtain the less thermodynamically stable cyclic alcohol. Advantages include higher yield of the less stable cyclic alcohol, low cost, ease of performance and the fact that no toxic material is formed upon workup (ultimately TiO_2). Further work is under way in order to extend the scope of these reactions to chemoselective carbonyl reductions.

Experimental Section

General Remarks: All reagents were commercially available research grade chemicals and used as received. The $TiCl_3$ solution (15% w/v, C. Erba) was standardised against 0.1 N Ce(IV) solution. All reactions were performed at 0 °C under a N_2 atmosphere: ^1H NMR spectra were recorded in $CDCl_3$ at 250 or 300 MHz. Gas chromatographic (GC) analyses of product mixtures and purified samples were performed on a 5% OV-17 on chromsorb W-HP 80/100 column.

General Procedure for the Reduction of Ketones (Table 1): To a well-stirred solution of 4-*t*Bu-cyclohexanone **5** (10 mmol) in methanol (40 mL), at 0 °C under N_2, a 15% aqueous acidic $TiCl_3$ solution (18 mL, ca. 20 mmol) was added with a syringe in one portion. To the resulting mixture, a 30% aqueous NH_3 solution (18 mL) was added dropwise (1 min) and the temperature (ice-water bath) was kept below 20 °C. After stirring for an additional 5 min, the resulting suspension was diluted with water (10 mL) and then extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product, upon addition of a weighed amount of an internal standard (anisole), was directly analysed. The ^1H NMR spectra indicated the presence of the unchanged **5** (24%) and of the isomeric alcohols (71%) with a *cis*/*trans* ratio of 66:34. ^1H NMR ($CDCl_3$) δ_{trans} 0.85 (s, 9 H, $3CH_3$), 3.45 (m, 1 H, C*H*OH); δ_{cis} 0.88 (s, 9 H, $3CH_3$), 3.95 (m, 1 H, C*H*OH). GC analysis revealed that the *cis* isomer was eluted first.

General Procedure for Chemoselective Reduction of an Aromatic versus an Aliphatic Ketone: To a well-stirred solution of 4-*t*Bu-cyclohexanone **5** (10 mmol) and α-tetralone **12** (10 mmol) in methanol (40 mL), at 0 °C under N_2, a 15% aqueous acidic $TiCl_3$ solution (18 mL, ca. 20 mmol) was added with a syringe in one portion. The other experimental conditions were the same as in the preceding procedure. After the usual work up, ^1H NMR and GC analyses of the crude product revealed a 98:2 mixture of α-tetralol and 4-*t*Bu-cyclohexanol respectively. After purification of the crude residue by flash chromatography (hexane/EtOAc 7:3), α-tetralol (1.4 g, 95% yield) was obtained.

General Procedure for Competition Experiments (Table 3): To a well-stirred solution of 4-*t*Bu-cyclohexanone **5** and 4-Me-cyclohexanone **2** (each 5.0 mmol) in methanol (20 mL), at 0 °C under N_2, a 15% aqueous acidic $TiCl_3$ solution (4.5 mL, ca. 5.0 mmol) was added with a syringe in one portion. NH_3 addition (4.5 mL) and work up was carried out as in the preceding procedures. To prevent loss of volatile compounds by evaporation, the combined organic extracts (3 × 25 mL) were directly submitted to GC analysis. The products identity was verified by comparison with authentic reference samples. The order of elution was (distribution normalized to 10 mmol and 200%): unchanged **2** (4.4 mmol, 88%), *cis* and *trans*-4-Me-cyclohexanol in a 65:35 ratio (0.39 and 0.21 mmol, 12% combined yield), unchanged **5** (4.0 mmol, 80%), *cis* and *trans*-*t*Bu-cyclohexanol in a 67:33 ratio (0.67 and 0.33 mmol, 20% combined yield). Within experimental error, the competitive reductions were entirely reproducible and the reported product distribution was the mean value of at least two runs.

Spectroscopic Data: All alcohols obtained by reduction of the ketones listed in Table 1 are known and/or commercial compounds, and were characterized by direct comparison of their physical and spectroscopic data with those of authentic commercial samples or with those reported in the literature.[31]

We report here the ^1H and ^{13}C NMR spectra of the *trans* and *cis* alcohols obtained from the reduction of ketone **18**, the former is not reported in the literature and data for the latter are unsatisfactory.[32]

***trans*-3-Methylindan-1-ol:** Isolated yield 0.26 g, 18%, white solid, m.p. 44−55 °C, (ref.[27] m.p. 44 °C). − ^1H NMR ($CDCl_3$): δ = 1.28 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.9 (br, 1 H, OH), 1.96 (dt, *J* = 6.8, 13.7 Hz, 1 H, CH_2), 2.25 (ddd, *J* = 3.1, 6.8, 13.7 Hz, 1 H, CH_2), 3.45 (sextet, *J* = 6.8 Hz, 1 H, C*H*CH_3), 5.24 (dd, *J* = 3.1, 6.8 Hz, 1 H, C*H*OH), 7.1−7.4 (m, 4 H, ArH). − ^{13}C NMR ($CDCl_3$): δ = 20.2 (CH_3), 36.4 (C-3), 44.2 (C-2), 75.1 (C-1), 123.3 (C-5), 124.4 (C-7), 126.9 (C-6), 128.2 (C-8), 144.1 (C-9), 148.4 (C-4).

***cis*-3-Methylindan-1-ol:** Isolated yield 1.0 g, 69%, white solid, m.p. 72−4 °C, (ref.[27] m.p. 72 °C). − ^1H NMR[32] ($CDCl_3$): δ = 1.36 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.48 (ddd, *J* = 6.8, 7.5, 12.5 Hz, 1 H, CH_2), 1.9 (br, 1 H, OH), 2.76 (ddd, *J* = 6.8, 7.5, 12.5 Hz, 1 H, CH_2), 3.06 (sextet, *J* = 6.8 Hz, 1 H, C*H*CH_3), 5.17 (t, *J* = 7.5 Hz, 1 H, C*H*OH), 7.1−7.4 (m, 4 H, ArH). − ^{13}C NMR ($CDCl_3$): δ =

20.1 (CH_3), 36.2 (C-3), 45.6 (C-2), 75.0 (C-1), 123.2 (C-5), 123.6 (C-7), 126.7 (C-6), 128.0 (C-8), 145.0 (C-9), 147.3 (C-4).

Acknowledgments

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