On the Ti-TADDOLate-Catalyzed Diels–Alder Addition of 3-Butenoyl-1,3-oxazolidin-2-one to Cyclopentadiene. General Features of Ti-BINOLate- and Ti-TADDOLate-Mediated Reactions

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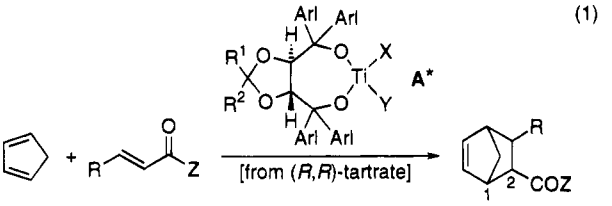
A systematic investigation of the enantioselective Diels–Alder addition of 3-butenoyl-1,3-oxazolidin-2-one to cyclopentadiene under the influence of catalytic amounts of dichloro-Ti complexes of α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs) is described. The influence of the mode of catalyst preparation, amount of catalyst, presence of molecular sieves, concentration of the reactands, temperature, solvent, and TADDOL structure on this reaction is studied. Best results (enantiomer ratio er 94:6) are obtained with the TADDOL-bearing Arl = C_6H_5 and C_6H_5/CH_3 substituents in the dioxolane 2-position (**47**) and with the C_2-symmetrical TADDOL with Arl = 2-naphthyl and two CH_3 groups on the dioxolane 2-position (**16**). A surprising reversal of the absolute topicity of the reaction is observed with TADDOLs (**15, 28, 32, 38**) bearing four 1-naphthyl groups: the 2(*R*)- instead of the 2(*S*)-bicyclo[2.2.1]hept-5-en-2-carboxylic acid derivatives are formed with enantioselectivities of up to 86:14. The crystal structures of several TADDOLs (**16, 28, 47**) and of the tetracyclohexylanalog **50** are described and compared with previously determined structures. A superposition of 29 structures reveals that the cyclic array of atoms of the TADDOLate moiety always has two *axial* and two *equatorial* aryl groups in a λ-type conformation when derived from (*R,R*)-tartrate and in a δ-type conformation when derived from (*S,S*)-tartrate. The binaphthols (BINOLs) show similar structural features (λ in (*P*) or (*S*) and δ in (*M*) or (*R*) enantiomers). A mnemonic rule is disclosed which applies to the steric course of Ti-BINOLate- and Ti-TADDOLate-mediated reactions involving monodentate and bidentate electrophiles. The possible structure of the reactive complex involved in enantioselective reactions mediated by Ti-BINOLates and -TADDOLates, *i.e.*, inter- and intramolecular [2 + 2] and [4 + 2] cycloadditions and ene reactions, is discussed.

Introduction

Ti-TADDOLate-Mediated Diels–Alder Additions. In 1986 and in 1987 it was found by two groups[4–6] that the Diels–Alder addition of acrylic and crotonic acid derivatives to cyclopentadiene (Scheme 1) can be rendered enantioselective in the presence of at least 1 equiv of a Ti-TADDOLate complex, which was and still is generally described by the formula **A***. It was also found that C_1-symmetrical derivatives with $R^1 \neq R^2$ in **A*** give better results than the C_2-symmetrical ones (for instance $R^1 = R^2$ = Me).[4–6] Since the TADDOLs (α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols) are readily available in both enantiomeric forms in two simple steps from tartrate ester, they were subsequently used as chiral ligands for Lewis acid catalysis not only in *inter-* and *intra*molecular Diels–Alder reactions but also in nucleophilic additions to aldehydes, ketones, and nitroolefins, aldol additions, hydrophosphonylations, cyanohydrin additions, [2 + 2] cycloadditions, *intra-* and *inter*molecular ene reactions, iodolactionizations, and transesterifications.[7,8]

Scheme 1. Ti-TADDOLate-Mediated Diels–Alder Addition of α,β-Unsaturated Carboxylic Acid Derivatives to Cyclopentadiene



(1)

Narasaka and his collaborators soon found that the C_1-symmetrical TADDOLate **A*** with Arl = Ph, X = Y = Cl, R^1 = Ph, R^2 = Me, can be used in catalytic amounts of 10 mol % for the reaction shown in Scheme 1, with the dienophile 3-((*E*)-2-butenoyl)-1,3-oxazolidin-2-one (BOX).[9] The best enantioselectivities were reported to be obtained in the presence of 4 Å molecular sieves and in toluene/

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(1) Part of the projected Ph. D. Theses of R.D. and F.N.M.K., ETH Zürich.

(2) Diplomarbeit (Master's Thesis) of R.E.M., ETH Zürich, 1992.

(3) Part of the dissertation No. 10283 of D.A.P., ETH Zürich, 1993.

(4) Narasaka, K.; Inoue, M.; Okada, N. *Chem. Lett.* **1986**, 1109–1112.

(5) Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954–974.

(6) This was observed previously for Ti-TADDOLate-mediated nucleophilic additions; see references cited in: Seebach, D.; Beck, A. K.; Schiess, M.; Widler, L.; Wonnacott, A. *Pure Appl. Chem.* **1983**, *55*, 1807–1822.

(7) For a review article with references to the original literature see: Dahinden, R.; Beck, A. K.; Seebach, D. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons: Chichester (expected publication date in early 1995; a copy of the manuscript may be requested from the corresponding author of the present paper).

(8) The (*R,R*) and the (*S,S*) forms of TADDOLs **1** and **16** are commercially available.

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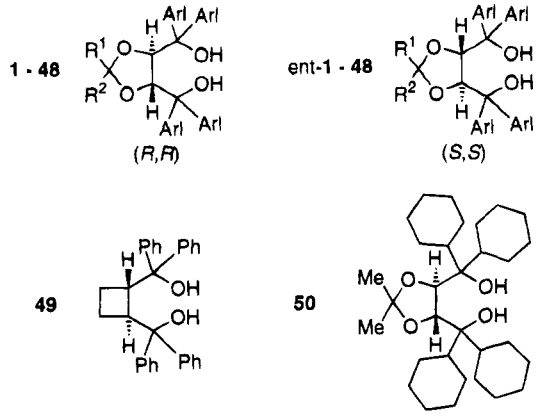
0022-3263/95/1960-1788$09.00/0

Chart 1. TADDOLs and Analogs



petroleum ether as solvent (enantiomer ratio er 97:3). The C_2-symmetrical TADDOLate **A*** (Arl = Ph, $R^1 = R^2 = Me$) did not perform nearly as well in this catalytic version of the reaction. In order to learn about the reasons for this striking difference between the simple TADDOL ligands of C_2- and of C_1-symmetry, we undertook a systematic investigation, varying the Arl group, R^1, and R^2 in **A***. We report here about our results, about the recognition of a simple general rule describing the stereochemical outcome of reactions in which Ti-TADDOLates are used as Lewis acids, and about a proposal of a model for the underlying mechanism. The conclusions are generalized and applied to titanates of other chiral diols such as BINOLs (1,1′-binaphthalin-2,2′-diol).

Results and Discussion

(1) Preparation of the TADDOLs. The TADDOLs **1**–**48** (Chart 1) prepared so far are collected in Table 1; 35 of them are C_2-symmetric. They all result from excess aryl Grignard additions to the corresponding acetals or ketals of tartrate esters.[10-12,14a] By now, more than half of these diols have been used for titanate-mediated Diels–Alder additions, and X-ray crystal structures of about a third of them have been determined. In the Experimental Section of the present paper, we describe the preparation and characterization of the representatives **12**, **13**, **19**, **32**, **35**, **47**, *ent*-**47**, and **48**. Ironically, the most frequently employed diol with a methyl and a phenyl group in the 2-position of the dioxolane ring, the Narasaka[9] ligand **47**, had not been fully characterized previously. We also included in our investigation the (*S,S*)-cyclobutane-1,2-dimethanol[28a] derivative **49** and the tetracyclohexyl substituted diol **50**, the product of hydrogenation[29] of the four benzene rings in the original TADDOL **1**.

(2) Diels–Alder Addition of the Crotonyl Derivative BOX to Cyclopentadiene in the Presence of Ti-TADDOLates. Since the first experiments in which chiral Lewis acids were used for enantioselective Diels–Alder additions[30,31] great progress has been made.[32] Enantioselectivities and *endo*/*exo* ratios over 99:1 have been reached in additions of α,β-unsaturated carbonyl compounds to cyclopentadiene.[33] The knowledge of structural detail (*cf.* X-ray column in Table 1) in the TADDOL series should make it worthwhile to do a thorough investigation of the reaction[34] shown in Scheme 1, with a chance of gaining mechanistic insight.

The *endo*/*exo* adducts **51**/**52** of the crotonic acid derivative BOX to cyclopentadiene were analyzed in the

(10) The original TADDOL **1** was first prepared by one of us (A.K.B.) in 1982. The procedure was first in ref 11. The procedures for the preparation of other TADDOLs and large-scale batches have been described in refs 5 and 12. For applications of Ti-**1** TADDOLate in enantioselecitve syntheses see refs 6 and 11. For a rediscovery of **1** see ref 14a.

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Table 1. TADDOLs 1–48 Derived from (*R,R*)- or (*S,S*)-Tartrate, Aldehydes R^1CHO, or Ketones R^1R^2CO and Aromatic Grignard Reagents ArlMgX

	TADDOLs			references		
no.	R^1	R^2	Arl	preparn and/or first use	use in Diels–Alder reactn	X-ray
1	Me		Ph	5, 11, 12	4, 5, 9, 13, this paper	12, 14d,f, 15b
ent-**1**	Me		Ph	12	16a, 17	
rac-**1**	Me		Ph	15a		15a,b
2	Me		2-MePh	14a		
3	Me		4-MePh	14a		15c
4	Me		4-CF_3Ph	15c		15c
5	Me		3,5-$(CF_3)_2$Ph	18		
6	Me		4-FPh	15c		15c
7	Me		3,5-F_2Ph	15c		15c
8	Me		F_5Ph	19		
9	Me		4-ClPh	15c		15c
10	Me		2-MeOPh	20	this paper	
11	Me		4-MeOPh	12, 20	this paper	
12	Me		4-Me_3CPh	this paper	this paper	
13	Me		3,5-Me_2Ph	this paper	this paper	
ent-**13**	Me		3,5-Me_2Ph	16a	16a	
14	Me		4-PhPh	12		
15	Me		1-naphth	12	16, this paper	
ent-**15**	Me		1-naphth	16c	16c	
16	Me		2-naphth	12	this paper	this paper
ent-**16**	Me		2-naphth	12	this paper	
17	Me		2-furyl	19		
18	Et		Ph	21	21	
19	Et		3,5-Me_2Ph	21, this paper	21, 22b,c, this paper	
ent-**19**	Et		3,5-Me_2Ph	16a	16a,c	
20	Et		3,5-$(CF_3)_2$Ph	21	21	
21	Et		3,5-Cl_2Ph	21	21	
22	Et		2-naphth	21	21	
23	Et		6-MeO-2-naphth	21	21	
ent-**24**	Et		9-phenanthryl	16b	16b,c	
25	Bu		Ph	9	9	
26	$-(CH_2)_4-$		Ph	14c		14e
27	$-(CH_2)_5-$		Ph	5, 12		14b
28	$-(CH_2)_5-$		1-naphth	12	this paper	this paper
29	H		Ph	5,12		
30	H		2-MeOPh	20		20
31	H		4-MeOPh	20		
32	H		1-naphth	this paper	this paper	
33	H		4-Me_2NPh	23	this paper	
34	Ph		Ph	15a	this paper	20, 24
35	9-fluorenylidene		Ph	15a, this paper	this paper	
36	Me	H	Ph	25		
37	*t*-Bu	H	Ph	5, 12	5, this paper	25
38	*t*-Bu	H	1-naphth	12	this paper	
39	*t*-Bu	H	2-naphth	12	this paper	
40	C_6H_{11}	H	Ph	5		
41	Ph	H	Ph	5, 23	this paper	25
42	4-MeO-Ph	H	Ph	26		
43	2,4,6-Ph	H	Ph	5		
44	1-naphth	H	Ph	25	this paper	
45	2-naphth	H	Ph	25		
46	Hexyl	Me	Ph	9	9	
47	Ph	Me	Ph	4, 9, this paper	9, 16a, 21, 22b,c, 27b,c, this paper	this paper
ent-**47**	Ph	Me	Ph	27a, this paper		
48	Ph	Me	2-naphth	this paper	this paper	

following way: the crude reaction mixture, after workup, was flash chromatographed to separate the TADDOL from the four norbornene derivatives **51a/b** and **52a/b** formed (Chart 2). Approximately 100 mg of the **51/52** mixture was reduced with lithium aluminum hydride[35] to give the primary alcohols **53**, R = H. These were then trifluoroacetylated to give **53**, R = $COCF_3$, and analyzed by gas chromatography on a γ-cyclodextrin column (see Experimental Section). This chiral stationary phase (CSP) analysis was employed throughout the present work. The GC peaks from the four stereoisomers are base line separated, with the *endo*-pair of enantiomers having the shorter retention time. For the assignment of the absolute and relative configurations of compounds **51** and **52** we rely on literature data.[9] Since TADDOLs

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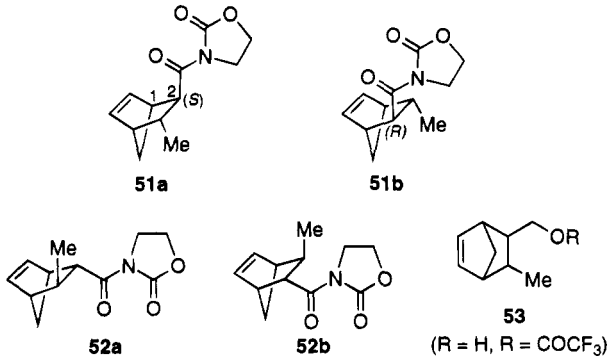
Chart 2. Products 51/52 from BOX Addition to Cyclopentadiene and Derivative 53 for er Determination

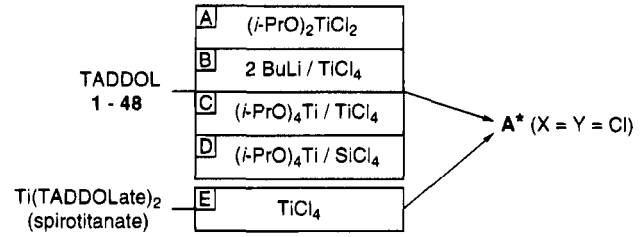


are known to enantioselectively form clathrates[15c,36] we have made sure that no enantiomer enrichment or decrease occurs during the workup procedure. It is also well known that head or tail enrichment may occur during chromatography on achiral columns of samples containing an excess of one enantiomer[37] (since most investigators are not aware of this fact, there are probably many false enantiomer ratios in the literature!). We therefore never analyzed certain fractions of the *endo*/*exo* mixtures but made sure that we had washed all the material **51/52** from the column before reduction, derivatization, and CSP analysis. Furthermore, the TADDOLs eluted from the SiO_2 column first (R_f *ca.* 0.6, toluene/EtOAc 10:1), were found by NMR spectroscopy not to contain any norbornene product (R_f *ca.* 0.25).

The conditions chosen for comparison of different TADDOLs in the reaction leading to the norbornenes **51/52** were carefully optimized; for this purpose, we used mainly the TADDOL ligand **16** bearing four 2-naphthyl groups. The optimization was necessary because various authors recommend widely differing procedures for Ti-TADDOLate-mediated intermolecular Diels–Alder additions. Thus, *catalytic*,[9,17,21,38] *stoichiometric*,[4,9,13,17] or *excess*[4,5,9,16,22] amounts of the chiral titanates are used by the groups of Narasaka,[4,9,34a-c,38] Seebach,[5] Corey,[21] Cativiela,[17] Engler,[22] Quinkert,[16] and Posner[13] (chronological order).[39] We used the catalytic version in the present study.

In particular, the *preparation of the titanate* was done in many different ways; see Scheme 2. Most authors mix the TADDOL with dichlorodiisopropoxy titanium[40,41] (A), in which case a mixture of **A*** and 2-propanol is present.[42] We also tested dichloro Ti-TADDOLates made with 2 equiv LiCl present (B) or in pure form (E).[25,43-45] The

Scheme 2. Different Modes of Catalyst A* Formation



sametype of dichloro Ti complex was assumed to be formed from diisopropoxy Ti-TADDOLate and $SiCl_4$ (D).[21] Finally, in one application, TADDOL, $(i\text{-PrO})_4Ti$, and $TiCl_4$ are mixed in a ratio of *ca.* 1:0.1:0.6 (by weight) (C).[22] We found none of these alternative recipes superior to method A in the BOX/cyclopentadiene cycloaddition.[46]

It is popular, but not always necessary, to add *molecular sieves* to reaction mixtures involving chiral Lewis acids;[47] occasionally, this additive needs to be around only during catalyst preparation,[41] but mostly it is left suspended in the solution while the actual reaction goes on.[9,34c,42] For our optimized reaction conditions (*vide infra*), we find that the presence of 4 Å molecular sieves increases the enantioselectivity of **51a/51b** slightly (91:9 without, 94:6 with), no matter whether it is kept in the reaction mixture after catalyst preparation or not.[48]

The best *solvents* for the Ti-TADDOLate-mediated Diels–Alder reactions are those with poor donor ability, such as toluene, petroleum ethers, methylene chloride, or mixtures thereof. For the addition of BOX to cyclopentadiene toluene is the solvent of choice,[49] and it was used in all our experiments. The influence of *concentration* is minimal: with 96, 54, and 38 mM BOX the er were constant within experimental error for the standard reaction. When studying the effect of *temperature*, we noticed that none of the catalysts **A*** gives rise to reasonable reaction rates below −50 °C, the ideal temperature range being −20 to 0 °C.[50]

In Scheme 3 our standard reaction conditions for preparing the catalyst and for carrying out the cycload-

(36) (a) Kaupp, G. *Angew. Chem.* **1994**, *106*, 768–770; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 728–729. (b) Toda, F.; Tanaka, K.; Ootani, M.; Hayashi, A.; Miyahara, I.; Hirotsu, K. *J. Chem. Soc., Chem. Commun.* **1993**, 1413–1415.

(37) (a) Tsai, W.-L.; Hermann, K.; Hug, E.; Rohde, B.; Dreiding, A. S. *Helv. Chim. Acta* **1985**, *68*, 2238–2243. (b) Diter, P.; Taudien, S.; Samuel, O.; Kagan, H. B. *J. Org. Chem.* **1994**, *59*, 370–373 and references cited therein.

(38) Narasaka, K.; Inoue, M.; Yamada, T. *Chem. Lett.* **1986**, 1967–1968.

(39) The effect of high pressure on Ti-TADDOLate-mediated reactions was also studied: Tietze, L. F.; Ott, C.; Gerke, K.; Buback, M. *Angew. Chem.* **1993**, *105*, 1536–1538; *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1485–1486.

(40) We also tested **A*** (Arl = 1- or 2-naphthyl, X = Y = Br) which did not give better results than the dichloro compounds (*cf.* ref 41).

(41) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949–3954.

(42) According to Narasaka *et al.* the alcohol is a "bystander" and does not react with **A*** (X = Y = Cl) to give the "real" catalyst: Iwasawa, N.; Hayashi, Y.; Sakurai, H.; Narasaka, K. *Chem. Lett.* **1989**, 1581–1584.

(43) (a) Schmidt, B.; Seebach, D. *Angew. Chem.* **1991**, *103*, 100–101; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 99–101. (b) Schmidt, B.; Seebach, D. *Angew. Chem.* **1991**, *103*, 1383–1385; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1321–1323.

(44) (a) Seebach, D.; Behrendt, L.; Felix, D. *Angew. Chem.* **1991**, *103*, 991–992; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1008–1009. (b) von dem Bussche-Hünnefeld, J. L.; Seebach, D. *Tetrahedron* **1992**, *48*, 5719–5730.

(45) Seebach, D.; Beck, A. K.; Schmidt, B.; Wang, Y. M. *Tetrahedron* **1994**, *50*, 4363–4384.

(46) Other variations of the catalyst preparation from **16**, which we tried without improving the enantioselectivity of **51** formation, are as follows: (i) addition of solid $(i\text{-PrO})_2TiCl_2$ rather than its standard solution in toluene (er 88:12); (ii) azeotropic removal of *i*-PrOH before carrying out the reaction (er 92:8); (iii) addition of 2 additional equiv of *i*-PrOH (er 93:7); (iv) addition of 1 or 2 equiv of $AgClO_4$ to the solution of **A*** (X = Y = Cl)/2 *i*-PrOH to generate a cationic Ti complex led to a great acceleration (reaction complete at −75 °C after 40 h) but decrease of enantioselectivity (er 78:22).

(47) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922–1925.

(48) (a) Under Narasaka's standard conditions with TADDOL **47** great differences have been reported for running the reaction with or without molecular sieves.[9,38] (b) Addition of both 4 and 10 Å molecular sieve does also not significantly change the enantioselectivity (10 Å molecular sieves should be able to entrap *i*-PrOH!).

(49) (a) With TADDOL **47**, addition of petroleum ether to the toluene gives no improvement within experimental error: er 95.5:4.5 vs 97:3 according to ref 9. We find the same for our standard reaction (er 93:7 vs 94:6). (b) In toluene/THF 1:1 no reaction was observed.

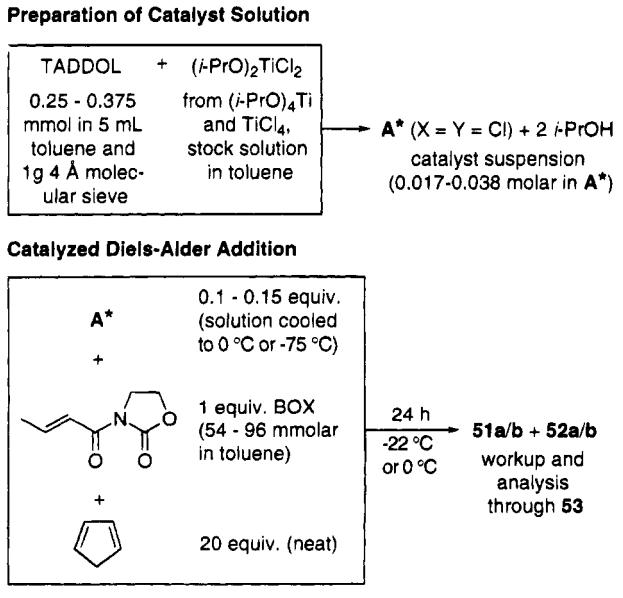
(50) The catalyst **A*** ($R^1 = R^2$ = Me, X = Y = Cl) causes the reaction to be complete within 24 h at −20 °C with Arl = 2-naphthyl and at 0 °C with Arl = Ph.

Table 2. Diels–Alder Addition of BOX to Cyclopentadiene in the Presence of 10–15 mol % Cl_2Ti-TADDOLates (*R,R*)-A* (see Schemes 1 and 3)[a]

	TADDOL					ratio of enantiomers er	
entry	no.	mol %[b]	reactn condns (°C) (time (h))	yield (%)	ratio of diastereomers dr **51/52**	**51a/51b**[c]	**52**[c]
1	**1**	15	−78 → −15 (24)	25	83:17	72:28	48:52
2	**10**	15	−21 (25) 3 (121)	20	74:26	51:49	50:50
3	**11**	10	−5 (24)	99[d]	84:16	75:25	53:47
4	**12**	10	0 (24)	95	83:17	67:33	64:36
5	**13**	15	−78 → −15 (26)	95[d]	89:11	91:9	76:24
6	**15**	15	−78 → −17 (24)	58	89:11	14:86	17:83
7	**16**	15	−78 → −16 (24)	94	87:13	94:6	89:11
8	**16**	10	−5 (24)	99[d]	88:12	89:11	82:18
9	**16**	15	−78 → −40 (47)	20[d]	88:12	94:6	79:21
10	**16**	15	−78 → rt (26)	99[d]	87:13	89:11	81:19
11	**16**	10	−78 (24)	0[d]			
12[e]	**16**	15	−78 → −13 (24)	96	90:10	94:6	91:9
13	*ent*-**16**	15	−74 → −18 (24)	94	88:12	7:93	14:86
14	**19**	15	−78 → −18 (26)	80[d]	90:10	94:6	85:15
15	**28**	10	−5 (24)	88[d]	85:15	18:82	15:85
16	**32**	15	−75 → −20 (24)	56	86:14	39:61	30:70
17	**33**	10	0 (24)	7	77:23	43:57[f]	
18	**34**[g]	10	0 (46)[h]	74	87:13	90:10	78:22
19	**35**	15	−78 → −17 (25)	75[d]	85:15	75:25	61:39
20	**37**	10	0 (24)	99[d]	84:16	70:30[f]	
21	**38**	10	−5 (24)	90	86:14	18:82	14:86
22	**39**	10	0 (24)	90	85:15	70:30	56:44
23	**41**	10	0 (24)	82	83:17	69:31	45:55
24	**44**	10	0 (24)	92	82:18	62:38	61:39
25	**47**	10	−5 (24)[h]	99[d]	88:12	94:6	88:12
26	**47**	10	−5 (24)	97[d]	87:13	93:7	86:14
27	**47**	10	−78 → −20 (22)	16[d]	85:15	85:15	80:20
28	**48**	15	−75 → −17 (24)	94	87:13	71:29	57:43
29	**48**	10	5 (24)	99[d]	87:13	67:33	54:46
30	**49**	15	−78 → −22 (71)	54	87:13	18:82	35:65
31	**50**	15	−21 (46) 0 (68) rt (45)	trace[d]			

[a] The catalyst was generated *in situ* as specified in Scheme 3 and, in more detail, in the Experimental Section (*cf.* A in Scheme 2). The reaction was carried out on a 2.5 mmol scale in toluene as outlined in Scheme 3, and the analysis of the resulting mixture is described in the accompanying text and in the Experimental Section. [b] In the experiments done with 10 mol % Ti-TADDOLate the concentration of BOX in the reaction mixture is 96 mM, in all other experiments it is 54 mM. [c] The absolute configuration of **51a/51b** was derived from literature data;[9] the absolute configuration of the exo-adducts **52a/52b** is unknown—as far as our literature searches go. [d] The product was not purified before reduction and er determination, the yield is calculated from the weight of the crude product and ^{1}H NMR integrations ("NMR yield"). [e] Scale up experiment with 28 mmol BOX. [f] Determined by HPLC (Chiralcel OD). [g] In a paper of Irurre et al. the TADDOL **34** was reported[24] to give **51** with an er of 99:1. [h] The solvent was toluene/petroleum ether 1:1.

Scheme 3



dition reaction are shown, in Table 2 the results are collected, and in Figure 1 the relationship between enantiomer purity of the catalyst **A*** from **16** and of the product **51** is plotted. The following comments seem appropriate. (i) The enantioselectivities reported for the catalysts from TADDOLs **19** and **47** (entries 14, 25) were not quite reached under the conditions chosen herein.[51] (ii) The 2-naphthyl derivative **16** (entry 7),[52] which is much easier to isolate in pure form than the ligand **47** (entry 25), and which, being C_2-symmetrical, does not create diastereotopic environments, gives almost the same results as does **47**. (iii) We have demonstrated, with the 2-naphthyl-TADDOL, that the norbornene derivative **51** of er 94:6 can be prepared on a 10–30 mM scale in >90% yield (entry 12 in Table 2) and that the enantiopurity can be raised to an er of 99:1 by two recrystallizations from hexane (50% yield, see Experimental Section). (iv) The C_1-symmetrical TADDOL with 2-naphthyl groups on the dimethanol unit and phenyl/methyl on the dioxolane 2-position is one of the poor ligands studied (er 71:29, entry 28). (v) A comparison of the very different performances of the tetraphenyldimethanols with Me/Me (**1**, er 72:28), Ph/Me (**47**, er 94:6), Ph/H (**41**, er 69:31), and Ph/Ph (**34**, er 90:10) in the 2-position of the dioxolane ring is puzzling. (vi) Perhaps the most striking result is that the sense of enantioselectivity reverses when we use catalysts **A*** made from the 1-naphthyl-substituted diols **15**, **28**, **32**, and **38**, as

(51) The discrepancy may come from the fact that the Narasaka[9] and Corey[21] groups used different methods for analysis of the resulting norbornenes **51** and **52**. Also, er 97:3 (their highest value) and er 94:6 (our highest value) may be within experimental error, after all!? Thus, in a small-scale experiment with 0.7 mmol BOX and 15 mol % **A*** (R^1 = Me, R^2 = Ar! = Ph, X = Y = Cl) as catalyst we observed the highest value in all of our experiments (er 95:5, compare entries 25–27 in Table 2).

(52) It is interesting to note that the TADDOL bearing 2-naphthyl groups also gives the best catalyst for the Ti-mediated addition of dialkyl zinc to aldehydes.[43b,45]

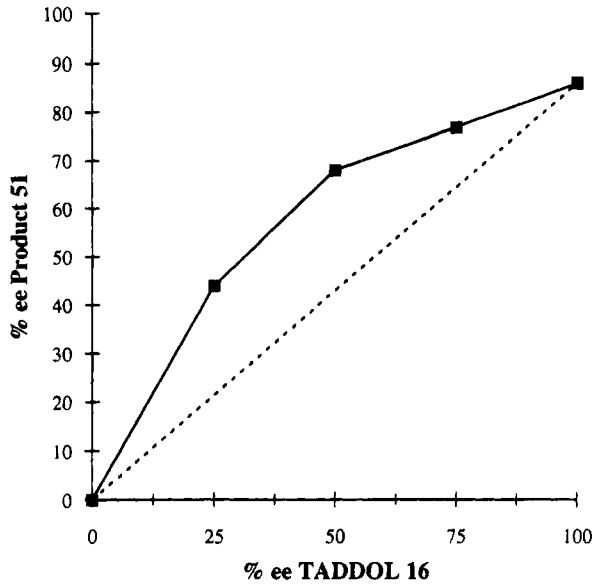


Figure 1. Nonlinear relationship between enantiomer purity of the catalyst **A*** from **16** and of the *endo*-product **51**. The reaction mixture is homogeneous (except for the molecular sieve) in all experiments from which this curve results. In reactions carried out with stoichiometric amounts of the TADDOL **47**, Narasaka et al.[42] also observed nonlinearity, but in their case, a precipitate is formed which contains (*R,R*)- and (*S,S*)-Ti-TADDOLates in a 1:1 ratio!

compared to all other TADDOLs hitherto tested for this reaction (entries 6, 15, 16, and 21). (vii) While the cyclobutane-derived diol **49** provides a catalyst which performs almost as well (entry 30) as those from the TADDOLs, the analog **50** bearing four cyclohexyl groups does not give an active catalyst at all (no product formation after 46 h/-21 °C, followed by 68 h/0 °C and 45 h/rt!). (viii) When discussing a mechanistic model for the present reaction,[53] caution should be employed because of the nonlinear relationship[54,55] shown in Figure 1.

(3) Crystal Structures of the Diols 16, 28, 47, and 50 and a Comparison with Other TADDOLs. On the basis of previous experience[25,56,57] we hoped to gain valuable insights from the X-ray crystal structures of the reagents involved. We managed to obtain suitable single crystals of the TADDOLs with 1- and 2-naphthyl groups (**28** and **16**), of the Narasaka ligand **47**, and of the tetracyclohexyldimethanol **50**. After many unsuccessful attempts we crystallized the TADDOLs **16**, **28**, and **47** as clathrates[58] with piperidine, ethanol, and methanol, respectively. The structures are shown in Figure 2. All four exhibit the typical general feature of TADDOLs, *i.e.*, a seven-membered ring containing a hydrogen bond, with *quasiaxial* and *quasiequatorial* substituents on the dimethanol moieties.[59] These rings are excellent models for the corresponding Ti-complexes: the TADDOLate part of the seven-membered rings containing a Ti-center in two crystal structures[19,25] is essentially identical with that in the free TADDOLs;[12,25] the *O,O* distance in the Ti-complexes is *ca.* 2.8 Å and *ca.* 2.6 Å in the TADDOLs themselves (*vide infra*); this is also true of a 7-ring phosphonite[60] derived from TADDOL **1**.

In Figure 3 we show MacMoMo presentations[61] of the TADDOLs and of the tetracyclohexyl analog **1/50**, **41/47**, and **16/28**, viewed from a direction perpendicular to the mean plane of the dioxolane rings. A comparison of the Me_2Ph_4-TADDOL **1** with the cyclohexyl analog. Me_2cHex_4-diol **50** reveals that the space above and below the supposed position of a Ti in the corresponding complex (in between the two oxygens) is occupied by CH_2 groups of the *axial* cyclohexyl ring; a somewhat different, but similarly encumbering position of the cyclohexyl ring is present in the second type of conformer present in the crystal of **50**. From the structure of **50** it is obvious why this ligand gives a totally inactive catalyst for the Diels–Alder reaction.[62]

Next we compare the Me_2Ph_4-TADDOL **1** with the Ph_5-TADDOL **41** and the $MePh_5$-TADDOL **47** in Figure 3. A striking difference is noticed between the dioxolanes bearing H/Ph and Me/Ph in the 2-position: the benzene ring on this acetal carbon is almost coplanar (17°) with the neighboring CH bond in **41** and is turned out of the plane (formed by *ipso*-C/acetal-C/Me-C), away from the neighboring Me group in **47** (65° and 78°, for the two independent molecules in the asymmetric unit). A comparison of the conformations around the C,C bonds between the *axial* benzene rings and the carbinol centers in **1**, **41**, and **47** shows that the *ortho*-hydrogens on the benzene rings are located more or less close to the supposed position of the Ti (between the two oxygens). In the $MePh_5$-TADDOL one of the benzene rings points an *ortho*-hydrogen straight toward the position in the middle between the two oxygens. The distances between the *ortho*-hydrogens and the neighboring O–H···O bridging hydrogens are 2.81 and 2.63 Å in **1** (average of structures, see Table 1), 2.9 and 3.3 Å in **41**, and 2.4 and 2.5 Å in **47**. Conformational changes due to substituent variation at the acetal center may cause dramatic changes in the steric hindrance of the Ti coordination sphere![63]

(53) Experiments done with other *N*-butenoyl-1,3-oxazolidin-2-ones such as the benzo derivative and the 4,4-dimethyl derivative gave much poorer results (30–70% ee). For the use of these oxazolidinones see: (a) Corey, E. J.; Houpis, I. N. *Tetrahedron Lett.* **1993**, *34*, 2421–2424. (b) Chapuis, C.; Jurczak, J. *Helv. Chim. Acta* **1987**, *70*, 436–440.

(54) For other examples of nonlinear plots between % ee of auxiliary and of product see: (a) Puchot, C.; Samuel, O.; Dunach, E.; Zhao, S.; Agami, C.; Kagan, H. B. *J. Am. Chem. Soc.* **1986**, *108*, 2353–2357. (b) Noyori, R.; Kitamura, M. *Angew. Chem.* **1991**, *103*, 34–55; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69. (c) Mikami, K.; Terada, M. *Tetrahedron* **1992**, *48*, 5671–5680. (d) Guillaneux, D.; Zhao, S.-H.; Samuel, O.; Rainford, D.; Kagan, H. B. *J. Am. Chem. Soc.* **1994**, *116*, 9430–9439.

(55) The Ti-TADDOLate-mediated additions of organozinc reagents to aldehydes show a linear relationship.[43b]

(56) Seebach, D. *Angew. Chem.* **1988**, *100*, 1685–1715; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624–1654.

(57) Seebach, D.; Lamatsch, B.; Amstutz, R.; Beck, A. K.; Dobler, M.; Egli, M.; Fitzi, R.; Gautschi, M.; Herradon, B.; Hidber, P. C.; Irwin, J. J.; Locher, R.; Maestro, M.; Maetzke, T.; Mourino, A.; Pfammatter, E.; Plattner, D. A.; Schickli, C.; Schweizer, W. B.; Seiler, B.; Stucky, G.; Petter, W.; Escalante, J.; Juaristi, E.; Quintana, D.; Miravitles, C.; Molins, E. *Helv. Chim. Acta* **1992**, *75*, 913–934.

(58) The guest molecules are all hydrogen bonded to that TADDOL OH-proton, which is not involved in intramolecular hydrogen bonding.

(59) Of more than two dozen structures there are only two exceptions from this general structural feature: **30** and **34** (solvent free).[20,24]

(60) (a) Sakaki, J.-i.; Schweizer, W. B.; Seebach, D. *Helv. Chim. Acta* **1993**, *76*, 2654–2665. (b) Seebach, D.; Hayakawa, M.; Sakaki, J.-i.; Schweizer, W. B. *Tetrahedron* **1993**, *49*, 1711–1724.

(61) Dobler, M. MacMoMo III–Molecular Modeling Program Version 1.1, Laboratory of Organic Chemistry, ETH Zürich, 1993.

(62) The titanate from **50** catalyzes the Et_2Zn addition to benzaldehydes, albeit with mediocre selectivity.[28a,45]

(63) Molecular Modeling and comparison of the many X-ray crystal structures we have in this series (Table 1 and section 5) tell us that the barrier to rotation around the aryl–C(OH) bond is quite small.[28a]

(64) Seebach, D.; Beck, A. K.; Roggo, S.; Wonnacott, A. *Chem. Ber.* **1985**, *118*, 3673–3682.

(65) Iwasawa, N.; Sugimori, J.; Kawase, Y.; Narasaka, K. *Chem. Lett.* **1989**, 1947–1950.

(66) (a) Mikami, K.; Motoyama, Y.; Terada, M. *J. Am. Chem. Soc.* **1994**, *116*, 2812–2820. (b) Terada, M.; Motoyama, Y.; Mikami, K. *Tetrahedron Lett.* **1994**, *35*, 6693–6696.

(67) (a) Hayashi, Y.; Narasaka, K. *Chem. Lett.* **1990**, 1295–1298. (b) Narasaka, K.; Hayashi, Y.; Shimada, S. *Chem. Lett.* **1988**, 1609–1612.

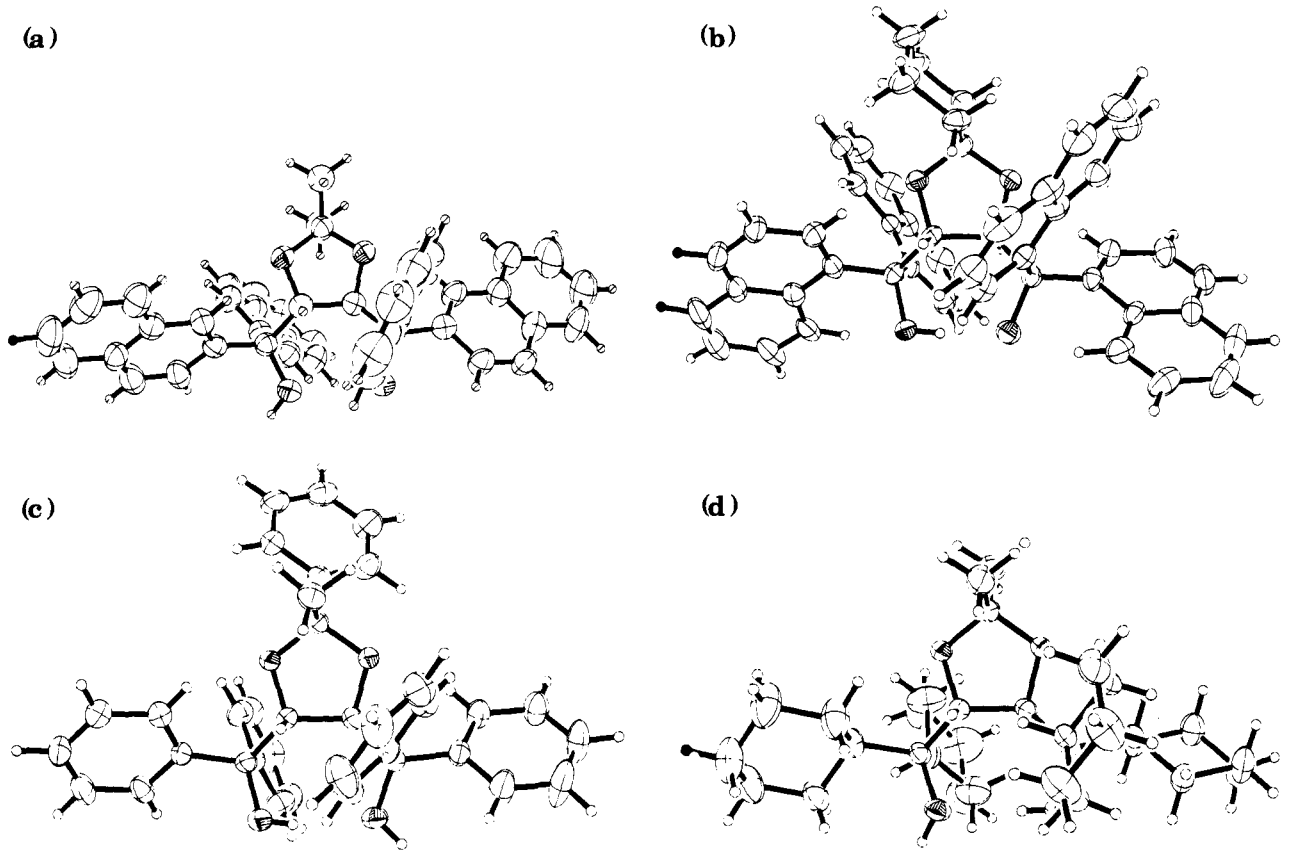


Figure 2. Crystal structures of four diols as ORTEP plots. The thermal ellipsoids are drawn at the 50% probability level. (a) Tetra(2-naphthyl)dimethanol (**16**). The guest molecule piperidine is not shown. (b) The TADDOL **28** with four 1-naphthyl groups and a spirocenter at the 2-position of the dioxolane. The clathrated ethanol is not shown. (c) The TADDOL **47** substituted by Ph/Me at the dioxolane 2-position. The crystal was composed of **47** and 0.5 MeOH (not shown). (d) Hydrogenation product **50** of the original TADDOL **1**. The asymmetric unit contains four independent, slightly different molecules of **50**, only one of which is shown here.

The presentation of the structures of the 1- and 2-naphthyl derivatives, the $(1\text{-Nt})_4$- and $(2\text{-Nt})_4$-TADDOLs **28** and **16** in Figure 3 shows that the latter is very similar to the Ph_4-TADDOL **1**; from a least-squares superposition we see that, in first approximation, there are just two additional benzene rings fused to the TADDOL **1** to give **16**. More drastic changes take place when going to the 1-naphthyl ligand **28**: the second benzene ring is fused-on in the back side, toward the dioxolane ring, on the *axial* aryl groups and in the front side on the *equatorial* aryl groups; thus, there is a great change of the steric hindrance around the complexing site with respect to the *equatorial* and essentially no change with respect to the *axial* aryl groups; rotation around the C-naphthyl bonds is greatly hindered, and hence this conformation is frozen. This change must be causing the reversal of the stereochemical course of the Diels–Alder reaction (Table 2).

Apart from the 1-naphthyl case, the effects of varying the aryl groups and the substituents on the acetal center upon the degree of enantioselectivity in the Diels–Alder addition studied herein is relatively small (er 94:6 to 62:38): at 0 °C 62:38 corresponds to a $\Delta\Delta G^{\ddagger}$ of 0.27 kcal/mol and at −20 °C 94:6 corresponds to 1.38 kcal/mol.

(4) Rule for Reproducing the Topicity of Ti-TADDOLate- and Ti-BINOLate-Mediated Reactions of Bidentate Electrophiles. In Chart 3 a collection of products formed by catalytic or stoichiometric chiral titanate Lewis acid activation of monodentate (products **54**, **55**) and of bidentate electrophiles (products **56**–**65**) with nucleophiles is shown. These products result from nucleophilic attack at aldehydes of organometallic species

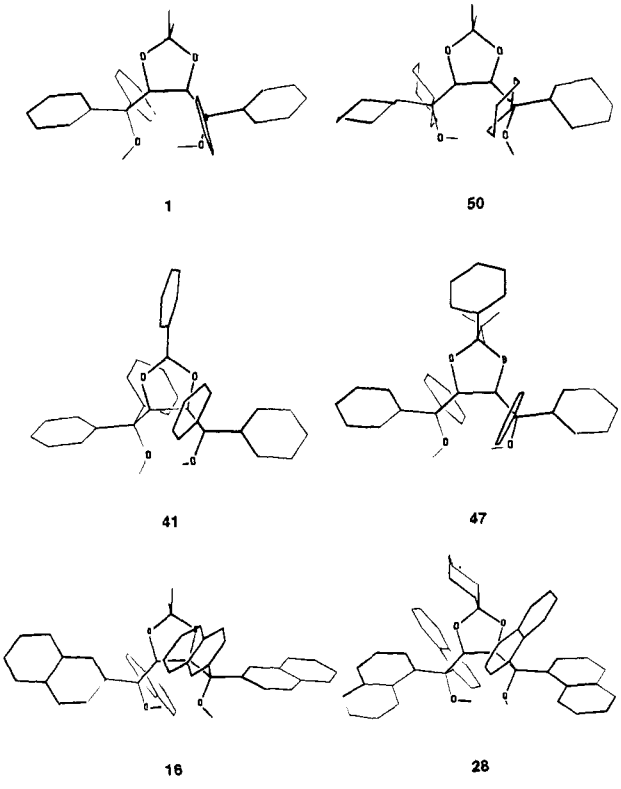
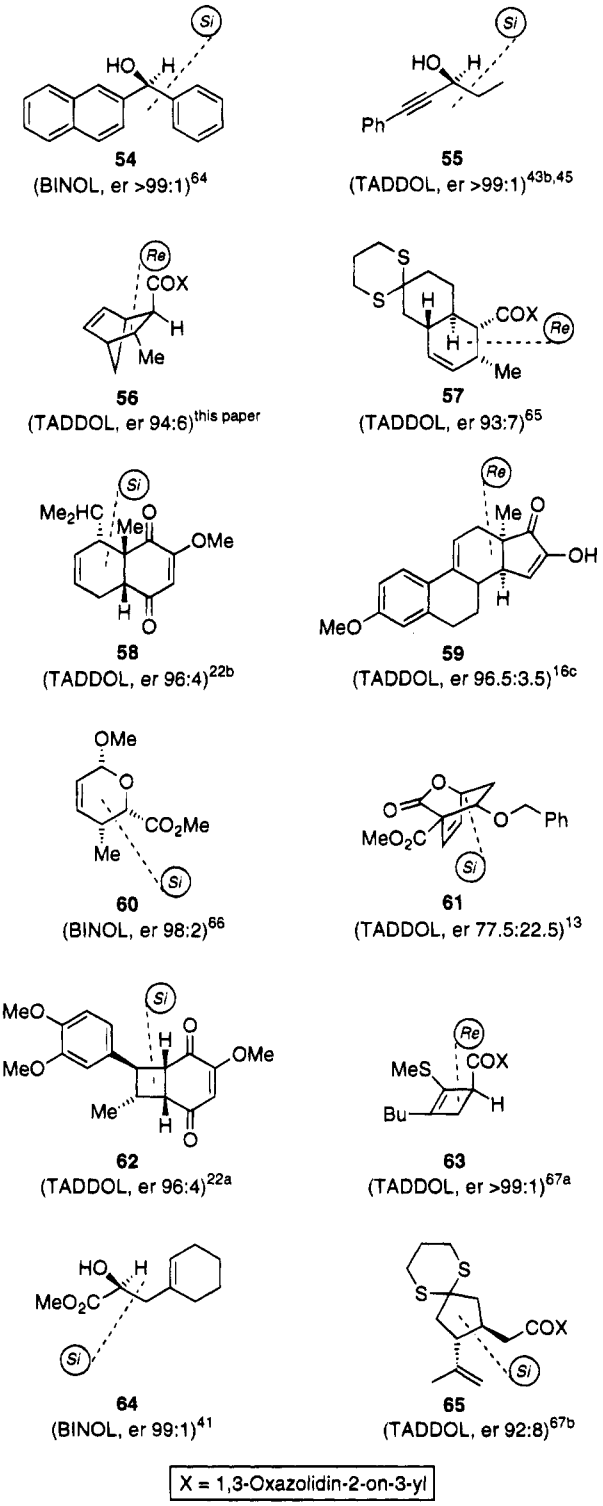


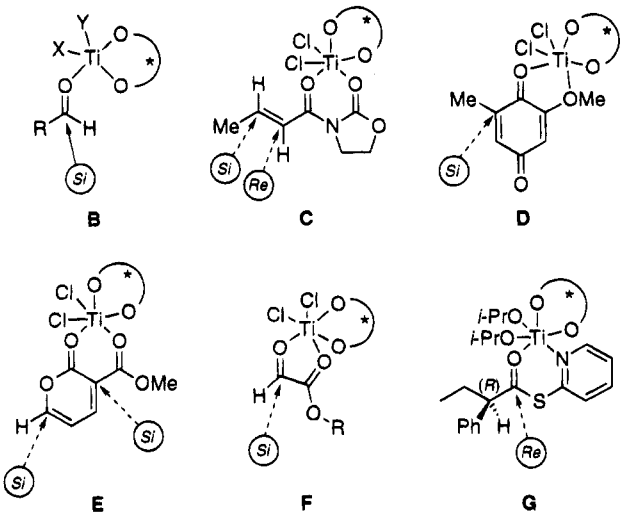
Figure 3. MacMoMo Presentations of the six diols **1**, **50**, **41**, **47**, **16**, and **28**. Hydrogen atoms (except for all OH hydrogens and the Me hydrogens in **47**) are omitted for clarity. For the structures of **1** and **41** see the references in Table 1.

Chart 3. Enantiomers Formed Preferentially with Ti-(*R,R*)-TADDOLate or Ti-(*P*)-BINOLate



(**54**, **55**), from inter- (**56**, **58**, **59**, **61**) or intramolecular (**57**) or hetero (**60**) Diels–Alder additions, from [2 + 2] cycloadditions (**62**, **63**), and from inter- (**64**) or intramolecular (**65**) ene reactions. The products **54**–**65** are those enantiomers which are formed with (*R,R*)-Ti-TADDOLates or with (*P*)-Ti-BINOLates (*P* in the revised CIP nomenclature corresponds to *S* in its old version).[68] The

Chart 4. Mnemonics for the Stereochemical Course of Reactions Mediated by Ti-(*R,R*)-TADDOLates or Ti-(*P*)-BINOLates



dotted lines and the *Re*/*Si* topicities in structures **54**–**65** indicate—for one of the trigonal carbons—the directions from which the nucleophilic attack with formation of a new C,C bond has taken place. At first sight, these results look random and confusing. It turns out, however, that with nonchelating electrophiles (aldehydes) the outcome of the reaction may be described by using the arrangement **B** in Chart 4, with the chiral titanate complexing on top, *cis* to hydrogen, and the nucleophile attacking from the *Si* face. For the chelating electrophiles the outcome of the reactions may be described by using the arrangements shown in **C**, **D**, and **E**, with the titanium center on top, the carbonyl group conjugated with the activated double bond to the left, and the additionally chelating heteroatom to the right (if the C,C double bond is not part of a ring, as in **C**, the most stable conformation is used); the nucleophile is then found to add from below the projection plane of these arrangements. With the (*S,S*)-TADDOLates and (*M*)-BINOLates the steric course of the reactions is, of course, reversed. Both the monodentate (**B**) and the bidentate (**F**) mnemonics apply to the ene reactions of glyoxylate[69] (Chart 4). The only example for which this simple rule does not hold is the Diels–Alder addition leading to the steroidal skeleton (**59** in Chart 3).[70] It does, however, hold for the enantioselective transesterification observed by Narasaka *et al.*[71] (**G** in Chart 4), assuming nucleophilic attack from below the projection plane in a Felkin–Anh–Bürgi–Dunitz trajectory.[72]

(5) Mechanistic Models for the Ti-BINOLate- and Ti-TADDOLate-Mediated Reactions. From numerous X-ray crystal structures of TADDOL derivatives and

(68) (a) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Experientia* **1956**, *12*, 81–94. (b) Prelog, V.; Helmchen, G. *Angew. Chem.* **1982**, *94*, 614–631; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 567–583. (c) Seebach, D.; Prelog, V. *Angew. Chem.* **1982**, *94*, 696–702; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654–660.

(69) The result described by **B** or **F** in Chart 4 (*cf.* **64** in Chart 3) is obtained with (*P*)-Ti-BINOLate; with the (*R,R*)-TADDOLate a poor (er 77:23) and reverse stereoselectivity was observed.[41]

(70) The published data[16a-c] do not indicate whether there is a reversal of the stereochemical course of reaction when going from normal aryl groups to 1-naphthyl and 9-phenanthryl. See also the discussion in section 5. The results described in the dissertation of W. Döring[16d] show that all TADDOLs used gave the same topicity in the Diels–Alder reaction leading to **59**.

(71) Narasaka, K.; Kanai, F.; Okudo, M.; Miyoshi, N. *Chem. Lett.* **1989**, 1187–1190.

(72) (a) Chérest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199–2204. (b) Chérest, M.; Felkin, H. *Ibid.* **1968**, 2205–2208. (c) Anh, N. T. *Topics Curr. Chem.* **1980**, *88*, 145. (d) Bürgi, H.-B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153–161. (e) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108–1117.

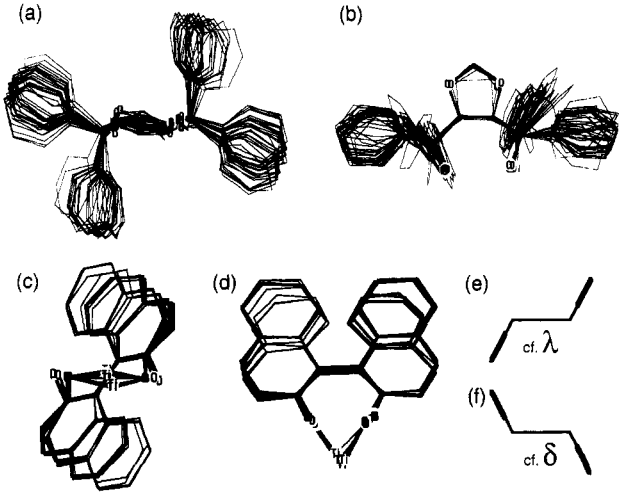
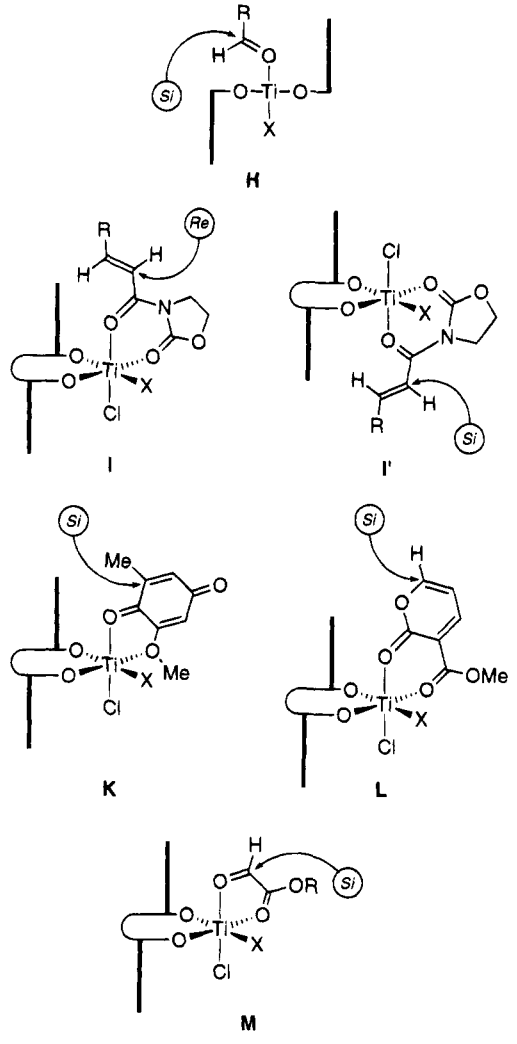


Figure 4. The superposition of 29 structures of TADDOLs and TADDOL analogs in the (*R,R*)-configuration is shown in (a) and (b) (the six-letter codes refer to the Cambridge Crystallographic database): EABGOD (**3**), EABGUJ (**6**), EABHEU, EABHIY (**9**), EABHOE (**7**), EABHUK, EABJAS, EABJEW, JOFSOM (**27**), JUPVIZ (**37**), JUPVOF (**41**), JUPWEW, KODWEF, KODWIJ, KOGJAR (**1**), KOMSAG, SADDUW, SADFAE, **16**, **28**, **34**, **47**, **49**, **2b** in ref 60a, **5c** and **5d** in ref 60b. The superposition of nine structures of BINOLs and Ti-BINOLates in the (*P*)-configuration is shown in (c) and (d): BEYKUL, BIRKOC, BIRKOC01, KOXGIN, KOXGOT, KOXGUZ, VOZXEN, WANNII. The arrangement of the *quasiaxial* aryl groups in (a) and (c) is designated λ, see (e); the enantiomers, *i.e.*, the (*S,S*)-TADDOL- or the (*M*)-BINOL-derivatives, would accordingly be designated δ, see (f).[73]

Ti-TADDOLates we know that the diolate part of these molecules has the oxygens in juxtaposition, with the neighboring aryl groups pointing in *axial* and *equatorial* directions. Since the *axial* aryl groups are *antiperiplanar* to the hydrogens on the chirality centers, the (*R,R*)-TADDOLs have these *axial* groups on the upper right and lower left side of the molecules, as viewed along the approximate C_2-axis with the oxygens in front and the dioxolane ring in the back; see Figure 4. We will refer to this arrangement as λ and to its mirror image (present in the (*S,S*)-TADDOLs) as δ in this paper.[73a] For a superposition of 29 different crystal structures in this projection see Figure 4a. Interestingly, the BINOLs and the Ti-BINOLates may also be described as having a λ arrangement of the aryl moieties when of *P* and a δ when of *M* configuration (Figure 4c), in agreement with the fact that the topicities of reactions mediated by Ti-(*R,R*)-TADDOLate and Ti-(*P*)-BINOLate are often the same (for instance, Chart 3, **54**/**55** and Ti-BINOLate-mediated reactions[53b,66,73b] leading to analogs of **56** and **58**). In Figure 4b and d the superpositions are shown in a projection perpendicular to the approximate C_2-axis demonstrating the great difference in available space on the left and right side of the center of these structures.

As proposed previously,[25,28a] the results with the monodentate aldehyde electrophiles would arise from nucleophilic attack in a penta- or hexacoordinate Ti-complex,[74] with the aldehyde held in the position pictured in **H** of Chart 5. This type of approach was observed with a great variety of different nucleophiles (*cf.* alkyl, allyl, enolate, cyanide, see refs in refs 25 and 34d).

Chart 5. Mechanistic Models for Ti-TADDOLate and Ti-BINOLate Mediated Enantioselective Reactions[a]



[a] The vertical heavy lines symbolize the *quasiaxial* aryl groups of the TADDOLate or the neighboring OArl benzene rings of the BINOLate moiety.

A model[25] for the bidentate electrophile ligands rests upon the following assumptions (see Chart 5)[75a]: (i) The titanium is octahedral, hexacoordinate, and neutral.[75b] (ii) The carbonyl oxygen, conjugated with the C,C double bond to be activated, is in a *trans* position with an electronegative chloride, rather than an alkoxide oxygen, thus placing this carbonyl oxygen near an *axial* aryl group and the second chelating oxygen of the electrophile in a position *trans* to an alkoxide oxygen. (iii) The resulting five- or six-membered chelate ring could now be positioned near an *axial* or near an *equatorial* aryl group; see **I** and **I'** in Chart 5; the latter arrangement would be expected to be more stable and the former one

(73) (a) This use of λ and δ to describe conformations of rings and of substitutents which they carry is different from the convention used for specifying the chirality sense of transition metal phosphine complexes: Kagan, H. B. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, pp 463–498 and references cited therein. (b) We realize that the analogy between BINOL and TADDOL must have its limitations, if not due to the fact that the former has OH groups of pK_a *ca.* 10, the latter of pK_a *ca.* 17.

(74) The fact that best results are obtained in the presence of excess (*i*-PrO)$_4$Ti was explained as a "cleansing" effect, removing product alkoxides from the Ti-center. This would exclude an intramolecular nucleophile transfer on a tetrahedral Ti as proposed in our previous paper (Figure 11 in ref 25).

(75) (a) The following discussion is given for TADDOL ligands, but would be analogous for the BINOL ligands. (b) The discussion would also hold for a model with pentacoordinate (trigonal bipyramidal) positively charged Ti, without the ligand X in Chart 5!

more reactive, with the nucleophile approaching in an area of space where there is an *axial* (**I'**) *vs* an *equatorial* (**I**) aryl group, respectively. For three other substrates the putative reactive complexes are pictured in **K**, **L**, and **M**[76] of Chart 5.

The reversal of the absolute topicity observed with the TADDOL, bearing 1-naphthyl groups is compatible with this model: if the crystal structure (Figures 2 and 3) is similar to the solution structure, the effective sizes of the *equatorial* and *axial* aryl groups have actually been reversed (see iii above).

With the dienophile 3-methyl-cyclopent-3-ene-1,2-dione leading to the steroidal product **59** there is also a reversal of the topicity if we apply the chelate model; this may be due to the very large diene component used in this particular case.[16,70]

A word of caution seems appropriate at this point: the observation that the Diels–Alder reactions catalyzed by Ti-TADDOLates (Figure 1) and Ti-BINOLates[66a] have a nonlinear relation between the enantiopurities of catalyst and product shows that the mechanistic model presented herein can only be a first trial.[77]

Conclusion

Common features of Ti-BINOLate- and Ti-TADDOLate-mediated reactions of a large variety of electrophiles with nucleophiles in as diverse transformations as simple nucleophilic organometallic additions to carbonyl groups, aldol additions, intra- and intermolecular [2 + 2] and [4 + 2] cycloadditions, and ene reactions have been disclosed. The mnemonic rule for the steric course followed by most of these reactions when mediated with titanates bearing the C_2-type λ or δ ligands suggests that there is a related mode by which the electrophiles are complexed in the coordination sphere of the titanium. The proposed model for the structure of the reactive complexes is based upon structural features found in the crystals of TADDOL and BINOL derivatives. Like the mnemonic rule, the model will be subject to further experimental results such as detailed NMR investigations of the solution structure of the complexes formed from the chiral Ti-complexes and various electrophiles,[78] extensions to other metals with the same or different coordination spheres,[79] and, of course, to other types of reactions[80] which are accelerated in the presence of Lewis acids. As mentioned in the introduction, the simple C_2-symmetrical geometry of BINOL and TADDOL ligands may be a most valuable prerequisite for eventually really understanding the reactions of their metal complexes.

Experimental Section

General. Abbreviations used: GP (general procedure), HV (high vacuum, 0.01–0.001 Torr), RV (evaporator). Dimethyl tartrate (Chemische Fabrik Uetikon) was used as received without prior purification. $(i\text{-PrO})_4$Ti (Hüls AG) and $TiCl_4$ (Fluka) were distilled under Ar. Toluene, petroleum ether (light fraction 30–50 °C), and hexane were distilled over Na with benzophenone as indicator under an Ar atmosphere immediately before use. Cyclopentadiene was freshly prepared before each experiment from dicyclopentadiene *via* a temperature bath of 180–200 °C and subsequent cooling in a *i*-PrOH/CO_2 slush bath. $(i\text{-PrO})_2TiCl_2$ was prepared from $TiCl_4$ and $(i\text{-PrO})_4$Ti according to the literature method;[41] the colorless solid was weighed in a glovebox and used as a 0.25 M stock solution. (*R,R*)-Dimethyl *O,O*-methylidenetartrate, (*R,R*)-dimethyl *O,O*-isopropylidenetartrate, (*R,R*)-dimethyl *O,O*-pentylidenetartrate,[21] and (*R,R*)-[9] and (*S,S*)-dimethyl *O,O*-(1-phenylethylidene)tartrate[27a] were prepared according to ref 12. TADDOLs **1**, **10**, **11**, **15**, **16**, *ent*-**16**, **28**, **33**, **34**, **37**, **38**, **39**, **41**, and **44** were prepared following reported procedures (see references in Table 1). Powdered molecular sieves (4 Å) (powdered MS) were purchased from Fluka and activated for 24 h at 350 °C/100 mbar. 3-((*E*)-2-Butenoyl)-1,3-oxazolidin-2-one was prepared according to the procedure of Evans;[81] spectral data and physical properties were identical to those given in ref 9. $LiAlH_4$ was procured from Chemetall in *purum* quality. All other commercially available chemicals used were of *puriss. p.a.* (pro analysi) quality, or purified and dried according to standard methods. The Diels–Alder reactions were carried out in a 100-mL two-neck flask with a three-way stopcock, septum, and magnetic stirrer under Ar atmosphere. The glassware was dried for at least 24 h in an oven at 130 °C. All reactions were performed using a cryostat Frigomix S (B. Braun). The temperatures given in Table 2 are measured as internal temperatures with a digital temperature detector. Analytical thin-layer chromatography (TLC) was performed on precoated silica gel 60 F_{254} plates (Merck). The compounds were visualized by UV_{254} light or by spraying with anisaldehyde solution (anisaldehyde 9.2 mL, AcOH 3.8 mL, EtOH 338 mL, H_2SO_4 12.5 mL) for aldehyde detection, or phosphomolybdic acid solution (phosphomolybdic acid 25 g, $Ce(SO_4)_2{\cdot}4H_2O$ 10 g, H_2SO_4 60 mL, H_2O 940 mL). Column chromatographic separations at normal pressure (NC) were executed using SiO_2 60 (0.063–0.200 mm, Fluka), and flash chromatographic (FC) separations at 0.2 bar were carried out using SiO_2 60 (0.040–0.063 mm, Fluka). The isolated products were distilled with a Büchi GKR-50 apparatus; boiling points correspond to uncorrected air bath temperatures. Melting points are mea-

(76) Note that the same *Si* approach of nucleophiles is compatible with both the nonchelating and the chelating model in the case of glyoxylate (**H** and **M**).

(77) To account for a second chiral ligand in the coordination sphere of the active center we could have a dimeric complex possibly formed through attachment at the position X in **I**–**M**. See also the recent report of an oxygen bridged dimeric complex formed upon heating in toluene a BINOLate $TiCl_2$/*i*-PrOH mixture, with no consequence for the topicity of the catalyzed ene reaction: Terada, M.; Mikami, K. *J. Chem. Soc., Chem. Commun.* **1994**, 833–834.

(78) (a) The DiMare group at the University of California, Santa Barbara, has done NMR experiments of complexes formed from Ti-TADDOLates and the dienophile BOX (see **I/I'** in Chart 5) to obtain information about the species involved in the reaction leading to **51**/**52**. The results are described in the accompanying paper. We thank Professor M. DiMare for sharing unpublished results with us. (b) For NMR investigations of complexes formed from a BOX derivative and Sn or Al Lewis acids see: Castellino, S. *J. Org. Chem.* **1990**, *55*, 5197–5200. Castellino, S.; Dwight, W. J. *J. Am. Chem. Soc.* **1993**, *115*, 2986–2987.

(79) For examples of reactions of BINOLates and TADDOLates with other metal centers such as boron (a), magnesium (b), aluminum (c), zirconium (d), molybdenum (e), and the lanthanides (f) see: (a) Reference 32. Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 1561–1562. (b) Weber, B.; Seebach, D. *Angew. Chem.* **1992**, *104*, 96–97; *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 84–86. Ibid. *Tetrahedron* **1994**, *50*, 6117–6128; 7473–7484. (c) References 18 and 32. Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709–6716. Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717–6725. Singh, V. K. *Synthesis* **1992**, 605–617. Dahinden, R. Diplomarbeit (Master's Thesis), ETH Zürich, 1991/92, unpublished results. (d) Reference 34d. (e) McConville, D. H.; Wolf, J. R.; Schrock, R. R. *J. Am. Chem. Soc.* **1993**, *115*, 4413–4414. (f) Reference 32c. Sasai, H.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1994**, *116*, 1571–1572. Kobayashi, S.; Ishitani, H. *Ibid.* **1994**, *116*, 4083–4084. Kobayashi, S.; Araki, M.; Hachiya, I. *J. Org. Chem.* **1994**, *59*, 3758–3759. Sasai, H.; Kim, W.-S.; Suzuki, T.; Shibasaki, M. *Tetrahedron Lett.* **1994**, *35*, 6123–6126. Kobayashi, S.; Ishitani, H.; Araki, M.; Hachiya, I. *Ibid.* 6325–6328. Kobayashi, S.; Ishitani, H.; Hachiya, I.; Araki, M. *Tetrahedron* **1994**, *50*, 11623–11636. Marko, I. E.; Evans, G. R.; Declercq, J.-P. *Ibid.* 4557–4574.

(80) In the reaction of quinones with styrenes furnishing [2 + 2] cycloadducts **62**, Engler and his collegues also observe the formation of [5 + 2] cycloadducts (bicyclo[3.2.1]oct-3-ene-2,8-diones) which have a configuration compatible with attack of the styrene to the 3- and 5-position of the quinone from the same face from which the [2 + 2] cycloaddition occurs (see **K** in Chart 5), see ref 22a and: (a) Engler, T. A.; Combrink, K. D.; Letavic, M. A.; Lynch, K. O., Jr.; Ray, J. E. *J. Org. Chem.* **1994**, *59*, 6567–6587. (b) Engler, T. A.; Wei, D.; Letavic, M. A.; Combrink, K. D.; Reddy, J. P. *Ibid.* 6588–6599.

(81) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238–1256.

sured in open glass capillaries with a Büchi 510 (Tottoli apparatus) using a 50 °C range Anschütz thermometer and are uncorrected. Optical rotations $[\alpha]_D$ were determined with a Perkin-Elmer 241 polarimeter at rt (*ca.* 20 °C) using *p.a.* solvents. Capillary gas chromatograms (CGC) were obtained with a MEGA HERGC 5160 (Carlo Erba) chromatograph using a γ-cyclodextrin column (20 m × 0.19 mm, self made, injector temperature 230 °C, detector temperature 250 °C, heating rate 55/0.2 °C per min, pressure 200 kPa H_2). IR spectra of $CHCl_3$ solutions were measured with a Perkin-Elmer 983 spectrometer. ^1H and ^{13}C NMR spectra were measured on a Varian Gemini 200 (200 or 50 MHz, respectively) or Bruker WM 300 (300 or 75 MHz, respectively). TMS (δ = 0) was used as a internal standard, and all chemical shifts (δ) are given in ppm downfield of TMS in $CDCl_3$ solutions, unless stated otherwise. The coupling constants (J) are given in Hz. Mass spectra were determined on a VG-Tribrid spectrometer, and the fragment ions are listed in m/z with relative intensities in parentheses. Elemental analyses were performed by the Microanalytical Service Laboratory of the Laboratorium für Organische Chemie (ETH).

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetrakis(4-*tert*-butylphenyl)-1,3-dioxolane-4,5-dimethanol (12). Following the known procedure[12] 4.36 g (20 mmol) of (*R*,*R*)-dimethyl-*O*,*O*-isopropylidenetartrate in 10 mL of THF was added to 90 mmol of 4-(*tert*-butylphenyl)magnesium bromide (prepared from 20.4 g of 4-*tert*-butylbromobenzene and 2.5 g of Mg) in 80 mL of THF. After workup and recrystallization from ethanol 8.14 g (59%) of a white powder of **12** was isolated: mp 222–223 °C; $[\alpha]^{rt}_D$ −64.5 (*c* = 1.0 in $CHCl_3$); ^1H NMR (200 MHz) δ 7.44 (d, J = 8 Hz, 4 H), 7.30 (m, 12 H), 4.56 (s, 2 H), 4.05 (br, 2 H), 1.33 (s, 18 H), 1.27 (s, 18 H), 1.02 (s, 6 H); ^{13}C NMR (50 MHz) δ 149.7, 149.5, 143.1, 139.4, 128.0, 127.0, 124.7, 123.8, 109.0, 80.9, 77.5, 34.2, 31.2, 31.1, 26.8; IR 3360, 2985, 2905, 2890, 1510, 1365, 1270, 1170, 1060, 1020, 890, 840, 830 cm^{-1}; MS (FAB) m/z 690 (M^+ − 1), 655 (M^+ − 2 OH). Anal. Calcd for $C_{47}H_{62}O_4$ (690.97): C, 81.69; H, 9.04. Found: C, 81.13; H, 9.37.

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetrakis(3,5-dimethylphenyl)-1,3-dioxolane-4,5-dimethanol (13). Following a procedure described previously[12] 4.0 g (18.3 mmol) of (*R*,*R*)-dimethyl *O*,*O*-isopropylidenetartrate in 45 mL of THF was added to 100 mmol of *m*-xylene-5-magnesium bromide (prepared from 20.94 g of 5-bromo-*m*-xylene and 2.5 g of Mg) in 70 mL of THF. After workup, 14.2 g of a brown syrup was isolated. This crude product was purified by FC (480 g SiO_2, hexane/ether 4:1) leading to 7.92 g of almost pure **13**. Recrystallization from MeOH/H_2O 1:1 afforded clathrates with water. To remove this water, the crystals were dissolved in ether and dried over $MgSO_4$. After the solvent was removed, 5.62 g (54%) of colorless solid **13** was obtained: mp 92.0–93.2 °C (lit.[78a] mp 82–85 °C); $[\alpha]^{rt}_D$ −42.6 (*c* = 1.0 in $CHCl_3$) (lit.[78a] $[\alpha]^{rt}_D$ −38.29 (*c* = 0.41 in $CHCl_3$)); ^1H NMR (300 MHz) δ 7.14 (s, 4 H), 6.93 (br s, 6 H), 6.84 (s, 2 H), 4.55 (s, 2 H), 3.79 (s, 2 H), 2.30 (s, 12 H), 2.23 (s, 12 H), 1.06 (s, 6 H); ^{13}C NMR (75 MHz) δ 145.96, 142.79, 137.33, 136.38, 129.16, 129.06, 128.71, 126.34, 125.31, 125.11, 109.28, 81.19, 77.95, 27.13, 21.53, 21.38; IR 3585, 3362, 3007, 2919, 2865, 1601, 1455, 1379, 1339, 1168, 1065, 941, 891, 854 cm^{-1}. Anal. Calcd for $C_{39}H_{46}O_4$ (578.79): C, 80.93; H, 8.01. Found: C, 80.68; H, 8.07.

(4*R*,5*R*)-2,2-Diethyl-α,α,α′,α′-tetrakis(3,5-dimethylphenyl)-1,3-dioxolane-4,5-dimethanol (19). Following the described procedure[12] 4.0 g (16 mmol) of (*R*,*R*)-dimethyl *O*,*O*-pentylidenetartrate in 45 mL of THF was added to 100 mmol of *m*-xylyl-5-magnesium bromide (prepared from 21.5 g of 5-bromo-*m*-xylene and 2.5 g of Mg) in 70 mL of THF. After workup, 14.5 g of a brown syrup was isolated. This crude product was purified by FC (400 g SiO_2), first with 5.36 L of toluene (134 fractions, each of 40 mL) and then with 1.6 L of ether (two fractions, each of 800 mL). The fractions 90–134 and the first ether fraction were combined and after removal of the solvent the product was recrystallized twice from MeOH/H_2O 1:1. The isolated clathrates with water were dissolved in ether and dried over $MgSO_4$. After filtering and evaporating 5.75 g (59%) of the colorless solid **19** was obtained, containing traces of water and ether. To obtain analytically pure **19**, 0.5 g of this sample was heated under HV at 160 °C. The resulting solid was stirred for several hours in pentane, decanted, and again heated under HV, furnishing 0.46 g of colorless **19**: mp 175.8–179.2 °C; $[\alpha]^{rt}_D$ −92.2 (*c* = 1.0 in $CHCl_3$) (lit.[21] $[\alpha]^{rt}_D$ −87.7 (*c* = 1.2 in $CHCl_3$)); ^1H NMR (300 MHz) δ 7.12 (s, 4 H), 6.96 (s, 4 H), 6.92 (s, 2 H), 6.86 (s, 2 H), 4.36 (s, 2 H), 4.10 (s, 2 H), 2.29 (s, 12 H), 2.23 (s, 12 H), 1.36–1.33 (m, 4 H), 0.73 (t, J = 7.5 Hz, 6 H); ^{13}C NMR (75 MHz) δ 146.32, 142.63, 137.31, 136.25, 129.07, 128.66, 126.38, 125.46, 111.97, 80.64, 78.05, 29.65, 21.53, 8.20; IR 3586, 3357, 3007, 2972, 2920, 1602, 1460, 1378, 1174, 1071, 1038, 941, 854 cm^{-1}. Anal. Calcd for $C_{11}H_{50}O_4$ (606.85): C, 81.15; H, 8.30. Found: C, 80.61; H, 8.44.

(4*R*,5*R*)-α,α,α′,α′-Tetra(1-naphthyl)-1,3-dioxolane-4,5-dimethanol (32). Following the known procedure[12] 14.28 g (75 mmol) of (*R*,*R*)-dimethyl *O*,*O*-methylidenetartrate in 200 mL of THF was added to 300 mmol of 1-naphthylmagnesium bromide (prepared from 68.44 g of 1-bromonaphthalene and 8.26 g of Mg) in 250 mL of THF. After workup, 55 g of a orange foam was isolated. This crude product was stirred in 250 mL of pentane for 1 h and evaporated (RV). The yellow solid was purified by FC (1.5 kg SiO_2, toluene) leading to two fractions of 16.45 g and 22.04 g of still impure **32**. The first fraction was dissolved in 800 mL and the second in 1 L of MeOH. With strong stirring to the first portion was added 800 mL and to the second 1 L of H_2O. Each precipitate was filtered off and recrystallized twice from toluene/hexane 1:1 yielding a total of 25.77 g (54%) of pure **32**. To obtain analytically pure **32**, 1.0 g was again recrystallized from toluene/hexane 1:1 furnishing 0.86 g of a colorless solid of **32**: mp 255–257 °C; $[\alpha]^{rt}_D$ −32.6 (*c* = 1.0 in $CHCl_3$); ^1H NMR (DMSO-d_6, 95 °C, 300 MHz) δ 8.43–5.75 (m, 28 H), 3.07 (s, 4 H); ^{13}C NMR (DMSO-d_6, 75 MHz) due to extremely broadened signals (rotamers) assignment is impossible; IR 3579, 3051, 3008, 2891, 1599, 1509, 1396, 1348, 1306, 1161, 1099, 1056, 966, 894 cm^{-1}. Anal. Calcd for $C_{45}H_{34}O_4$ (638.76): C, 84.62; H, 5.37. Found: C, 84.42; H, 5.49.

Preparation of TADDOL 35 from (*R*,*R*)-Dimethyl Tartrate. (*R*,*R*)-Dimethyl *O*,*O*-fluorenylidenetartrate was prepared following procedures taken from the literature: fluorenone → 9,9-dichlorofluorene (99%)[82a] → fluorenone dimethyl acetal (63% yield)[82b] + (*R*,*R*)-dimethyl tartrate → (*R*,*R*)-dimethyl *O*,*O*-fluorenylidenetartrate (49% yield).[82c](4*R*,5*R*)-2-(9-Fluorenylidene)-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol (35). Following a described procedure[12] 8.51 g (25 mmol) of (*R*,*R*)-dimethyl *O*,*O*-fluorenylidenetartrate in 70 mL of THF was added to 110 mmol of phenylmagnesium bromide (prepared from 15.7 g of bromobenzene and 2.75 g of Mg) in 90 mL of THF. After workup, 15.6 g of a yellow foam was isolated. This crude product was purified by NC (700 g SiO_2, pentane/ether 2:1) leading to 12.06 g of still impure **35**. After recrystallization from MeOH/H_2O 1:1 and drying under HV at 70 °C for 5.5 h 6.65 g (45%) of **35** was isolated: mp 225.0–226.4 °C (lit.[15a] mp 128–130 °C). $[\alpha]^{rt}_D$ −62.9 (*c* = 1.0 in $CHCl_3$) (lit.[15a] $[\alpha]^{rt}_D$ −40.6 (*c* = 1.0 in $CHCl_3$); ^1H NMR (300 MHz) δ 7.76–7.01 (m, 28 H), 6.42 (d, J = 7.5 Hz, 2 H), 4.95 (s, 2 H), 4.71 (s, 2 H); ^{13}C NMR (75 MHz) δ 145.70, 143.89, 142.24, 139.62, 130.07, 129.12, 128.23, 128.00, 127.72, 127.57, 127.41, 124.50, 119.55, 111.82, 81.28, 78.34; IR 3583, 3358, 3063, 3008, 2900, 1954, 1811, 1611, 1495, 1449, 1298, 1118, 1070, 1051, 1005, 924, 897, 648 cm^{-1}. Anal. Calcd for $C_{41}H_{33}O_4$ (589.71): C, 83.51; H, 5.64. Found: C, 83.30; H, 5.83.

(4*R*,5*R*)-2-Methyl-2-phenyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol (47). Following the known procedure[12] 14.14 g (50.5 mmol) of (*R*,*R*)-dimethyl *O*,*O*-(1-phenylethylidene)tartrate in 130 mL of THF were added to 227 mmol of phenylmagnesium bromide (prepared from 24 mL of bromobenzene and 5.8 g of Mg) in 130 mL of THF. After workup and FC (480 g SiO_2, hexane/ether 4:1) 19.42 g of a yellow solid contaminated with an unknown impurity was obtained. Sixteen g of this product was dissolved in 600 mL of MeOH and to this solution was added during 2.5 h 600 mL of H_2O with vigorous stirring. The formed white precipitate was filtered off, dissolved in 150 mL of CH_2Cl_2, and dried with $MgSO_4$.

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After solvent was removed and the precipitate dried overnight under HV at 60 °C 13.0 g of **47** was obtained: mp 96–99 °C. $[\alpha]^{rt}_D$ +71.44 (c = 1.22 in $CHCl_3$) (lit.[9] $[\alpha]^{rt}_D$ +83 (c = 1.3 in $CHCl_3$); ^1H NMR (400 MHz) δ 7.55–6.97 (m, 25 H), 5.17 (d, J = 5.6 Hz, 1 H), 5.09 (d, J = 5.6 Hz, 1 H), 2.40 (s, 1 H), 2.27 (s, 1 H), 1.33 (s, 3 H); ^{13}C NMR (100 MHz) δ 145.10, 145.06, 145.03, 143.42, 143.30, 128.48, 128.29, 128.07, 128.04, 127.96, 127.82, 127.60, 127.45, 127.31, 127.21, 127.18, 127.00, 126.95, 126.78, 126.53, 124.70, 111.32, 83.22, 81.62, 78.91, 78.42, 29.97; IR 3544, 3087, 3008, 1600, 1493, 1448, 1372, 1177, 1134, 1070, 1045, 914 cm^{-1}; MS (FAB) m/z 300 (13), 299 (44), 195 (15), 183 (43), 179 (32), 168 (15), 167 (71), 165 (18), 121 (45), 106 (12), 105 (100), 77 (34). Anal. Calcd for $C_{36}H_{32}O_4$ (528.61): C, 81.79; H, 6.10. Found: C, 81.75; H, 6.23.

(4S,5S)-2-Methyl-2-phenyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol (*ent*-47). The preparation was done as for **47**, but instead of the (*R,R*)- the (*S,S*)-dimethyl *O,O*-(1-phenylethylidene)tartrate was used: mp 99.0–100.5 °C; $[\alpha]^{rt}_D$ −71.8 (c = 2.0 in $CHCl_3$). The spectroscopic data (^1H NMR (300 MHz), ^{13}C NMR (75 MHz), and IR) are identical to those shown for **47**.

(4*R*,5*R*)-2-Methyl-2-phenyl-α,α,α′,α′-tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol (48). Following a previous procedure[12] 11.20 g (40 mmol) of (*R,R*)-dimethyl *O,O*-(1-phenylethylidene)tartrate in 100 mL of THF was added to 164 mmol of 2-naphthylmagnesium bromide (prepared from 33.94 g of 2-bromonaphthalene and 4.00 g of Mg) in 150 mL of THF. After workup and FC (360 g SiO_2, toluene) the yellow solid was dissolved in 950 mL of MeOH and the resulting precipitate washed with ether to remove the yellow impurity. After the precipitate was dried under HV at 110 °C 5.28 g (18%) of **48** was obtained; mp 160–170 °C; $[\alpha]^{rt}_D$ +289.9 (c = 1.55 in $CHCl_3$); ^1H NMR (300 MHz) δ 8.25–7.06 (m, 29 H), 6.48–6.40 (m, 2 H), 6.32–6.27 (m, 2 H), 5.79 (d, J = 4.2 Hz, 1 H), 5.76 (d, J = 4.2 Hz, 1 H), 3.03 (s, 1 H), 2.14 (s, 1 H), 1.64 (s, 3 H); ^{13}C NMR (100 MHz) δ 145.33, 143.29, 142.63, 139.87, 139.22, 132.79, 132.70, 132.63, 132.45, 132.24, 132.03, 131.81, 128.76, 128.49, 128.45, 128.27, 128.04, 127.98, 127.60, 127.47, 127.46, 127.36, 127.32, 127.29, 127.24, 127.22, 126.45, 126.16, 126.11, 126.07, 125.85, 125.80, 125.78, 125.76, 125.69, 125.65, 125.61, 125.48, 124.88, 124.70, 124.26, 124.03, 123.70, 112.30, 83.44, 81.89, 79.74, 79.57, 31.15; IR 3539, 3060, 3008, 1600, 1506, 1448, 1436, 1372, 1361, 1313, 1270, 1178, 1123, 1070, 937, 903, 858, 818 cm^{-1}; MS (FAB) m/z 711 (3), 429 (7), 399 (29), 309 (15), 308 (35), 283 (61), 279 (32), 268 (19), 155 (100), 154 (30), 152 (19), 136 (22), 128 (15), 127 (50), 77 (13). Anal. Calcd for $C_{52}H_{40}O_4$ (728.89): C, 85.69; H, 5.53. Found: C, 85.79; H, 5.43.

Typical Procedure for the Diels–Alder Reaction Performed at 0 or −5 °C. An experiment using TADDOL **16** is outlined in Table 2 (entry 8). To a toluene (3 mL) suspension of 1.0 g of powdered MS, and 185 mg (0.277 mmol) of TADDOL **16** was added *via* syringe 1.0 mL (0.25 mmol) of 2.5 M $(i\text{-PrO})_2TiCl_2$ in the same solvent. The mixture was stirred at rt for 1 h, diluted with 5 mL of toluene, and cooled to −5 °C. A toluene solution (12 mL) of 3-((*E*)-2-butenoyl)-1,3-oxazolidin-2-one (388 mg, 2.5 mmol) and 5 min later 4.4 mL (55 mmol) of cyclopentadiene were added. After being stirred for 24 h at −5 °C (± 0.5 °C) the reaction was quenched with 50 mL of 1 N HCl solution, stirred for 15 min, and filtered through celite, and the celite residue was washed with 50 mL of 1 N HCl solution and 50 mL of ether. The organic phase was separated and the aqueous layer was extracted with 3 × 100 mL of ether. The combined organic phases were washed with 100 mL of saturated NaCl solution, dried over $MgSO_4$, evaporated (RV), and dried overnight under HV. The spectral data and physical properties of the cycloadducts are identical to those in ref 9.

Typical Procedure for the Diels–Alder Reaction Performed at *ca.* −20 °C. An experiment using TADDOL **16** is outlined in Table 2 (entry 7). To a toluene suspension (5 mL) of 1.0 g of powdered MS and 260 mg (0.39 mmol) of TADDOL **16** was added *via* syringe 1.5 mL (0.375 mmol) of 2.5 M $(i\text{-PrO})_2TiCl_2$ in the same solvent. The mixture was stirred at rt for 1 h, diluted with 15 mL of toluene, and cooled to −78 °C with a i-PrOH/CO_2 cooling bath. A toluene solution (20 mL) of 3-((*E*)-2-butenoyl)-1,3-oxazolidin-2-one (388 mg, 2.5 mmol) was added. Five min later 4.4 mL (55 mmol) of cyclopentadiene was added. The mixture was allowed to warm to −16 °C (± 0.5 °C) and was stirred for 24 h. After workup (same procedure as for the experiment above) the resulting light yellow oil was purified by FC (3.5 cm i.d., 140 g of SiO_2) with toluene/AcOEt 10:1 as eluent. After the oil was dried overnight under HV 0.52 g (94%) of **51/52** was isolated as a white powder. The TADDOL **16** was recovered (during FC) with a yield of 92% and checked to be free of the Diels–Alder product by ^1H NMR.

Reduction of the Diels–Alder Products 51/52 to 53 (R = H).[35] To an ether solution (40 mL) of 100 mg (0.45 mmol) of **51/52** 250 mg (6.6 mmol) of $LiAlH_4$ was added. This solution was stirred for 4 h at rt and subsequently hydrolyzed with 2.5 mL of 10% NaOH solution and dried with $MgSO_4$. This suspension was filtered through SiO_2 (5 × 1 cm, the SiO_2 was covered with a filter paper) and washed with 200 mL of ether. The organic layer was evaporated (RV) and after distillation at 55–110 °C/40 mbar 46 mg (73%) of **53** (R = H) was obtained as a colorless oil.

Preparation of the Trifluoroacetate Derivative[83] 53 (R = COCF$_3$). To a solution of 1 μL of alcohol **53** (R = H) in 200 μL of CH_2Cl_2 was added 50 μL of trifluoroacetic anhydride. The solution was stirred overnight at rt and then nitrogen gas was passed through for several minutes to remove the solvent. After 1 mL of ether was added the obtained sample was used directly for CGC (retention times (t_R) for **53** (R = $COCF_3$): t_R = 48.18 (corresponding to **51a**), t_R = 48.97 (corresponding to **51b**), t_R = 52.9, t_R = 53.56 (corresponding to **52**)).

Enantiomer Enrichment of 51/52 by Recrystallization. After two recrystallizations of 0.5 g of a mixture of **51/52** (dr 9:1, er **51a/51b** 94:6, er **52** 91:9, Table 2, entry 12) from hexane, i-PrOH/hexane 5:95, or ether/hexane 1:9 the enantiomer, enriched products **51/52** were obtained with yields of 50%, 48%, and 33%, respectively. CGC analysis showed diastereomer ratios of 98:2, 98:2, and 98.5:1.5 and enantiomer ratios of **51a/51b** 99:1, 98.5:1.5, and 98.5:1.5, respectively. In all three cases er >99:1 were obtained for the *exo*-product **52**.

X-ray Crystal Structure Analysis. Details of the crystal structure investigation are available on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK, on quoting the full journal citation.

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