176 (M^+, 100), 150 (8), 88 (35), 75 (16).

On elution with benzene 5*H*-cyclopenta[*cd*]phenalen-5-one (**3**) (25 mg, 0.12 mmol, 12%) was obtained: mp 158–159 °C (lit.[6] mp 154–156 °C); NMR, UV, and IR according to ref 6; mass spectrum, *m/e* (relative intensity) 204 (M^+, 70), 176 (100), 150 (16), 88 (60), 75 (35).

By further elution with ethyl acetate the starting materials **1** or **2** (76 mg, 0.33 mmol, 33%) could be recovered.

Acknowledgment. This work was supported by a grant from the Deutsche Forschungsgemeinschaft, which is gratefully acknowledged.

Registry No. **1**, 1785-51-9; **2**, 2304-85-0; **3**, 23353-92-6; **4**, 187-78-0.

Stereochemistry of Lithium Trimethoxyaluminohydride Reduction of Cyclic Ketones. A Comparison of Its Stereochemical Character with That of Lithium Aluminum Hydride

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Received March 18, 1983

Lithium trimethoxyaluminohydride (LTMAH) was assumed[1] to have a greater effective bulk than lithium aluminum hydride (LAH) in their reaction with ketones, presumably owing to the greater steric requirement of the reducing species, $AlH(OCH_3)_3^-$. For instance, hydride reduction of 3,3,5-trimethylcyclohexanone produces a trans/cis alcohol ratio of 79.8:20.2 by LAH; the ratio increases to 95.8:4.2 by LTMAH reduction[1,2] in tetrahydrofuran.[1,2] Likewise, in the hydride reduction of norbornanone,[3] 89% of the endo alcohol was obtained by the use of LAH while 98% of the endo alcohol was obtained by LTMAH. However, in the case of 4-*tert*-butylcyclohexanone,[2,3] the trans/cis alcohol ratio of 88.5:11.5 by LAH is decreased to 61:39 by LTMAH. Here the trend is the same in that the formation of the less stable alcohol (axial or endo alcohol) increases with the replacement of LAH by LTMAH.

These results were generally attributed[2,3] to the greater contribution of steric strain control at the transition states and, hence, a lesser degree of product stability control by the bulkier LTMAH than by LAH.

Through a principle of linear combination of free energies of steric strain and product stability differences, we derived the empirical equation[4]

$$\Delta(\Delta G^{\ddagger})_H = \Delta\sigma + \Delta\pi = \Delta(\Delta G^{\ddagger})_{Me} + 1.4\Delta G^{\circ}$$

This equation has successfully provided both qualitative and quantitative explanations of the stereochemistry of the hydride reduction of cyclic ketones with LAH.[5] Furthermore, this equation enables one to estimate both steric strain contribution ($\Delta\sigma$) and product stability contribution ($\Delta\pi$) to the energy difference at the transition states, $\Delta(\Delta G^{\ddagger})_H$. In the case of LAH, $\Delta\sigma$ was estimated from the reaction of methyllithium with the same ketone, $\Delta(\Delta G^{\ddagger})_{Me}$ while $\Delta\pi$ was found to be 1.4 ΔG°_H of the two isomeric alcoholic products.

We, therefore, decided to examine the steric strain factor, $\Delta\sigma'$, for the LTMAH reduction of nine cyclic ketones. Unexpectedly, we found that both LAH and LTMAH have about the same steric strain contribution to the energy difference of transition states. The observed stereochemical character of LTMAH is, therefore, best attributed to the diminishing of product stability control.

Results and Discussion

We have chosen nine cyclic ketones ranging from flexible and less hindered substituted cyclohexanes to semirigid and crowded cyclopentanones and to the rigid methyl-substituted norbornanones and studied their reactions with LAH, LTMAH, and methyllithium (MeLi). It was claimed that the stereospecificity of LTMAH becomes particularly effective in the rigid and hindered systems such as 3,3,5-trimethylcyclohexanone[2] and norbornanone;[3] these ketones should provide a clue for estimating the contribution of steric strain and its possible variation from system to system as their steric environment becomes more rigid and congested. A literature method for the preparation of LTMAH in THF[6] was used for this study; the reduction was carried out at 0 °C as reported before. The results are presented in Table I together with the stereochemistries of reactions of these ketones with LAH and with MeLi reported in the literature.[4]

In general, when LAH is replaced by LTMAH, the stereospecificity decreases in the relatively open and flexible system but it becomes larger in the rigid and congested system as reported in the literature.[2,3]

For estimation of $\Delta\sigma'$ and $\Delta\pi'$ for LTMAH reductions of cyclic ketones, the following equation was subjected to linear regression analysis:

$$\Delta(\Delta G^{\ddagger})_{H'} = \Delta\sigma' + \Delta\pi' \quad (1)$$

$$y = ax + b \quad (2)$$

with $x = \Delta(\Delta G^{\ddagger})_{Me}/\Delta G^{\circ}_H$ and $y = \Delta(\Delta G^{\ddagger})_{H'}/\Delta G^{\circ}_H$

Both x and y are calculated from $\Delta(\Delta G^{\ddagger})_{H'}$, $\Delta(\Delta G^{\ddagger})_{Me}$, and ΔG°_H listed in Table I; a best fit for the analysis requires $a = 1.0$ and $b = 0.4$ with a correlation coefficient of 0.9713 (Figure 1). Consequently, a new empirical equation for the LTMAH reduction can now be expressed as

$$\Delta(\Delta G^{\ddagger})_{H'} = \Delta\sigma' + \Delta\pi' = \Delta(\Delta G^{\ddagger})_{Me} + 0.4\Delta G^{\circ}_H \quad (3)$$

In the LAH reduction, the corresponding empirical equation[4] is

$$\Delta(\Delta G^{\ddagger})_H = \Delta\sigma + \Delta\pi = \Delta(\Delta G^{\ddagger})_{Me} + 1.4\Delta G^{\circ}_H \quad (4)$$

Comparison of eq 3 and 4 leads one to conclude that while both LAH and LTMAH have equal steric strain contribution to the transition-state complexes, the transition-state complexes from LAH reduction is under greater influence of product stability difference than is LTMAH reduction. Moreover, Figure 1 shows that irrespective of the steric environment and rigidity of ketones, the effect of steric strain on the transition-state complexes is uniform.

The observed changes in the stereospecificity from the LAH to LTMAH reduction can now be attributed to the diminishing contribution of product stability control, not the enhanced contribution of steric strain from LTMAH.

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Table I. Stereochemistry of the Reactions of Methyl-Substituted Cyclic Ketones with MeLi, LAH, and LTMAH at 0 °C[a]

ketones	trans alcohol,[b] %			energy difference at transition states,[a] kcal/mol			$G°_H$,[d] kcal/mol	trans[k] ROC, calcd, % (LTMAH)
	MeLi[d]	LAH[d]	LTMAH	$\Delta(\Delta G^{\ddagger})_{Me}$[g]	$\Delta(\Delta G^{\ddagger})_{H}$[h]	$\Delta(\Delta G^{\ddagger})_{H'}$[i]		
1	35	88.5	58 61[e,f]	−0.34	1.11	0.17 0.24	0.94	52
2	61	75[e]	31[e]	−0.90	0.60	−0.43	1.15	31
3	99.7	78.5[f]	95.8[f]	3.17	0.74	1.84	−2.01	99
4	77.5	95.6 95.8[f]	80[l] 78.2[f]	0.67	1.70	0.75	0.58 0.87	84
5	33	79	56[e]	−0.38	0.72	0.13	0.87	49
6	67	91.5	76.5[l]	0.38	1.26	0.64	0.90	80
7	99.3	89	98[e]	2.69	1.13	2.11	−1.08	98
8	98	92.7	96[j]	2.11	1.38	1.72	−0.51	97
9	2	8	1[e]	−2.11	−1.33[e]	−2.49	0.66	3

[a] The following comments were made by one of the reviewers: The product analysis from reduction by LAH may not reflect reduction by the AlH_4-species itself, this would depend on the conditions of the reaction (work of S. Smith et al.) [b] For the bicyclic compound, it represents % endo alcohols. [c] Calculated by following $\Delta(\Delta G^{\ddagger}) = \Delta G^{\ddagger}_{cis} - \Delta G^{\ddagger}_{trans}$ or $\Delta G^{\ddagger}_{endo}$. [d] Reference 4. [e] Reference 3. [f] Reference 2. [g] For methyllithium. [h] For LAH. [i] For LTMAH. [j] K. T. Liu, private communication, Department of Chemistry, National Taiwan University. [k] Calculated according to $\Delta(\Delta G^{\ddagger})_H = \Delta(\Delta G^{\ddagger})_{Me} + 0.4\ \Delta G°_H$. [l] This work. [m] Reference 5.

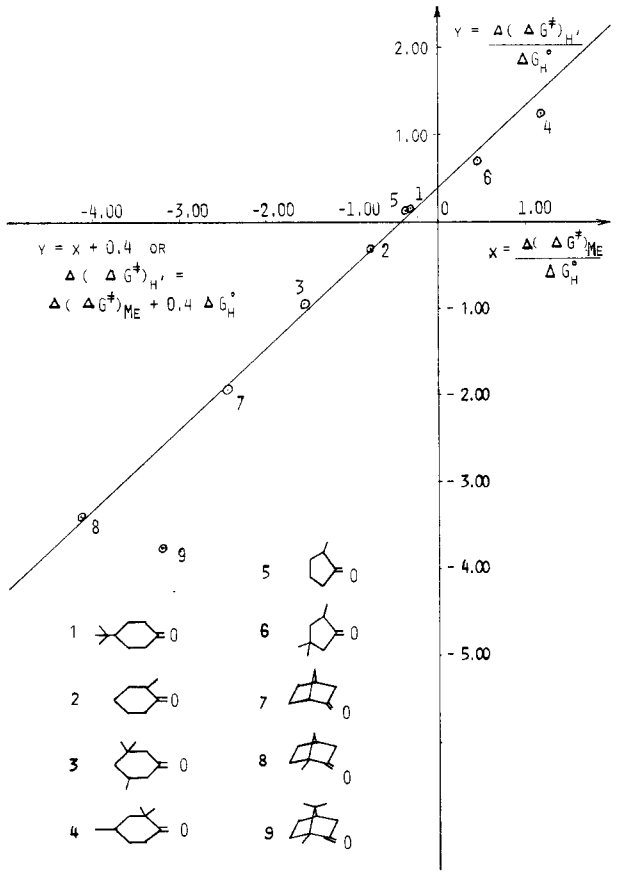


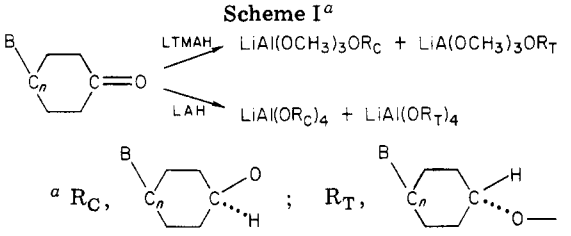
Figure 1. Evaluation of $\Delta\sigma'$ and $\Delta\pi'$ through the linear plot $\Delta(\Delta G^{\ddagger})_{H'}/\Delta G°_H$ vs. $\Delta(\Delta G^{\ddagger})_{Me}/\Delta G°_H$ in the LTMAH reductions.

The data in column 3 of Table I provide a ready explanation for the observed results by the use of eq 3.

When $\Delta(\Delta G^{\ddagger})_{Me}$ (or $\Delta\sigma$) and $\Delta G°_H$ differ in sign and the absolute value of $\Delta\sigma$ is smaller than $\Delta\pi$, $\Delta(\Delta G^{\ddagger})_{H'}$ is expected to be smaller than $\Delta(\Delta G^{\ddagger})_H$ when LTMAH replaces LAH. A decrease in the stereoselectivity is thus expected as shown in ketones **1**, **2**, and **5**. On the other hand, if the absolute value of $\Delta\sigma$ is larger than $\Delta\pi$ even if they are different in sign, $\Delta(\Delta G^{\ddagger})_{H'}$ will be larger than is $\Delta(\Delta G^{\ddagger})_H$ and the hydride reactions becomes more stereospecific by the replacement of LAH with LTMAH (ketones **3** and **7–9**).

The first case is often refered as a stability-controlled reduction[3] because the major reaction product always is the more stable product (e.g., large $\Delta\pi$ contribution). The second case is a steric strain controlled reduction and will prefer the product having the less stericly strained transition-state complex (e.g., $\Delta\sigma$ overwhelms $\mu\Delta\pi$). Therefore, a weaker effect from product stability (0.4 $\Delta G°_H$ vs. 1.4 $\Delta G°_H$) will bring about a decrease in the stereoselectivity, case one (or product stability controlled reduction). In case two (or steric strain controlled reduction), a diminishing product stability factor will allow the steric strain effect to be even more effective and result in an increase of stereoselectivity.

Scheme I[a]



Ketones **4** and **6** deserve special attention because they belong to neither one of the above two cases. In the hydride reduction, both $\Delta\sigma$ and $\Delta\pi$ have the same sign. Therefore, $\Delta(\Delta G^{\ddagger})_H$ ($\Delta\pi = 1.4\Delta G°_H$) is larger than $\Delta(\Delta G^{\ddagger})_H$ ($\Delta\pi = 0.4\ \Delta G°_H$), which in turn is still larger than $\Delta(\Delta G^{\ddagger})_{Me}$ ($\Delta\pi = 0$). In terms of stereoselectivity, LAH reduction is the most stereospecific one followed by LTMAH; stereochemistry of MeLi reaction becomes the least specific one of the three even if it is always steric strain controlled.

If LTMAH were to have greater effective bulk than LAH, then hydride reduction of **4** and **6** would have larger stereospecificity by LTMAH than will LAH. This expectation is not supported by our data. Therefore, we prefer the explanation derived from eq 3 that the stereochemical character of LTMAH reduction is its diminishing effect of product stability control rather than the enhanced steric strain control.

The cause of diminishing product stability difference ($\Delta\pi$) can perhaps be speculated in Scheme I.

According to the original definition of $\Delta\pi$, it is a measure of the stability difference of the two isomeric metal alkoxides. In the case of LAH reduction, all four alkoxide groups OR are derived from the ketone itself, whereas in the LTMAH reduction, of the four alkoxide groups, only one is derived from the ketone itself, the other three being the smaller methoxide groups. Consequently, the stability difference of $LiAl(OCH_3)_3OR_C$ and $LiAl(OCH_3)_3OR_T$ can

be smaller than that of $LiAl(OR_C)_4$ and $LiAl(OR_T)_4$.

The steric strain factor, $\Delta\sigma$, is a measure of the difference of steric strain between the approaching hydride and the ketone[4] at the transition states having a steric environment resembling the starting ketone. The fact that both $\Delta\sigma$ and $\Delta\sigma'$ are equal implies that it is the singular hydride alone, not $LiAlH_4$ or $LiAlH(OCH_3)_3$ as a whole, that is responsible for the difference in the steric strain between the ketone and the reducing agent.

In conclusion, the hydride reduction with lithium trimethoxyaluminohydride is characterized by its reduced contribution from the product stability difference to the final stereoselectivity. Whether the stereoselectivity increases or decreases when LAH is substituted by LTMAH is decided by the signs of $1.4\Delta G°H$ and $\Delta(\Delta G^{\ddagger})_{Me}$ and their relative magnitudes. The empirical equation $\Delta(\Delta G^{\ddagger})_{H'} = \Delta(\Delta G^{\ddagger})_{Me} + 0.4\Delta G°_{H}$ appears to provide a satisfactory explanation for all the available data bath qualitatively and quantitatively.

Experimental Section

Chemicals. Lithium aluminum hydride (LAH), used to prepare lithium trimethoxyaluminohydride (LTMAH), was purchased from Merck & Co. Inc. Tetrahydrofuran (THF) and methanol were the products of Alps Chemical Co. (Taipei, Taiwan). The THF solution of LTMAH (1.2 M) was prepared according to a literature method[6] by adding 3 mol of metanol to 1 mol of LAH in THF. All of the ketones used in this study have been characterized and reported in the literature. 2,2-Dimethyl-4-*tert*-butylcyclohexanone was purified by gas chromatography and gave a satisfactory ^1H NMR spectrum. 2,4,4-Trimethylcyclopentanone was purchased from Chemical Sample Co.

LTMAH Reduction. The method used by Brown and Deck was followed in this study. Typically, 2,4,4-trimethylcyclopentanone (1.2 M in THF) was placed in a round-bottomed flask and thermosatted to 0 °C by an ice–water mixture. An equal molar solution of LTMAH in THF was added dropwise into the ketone solution while the reaction mixture was magnetically stirred. After 3 h of reaction the products were hydrolyzed, decanted, and dried; the products were analyzed by GLPC[4] for distribution (76.5% trans alcohol) and characterized by ^1H NMR.[7]

Acknowledgment. Financial support from the National Science Council to allow preparation of 2,2-dimethyl-4-*tert*-butylcyclohexanone is acknowledged. I also express sincere gratitude to Miss Y. C. Kong for her help with the GLPC analysis.

Registry No. 1, 98-53-3; 2, 583-60-8; 3, 873-94-9; 4, 35413-38-8; 5, 1120-72-5; 6, 4694-12-6; 7, 497-38-1; 8, 10218-04-9; 9, 76-22-2; lithium trimethoxyaluminohydride, 12076-93-6; lithium aluminum hydride, 16853-85-3.

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Anthracene Pillared Cofacial Diporphyrin

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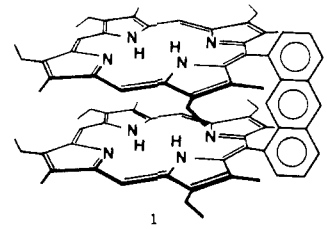
Received July 11, 1983

Porphyrin dimers whose macrocyclic rings are covalently linked in a cofacial configuration have recently received considerable attention.[1,2] They have been successfully applied to model photosynthetic reaction centers[3,4] as well as to effect electrocatalytic reduction of dioxygen on graphite electrode.[5,6] Our previous examples of diporphyrin were prepared by coupling monomeric porphyrin diacids and diamines under high dilution condition. While this method remains popular,[7] our continued interest in these compounds has resulted in the synthesis of a new type of cofacial diporphyrin. As shown by the example, 1,8-anthryldiporphyrin 1, the two porphyrin rings are anchored



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to a single rigid spacer; there are no amide linkages and the cofacial configuration is enforced by steric confines. It is anticipated that the stability and conformation of the new system would complement those of the existing amide type and thus may impart interesting new properties to the metallo complexes derived therefrom. We report here a rational synthesis of monoarylporphyrins in general and the anthryldiporphyrin in particular, via a dipyrrylmethane–dipyrrylmethene condensation.

In spite of the vast amount of literature on porphyrins, reliable syntheses of meso-substituted monoarylporphyrins hardly exist. Ogoshi et al.[8] reported 5-aryl-2,3,7,8,12,13,17,18-octaethylporphyrins as side products in the condensation of α,α'-unsubstituted dipyrrylmethane and benzaldehydes. Others[9,10] have used mixed benzaldehydes to react with pyrrole to obtain mixtures of *meso*-tetraphenylporphyrins from which the desired compound bearing a dissimilar aryl group may be isolated through chromatography. Both of these approaches, in our hands, failed to meet the demand of 1,8-anthracenedicarboxaldehyde and yielded no diporphyrin.[11] We are therefore forced to adopt a stepwise approach.

1,8-Anthracenedicarboxaldehyde (**2**)[12] reacted with 4 equiv of ethyl 3-ethyl-4-methyl-2-pyrrolecarboxylate (**3**)[13]

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(11) In the former case, when the dialdehyde **2** and 4 equiv of (3,4,3',4'-tetraethyl-2,2'-dipyrryl)methane (ref 8) were heated in propionic acid, with or without zinc acetate, only small amounts of OEP were yielded. In the latter approach using mixtures of various ratios of **2**, benzaldehyde, and (3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrryl)methane, only etioporphyrin II, phenyl etioporphyrin **8**, and 5,15-diphenyl-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphine were isolated.

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