Solution Structures of Sharpless Epoxidation Catalysts

Pierre G. Potvin,*[a] Patrick C. C. Kwong,[a] and Michael A. Brook [b]

[a] *Department of Chemistry, York University, 4700 Keele St., North York, Ontario, Canada M3J 1P3.*

[b] *Department of Chemistry, McMaster University, 1280 Main St., W., Hamilton, Ontario, Canada L8S 4M1*

Over the range −43 °C to room temperature, *R,R*-di-isopropyl tartrate (**4**) and $Ti(OPr^i)_4$ form a monocyclic 2 : 2 complex in $CDCl_3$ solution while three sugar derivatives (**1**)—(**3**) form tricyclic dimers.

The Sharpless† epoxidations of geraniol[4] with 1 : 1 complexes of the sugar derivatives 1,4-di-*O*-methyl-L-threitol[5] (**1**), 1,2,5,6-tetra-*O*-methyl-D-mannitol[6] (**2**) and 1,2,5,6-di-*O*-isopropylidene-D-mannitol[7] (**3**), or of α-phenylcinnamyl alcohol with other sugar derivatives,[1] were found to give poorer enantioselectivities than with *R,R*-di-isopropyl tartrate (**4**), and exhibited no apparent correlation with side-chain structure. We suspected that different mechanisms and/or reactive intermediates were involved in the two classes of compounds and herein report n.m.r. studies on 1 : 1 Ti^{4+} complexes of these ligands that support this view.

^1H and ^{13}C n.m.r. spectra were obtained for $CDCl_3$ solutions of $Ti(OPr^i)_4$ and ligands (**1**), (**2**), (**3**), or (**4**) in 1 : 1 ratios, both at room temperature and at −23 °C (the usual temperature for the Sharpless reaction[1]). A 2 : 1 Ti : (**4**) complex[2] was also examined. It is important to note that the spectra of the complexes of (**4**) displayed ligand symmetry, while those of the sugar complexes did not. The downfield displacements of selected ligand signals upon complexation (Table 1) suggest rigid tricyclic structures (**5**), (**6**),‡ and (**7**)‡

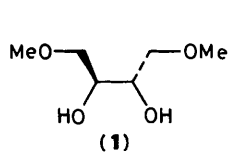
† The Sharpless epoxidation involves the enantioselective epoxidation of allylic alcohols by t-butyl hydroperoxide under catalysis by 1 : 1 Ti^{4+} complexes of tartaric acid derivatives.[1] It and related oxidations[2] are rare examples of non-enzymatic chiral catalysis[3] and proceed with high enantiomeric excesses.

‡ For the sake of economy of space, (**6**) and (**7**) are depicted as the enantiomers of the complexes actually studied.

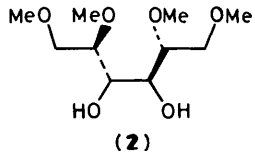
Table 1. Displacements (in p.p.m.) and assignments of selected ligand ^{13}C and ^{1}H n.m.r. signals upon formation of complexes.

Ligand	C_α[a]	C_β	C_γ	OCH_3	H_α	OCH_3
(4)	13.62[b]				0.64[b]	
	13.50[c]				0.64[c]	
(1)	17.30 (α)	2.79 (β′)		0.58 (β′)	0.86 (α)	0.05 (β)
	11.30 (α′)	−0.28 (β)		−0.16 (β)	0.55 (α′)	−0.01 (β′)
(2)	18.48 (α)	3.61 (β′)	1.37	0.00 (β′)	0.73 (α)	0.07 (β)
	12.19 (α′)	0.89 (β)	1.14	−0.25	0.45 (α′)	0.04 (β′)
				−0.29		0.00
				−0.38		−0.05
(3)	19.37 (α)	1.60 (β′)	1.21		0.91 (α)	
	15.87 (α′)	0.21 (β)	0.93		0.50 (α′)	

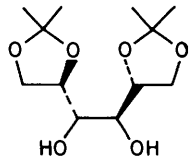
[a] Assignments were made with the help of ^{1}H–^{1}H decoupling, ^{1}H-coupled ^{13}C spectra, and ^{1}H–^{1}H (COSY) and ^{13}C–^{1}H (XHCORR) *J*-resolved correlation spectra. [b] Data for the 1 : 1 complex. [c] Data for the 2 : 1 Ti : (**4**) complex.



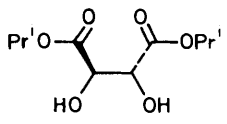
(**1**)



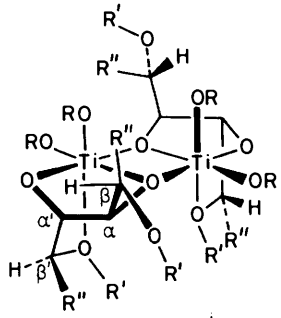
(**2**)



(**3**)

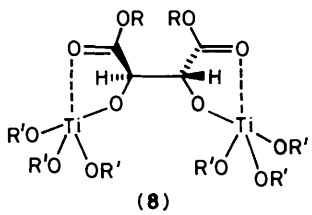


(**4**)



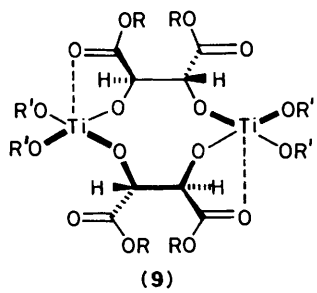
for the 1 : 1 sugar complexes, similar to solid-state structures of tartaric acid derivatives.[8] Our reasoning is as follows: (i) mass spectral data support the assignment of dimeric structures in all cases, as had been found with tartaric acid derivatives,[8,9] and; (ii) in (**5**)—(**7**), H_α is flanked by two Ti^{4+} centres while $H_{\alpha'}$ is near to only one; these protons and the attached carbons should have very different electronic environments and chemical shifts, as is only observed in the sugar complexes. In contrast, the data suggest an acyclic structure (**8**) for the 2 : 1 Ti: (**4**) complex, as has been assumed,[2] and a fluxional monocyclic dimer (**9**) for the 1 : 1 Ti: (**4**) complex, similar to that originally postulated.§ We base this assessment upon: (i) the downfield displacements of C_α of the 1 : 1 and 2 : 1 Ti : (**4**) complexes (13.5—13.6 p.p.m.) being less than the averaged displacement of the $C_\alpha/C_{\alpha'}$ signals in the sugar complexes (14.3—17.6 p.p.m.); the symmetry in the 1 : 1 Ti : (**4**) complex is thus not likely due to a rapidly equilibrating tricyclic structure, and; (ii) in (**8**) and (**9**), both diolate oxygens are each bound to one Ti^{4+}, and the downfield displacements of the H_α and C_α signals should be similar to those of the $H_{\alpha'}$ and $C_{\alpha'}$ signals in (**5**)—(**7**), as observed.

Of particular interest with regard to the epoxidation reactions are the structures of the 1 : 1 complexes at −23 °C. The spectra of the sugar complexes were almost invariant with decreasing temperature. The spectra of the 1 : 1 complex of (**4**), however, became asymmetric at −23 °C: there was a 0.012 p.p.m. difference in shifts between H_α and $H_{\alpha'}$ signals and less



(**8**)

R = R' = Pr'



(**9**)

R = R' = Pr'

than 0.2 p.p.m. difference for C_α and $C_{\alpha'}$ signals. This can be compared to ranges of 0.28—0.41 p.p.m. for H_α–$H_{\alpha'}$ or of 3.50—6.27 p.p.m. for C_α–$C_{\alpha'}$ in the sugar complexes at room temperature. Moreover, only single signals, albeit somewhat broad, were observed at −23 °C for ester and isopropoxide OCH and $CHCH_3$ and for the carbonyl carbons in the complex of (**4**). The H_α and $H_{\alpha'}$ signals did widen upon further cooling into an AB pattern, but the shift difference was no greater than 0.05 p.p.m. even at −43 °C. We conclude that tricyclic forms were not formed at −23 °C, but that the fluxional process was slowed, as has been observed before.[9] Because of close spectral similarities between the 1 : 1 and the 2 : 1 Ti : (**4**) complexes, bridged structures can also be ruled out in the latter at −23 °C.

The data also indicate axial complexation by the β′ oxygens of the sugar derivatives, as found in complexes of tartaric acid derivatives in the solid state,[8] rather than the β, γ, or γ′

§ Since a crystalline vanadyl tartrate complex was found to possess a (ten-membered) monocyclic dimeric structure,[10] and because the active complexes are dimeric in solution,[8,9] a monocyclic structure (**9**) was initially assumed to be the active catalyst.[9]

oxygens. The smaller displacement of $C_{\beta'}$ of (**7**), relative to the other two sugar complexes [(**5**), (**6**)] may indicate weaker axial binding.

These results contrast with the current mechanistic understanding of the Sharpless reaction, in which tricyclic dimers are thought to be involved, based on the isolation in the solid state of tricyclic dimeric structures,[8] and on molecular mechanical calculations which have recently provided an explanation of the observed enantioface selection in a mechanism involving such species.[11] While our studies of the precatalyst complexes cannot address directly the mechanism of the Sharpless reaction, they do throw into question the current hypothesis. In light of these findings, the original mechanistic postulates[9] may regain relevance for tartaric acid derivatives, while the modified mechanism[10,11] may have relevance for the sugar derivatives.

We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

Received, 12th January 1988; Com. 8/00114F

References

1 T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5976; M. G. Finn and K. B. Sharpless, in 'Asymmetric Synthesis,' ed. J. D. Morrison. Academic Press, New York, 1985, vol. 5, ch. 8.

2 L. D. L. Lu, R. A. Johnson, M. G. Finn, and K. B. Sharpless, *J. Org. Chem.*, 1984, **49**, 728; S. Miyano, L. D. L. Lu, S. M. Viti, and K. B. Sharpless, *ibid.*, 1983, **48**, 3608; P. Pitchen, E. Duñach, M. N. Deshmukh, and H. B. Kagan, *J. Am. Chem. Soc.*, 1984, **106**, 8188; F. Di Furia, G. Modena, and R. Seraglia, *Synthesis*, 1984, 325.

3 Others include K. Narasaka, M. Inoue, and N. Okada, *Chem. Lett.*, 1986, 1109, and references cited therein.

4 P. G. Potvin, P. C. C. Kwong, and M. A. Brook, to be published elsewhere.

5 A. H. Haines and C. S. P. Jenkins, *J. Chem. Soc., Perkin Trans. 1*, 1972, 273; P. Nanasi and A. Liptak, *Carbohydr. Res.*, 1973, **29**, 201; D. Seebach, H. O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Doerr, N. P. DuPreez, V. Ehrig, and W. Langer, *Helv. Chim. Acta*, 1977, **60**, 301.

6 J. C. Irvine and B. M. Paterson, *J. Chem. Soc.*, 1914, **105**, 898.

7 G. Kohan and G. Just, *Synthesis* 1974, 192.

8 I. D. Williams, S. F. Pedersen, K. B. Sharpless, and S. J. Lippard, *J. Am. Chem. Soc.*, 1984, **106**, 6430.

9 K. B. Sharpless, S. S. Woodard, and M. G. Finn, *Pure Appl. Chem.*, 1983, **55**, 1823.

10 R. E. Tapscott and G. L. Robbins, *Inorg. Chem.*, 1976, **15**, 154; R. E. Tapscott, R. L. Belford, and I. C. Paul, *Coord. Chem. Rev.*, 1969, **4**, 323; S. K. Hahs, R. B. Ortega, R. E. Tapscott, C. F. Campana, and B. Morosin, *Inorg. Chem.*, 1982, **21**, 664; R. B. Ortega, R. E. Tapscott, and C. F. Campana, *ibid.*, p. 672.

11 K. A. Jorgensen, R. A. Wheeler, and R. Hoffmann, *J. Am. Chem. Soc.*, 1987, **109**, 3240.