Preparation and Characterization of New C_2- and C_1-Symmetric Nitrogen, Oxygen, Phosphorous, and Sulfur Derivatives and Analogs of TADDOL[1])

Part I

Compounds Containing One or Two Sulfur-Containing Substituents and Use in Cu-Catalyzed Enantioselective Conjugate Additions to Cyclic Enones

by **Arkadius Pichota**[2]), **Volker Gramlich**[3]), **Albert K. Beck**, and **Dieter Seebach***

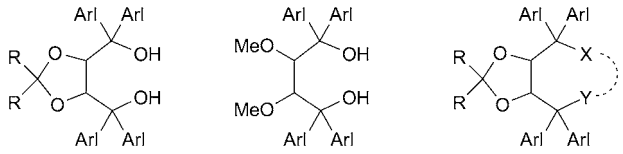
Laboratorium für Organische Chemie, Departement für Chemie und Angewandte Biowissenschaften, ETH-Zürich, Hönggerberg HCI, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich
(phone: +41-44-632-2990; fax: +41-44-632-1144; e-mail: seebach@org.chem.ethz.ch)

The chloro alcohols **4**–**6** derived from TADDOLs (=$\alpha,\alpha,\alpha',\alpha'$-tetraaryl-1,3-dioxolan-4,5-dimethanols) are used to prepare corresponding sulfanyl alcohols, ethers, and amines (*Scheme 1* and *Table 1*). The dithiol analog of TADDOL and derivatives thereof, **45**–**49**, were also synthesized. The crystal structures of 16 representatives of this series of compounds are reported (*Figs. 1–3* and *Scheme 2*). The thiols were employed in Cu-catalyzed enantioselective conjugate additions of *Grignard* reagents to cyclic enones, with cycloheptenone giving the best results (er up to 94:6). The enantioselectivity reverses from *Si*-addition with the sulfanyl alcohol to *Re*-addition with the alkoxy or dimethylamino thiols (*Table 4*). Cu^I-Thiolates, **50**–**53**, could be isolated in up to 84% yield (*Scheme 2*) and were shown to have tetranuclear structures in the gas phase (by ESI-MS), in solution (CH_2Cl_2, THF; by vapor-pressure osmometry and by NMR pulsed-gradient diffusion measurements; *Table 5*), and in the solid state (X-ray crystal structures in *Scheme 2*). The Cu complex **50** of the sulfanyl alcohol is stable in air and in the presence of weak aqueous acid, and it is a highly active catalyst (0.5 mol-%) for the 1,4-additions, leading to the same enantio- and regioselectivities observed with the *in situ* generated catalyst (6.5 mol-%; *Scheme 3*). Since the reaction mixtures contain additional metal salts (MgX_2, LiX) it is not possible at this stage, to propose a mechanistic model for the conjugate additions.

1. Introduction. – Since the first preparation in 1982 of the parent TADDOL **A**, Arl = Ph, R = Me, by one of us (*A. K. B*), and its use as bis(alkoxide) ligand in enantioselective organotitanium reagents [2], this skeleton has experienced numerous applications for inducing chirality in the most general sense. In addition, the conformational fixing effect of diarylmethanol groups (*cf.* the *Thorpe–Ingold* effect) and the steric effect of the diastereotopic geminal aryl groups in chiral molecules were

[1]) Partially mentioned in preliminary communications [1].
[2]) Part of the Ph.D. Thesis of *A. P.*, ETH Dissertation No. 14015 (2000).
[3]) Laboratorium für Kristallographie, Sonnegstrasse 5, ETH Zürich, CH-8092 Zürich.

subsequently exploited for the same purpose[4]). The structural diversity of TADDOL and its derivatives **A** is huge: the aryl (or heteroaryl) groups can be varied widely, the substituents R on the dioxolane ring may be H, alkyl, or aryl, yea, the heterocyclic ring may be opend as in **B** [7]. This is due to the simplicity of preparing these compounds: (*R*,*R*)- or (*S*,*S*)-tartrates are converted to acetals or ketals by treatment with aldehydes or ketones, followed by reaction with an excess of aryl *Grignard* reagent. The diversity is further enhanced by modification (OH → OR) or substitution (OH → X) of one or both TADDOL OH group(s) to give C_1- or C_2-symmetrical analogs of type **C**, which can be used for stoichiometric (*cf.* **C**, X = OH, Y = OOH, TADOOH [8]) or catalytic [1a,c] enantioselective transformations, which would not be possible with the TADDOLs themselves. For details, we refer to two comprehensive articles[5]) [9] and a number of reviews addressing various aspects[6]) of the use of TADDOLs [10–19].



A **B** **C**

absolute configuration (*R*,*R*) or (*S*,*S*)

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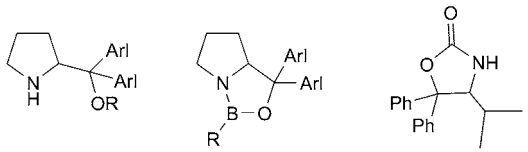
[4]) *Cf.* the diaryl-prolinol-derived organocatalysts **i** [3] and oxaborolidines **ii** [4], and the diaryl-imidazolidinone (DIOZ) **iii** [5], to name only a few. See also '*The 'Magic' Diarylhydroxymethyl Group*' (*M. Braun* [6a]), '*The* gem-*Diaryl Effect in Enantioselective Synthesis*' (*D. S.* and *A. K. B.* [6b]), and the discussion in Sect. D of [6c].



i **ii** **iii**

[5]) '*TADDOLs, their derivatives, and TADDOL analogs: versatile chiral auxiliaries*' [9a]; '*Use of TADDOLs and Their Derivatives in Asymmetric Synthesis*' [9b]; '*TADDOLate Ligands*' [9c].

[6]) '*Tartrate-Derived Ligands for Enantioselctive $LiAlH_4$ Reduction of Ketones – A Comparison of TADDOLs and BINOLs*' [10a,b]; '*TADDOLs – from enantioselective catalysis to dendritic crosslinkers to cholesteric liquid crystals*' [10c]; '*TADDOL and its derivatives – our dream of universal chiral auxiliaries*' [11]; '*Developing catalytic enantioselective fluorination*' [12a]; '*Development of the titanium-TADDOLate-catalyzed asymmetric fluorination of β-ketoesters*' [12b]; '*Cp Titanium TADDOLate*' [13]; '*Catalytic asymmetric organozinc additions to carbonyl compounds*' [14]; '*Preparation of Polymer-Supported Ligands and Metal Complexes for Use in Catalysis*' [15]; '*Recent progress in chiral* Brønsted acid *catalysis*' [16]; '*Crown ethers, TADDOL, Nobin and Metal(salen) compexes as chiral phase-transfer catalysts for asymmetric synthesis*' [17]; '*Noncovalent organocatalysis based on hydrogen bonding*' [18]; '*TADDOL-Derived Phosphonites, Phosphites, and Phosphoramidites in Asymmetric Catalysis*' [19].

In the present series of three papers[7]) [20], we describe the preparation of hitherto unpublished or non-characterized TADDOL derivatives (mainly of the parent structure **A**), in which OH groups are replaced by N- or S-containing substituents; we also present crystal structures, an application for enantioselective conjugate addition, and the determination of pK_a values of TADDOL derivatives.

2. Preparation of the S- and N-Derivatives. – The conversions leading from TADDOLs to these derivatives are outlined in *Scheme 1*, and the results were compiled in *Table 1*. The central starting materials for mono-substitutions on TADDOL skeletons are chloro-hydroxy compouds such as those from the parent TADDOL **1** [21a], the naphthalen-2-yl-TADDOL **3** [21a,b] and the hexaphenyl analog **2** [21c,d]. One of the OH groups can be replaced with Cl by the *Appel* reaction (PPh_3/CCl_4/pyridine [22]), which stops at the stage of mono-substitution[8])[9]); the yields drop from those obtained with the parent TADDOL (*i.e.*, **1** → **4**), when the procedure is applied to the naphthalen-2-yl (*i.e.*, **3** → **6**) and the hexaphenyl derivative (*i.e.*, **2** → **5**), and complex mixtures were obtained with the TADDOLs carrying naphthalen-1-yl or 4-tolyl groups.

With the mono-chloro compounds **4**–**6** available, we have prepared other C_1-symmetrical TADDOL derivatives, **7**–**17**, by nucleophilic replacement of the Cl-atom. Thus, treatment with excess thiourea, followed by hydrolysis under basic conditions, yields the sulfanyl derivatives **7** and **8**, reaction with NH_3, $MeNH_2$, or Me_2NH[10])[11]) provides the amino alcohols **9**–**12**, and with alcohols or phenols (in the presence of Et_3N), the alkoxy and aryloxy alcohols **13**–**17** are formed[12]).

The OH-group of the amino, alkoxy and aryloxy alcohols **9**–**17** could be replaced by nucleophilic substitutions *via* the corresponding Cl-derivatives, which are formed by

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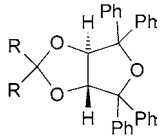
[7]) a) Part II: '*TADDAMIN-Derived and Phosphorous-Containing Compounds*' (p. 1273 of this HCA issue); b) Part III: '*Some New Chiral* Brønsted Acids *for Organocatalysis and p*K_a *Values in MeO–*$(CH_2)_2$*–OH/*H_2O *– A Survey*' (p. 1303 of this HCA issue).

[8]) .....even when excess reagent was employed.

[9]) Considering that this reaction is expected to occur *via* an S_N1 mechanism, and that the intermediate cation could undergo rearrangements (Scheme 4 in [9a] and [23]), the 90% yield of crude product **4** is remarkable. For previous reports on **4**, see [24].

[10]) The yields of this reaction and its selectivity (with respect to the tetrahydrofuran by-product **iv**) could be greatly improved by using DMF as solvent and carrying out the reaction at lower temperatures than previously reported [24b]. For preparation of TADDAMINs (= (4*S*,5*S*)-2,2,*N*,*N*′-tetramethyl-*a*,*a*,*a*′,*a*′-tetraphenyl-1,3-dioxolan-4,5-diamines) *via* azido-derivatives see [24a].



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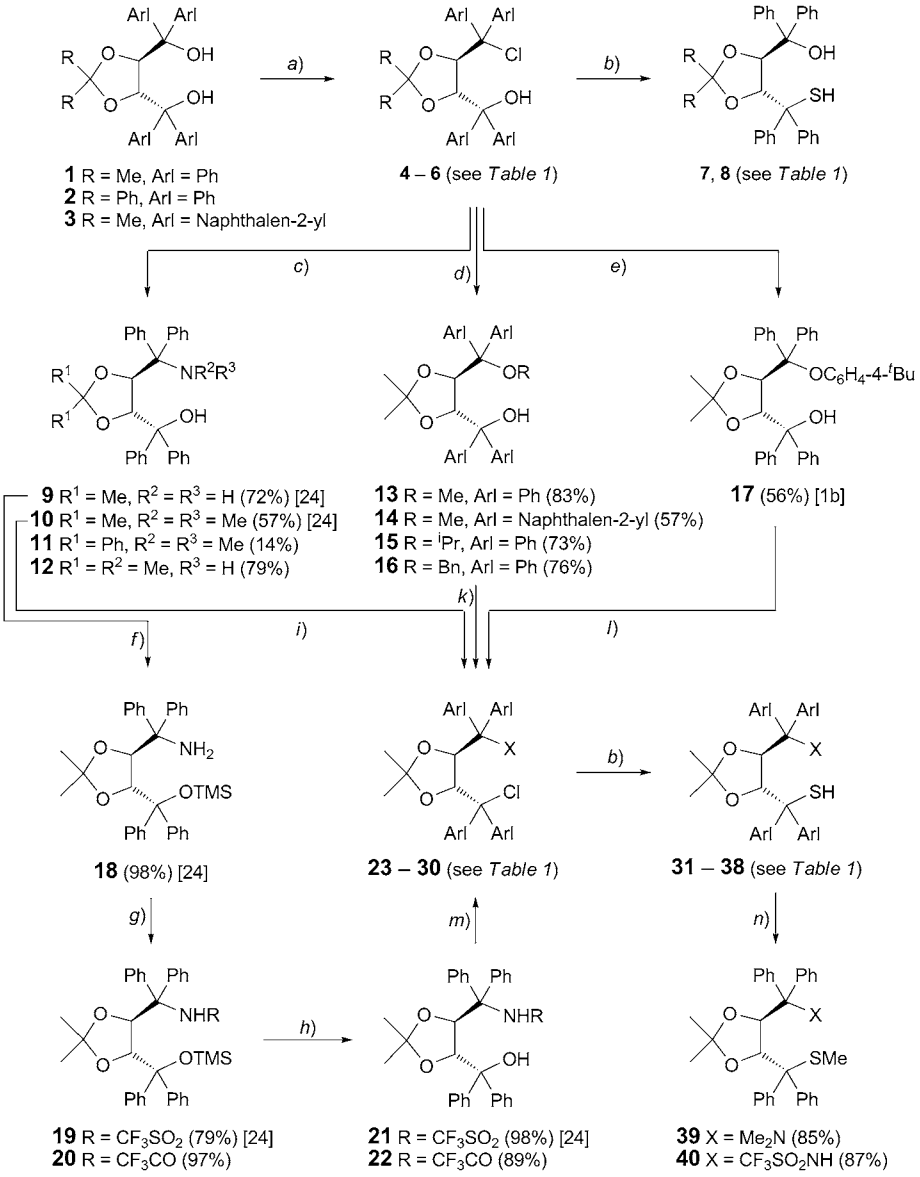
[11]) For *Friedel–Crafts*-type reactions with anilines (leading to trityl-substituted dioxolanes), see [1b].

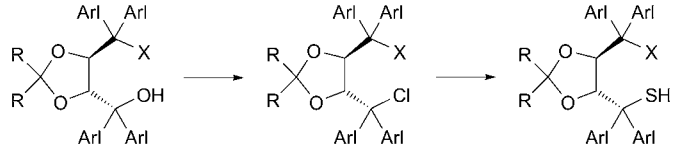
[12]) Interestingly, the phenoxy group in **17** acts as a leaving group under mild conditions: when dissolved in MeOH, **17** is converted to **13** under acid catalysis.

Scheme 1. *Preparation of Sulfur-Containing Derivatives* **7**, **8**, **19**, **21**, *and* **31**–**40** *from TADDOLs* **1**–**3**



a) 2 equiv. PPh_3, 10 equiv. CCl_4, CH_2Cl_2, r.t. *b*) 1. 20–30 equiv. $SC(NH_2)_2$, DMF, r.t.; 2. NaOH. *c*) HNR_2, autoclave, 50–80°. *d*) MeOH Reflux or ROH 50°, 1–1.5 equiv. Et_3N. *e*) 5 equiv. 4-^{t}Bu–C_6H_4OH, 2 equiv. Et_3N, CH_2Cl_2, r.t. *f*) Me_3SiCl (TMSCl), Et_3N, CH_2Cl_2, r.t. *g*) $(CF_3SO_2)_2O$ or $(CF_3CO)_2O$, Et_3N, CH_2Cl_2, –78° → r.t. *h*) Bu_4NF (TBAF), THF, r.t. *i*) $SOCl_2$, CH_2Cl_2. *k*) $SOCl_2$, Et_3N, CH_2Cl_2. *l*) BuLi, –78° → r.t., $SOCl_2$, THF. *m*) 5 equiv. $SOCl_2$, 10 equiv. LiCl, THF, reflux. *n*) MeI, K_2CO_3, MeCN, CH_2Cl_2.

Table 1. *Preparation of Monothiols* **7**, **8**, *and* **31**–**38** *Obtained from Monohydroxy TADDOLs* **1**–**3**, **10**, **13**–**17**, **21**, *and* **22** via *Replacement of Cl of the Corresponding Monochloro Compounds* **4**–**6** *and* **23**–**30** *with Thiourea*

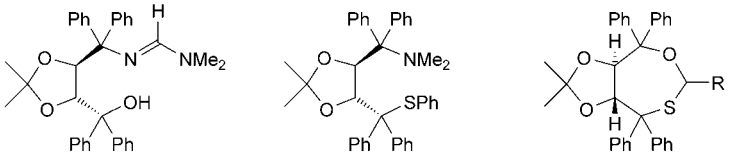


1–**3**, **10**, **13**–**17**, **21**, **22** → **4**–**6**, **23**–**30** → **7**, **8**, **31**–**38**

R	ArI	X	OH Derivative	Cl Derivative (yield [%])	SH Derivative (yield [%])
Me	Ph	OH	**1**	**4** (76)	**7** (75)
Ph	Ph	OH	**2**	**5** (56)	**8** (63)
Me	Naphthalen-2-yl	OH	**3**	**6** (64)	–
Me	Ph	Me_2N	**10**	**23** (98)	**31** (79)
Me	Ph	MeO	**13**	**24** (quant.)	**32** (66)
Me	Naphthalen-2-yl	MeO	**14**	**25** (97)[a])	**33** (47)
Me	Ph	^{i}PrO	**15**	**26** (75)	**34** (74)
Me	Ph	BnO	**16**	**27** (quant.)	**35** (65)
Me	Ph	4-^{t}Bu–C_6H_4O	**17**	**28** (quant.)	**36** (43)
Me	Ph	CF_3SO_2NH	**21**	**29** (81)	**37** (74)
Me	Ph	CF_3CONH	**22**	**30** (quant.)	**38** (75)

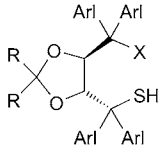
[a]) Conversion (determined by ^{1}H-NMR).

the previously reported treatment with $SOCl_2$ [24a] (→**23**–**30**); even the dimethylamino- (**23**) and the 4-(*tert*-Butyl)-phenoxy chloro derivative (**28**) could be prepared by this procedure. These Cl compounds were mainly used to prepare the thiols **31**–**38** (*Scheme 1* and *Table 1*) by reaction with excess thiourea in DMF at room temperature, followed by alkaline hydrolysis (*Table 1–3*). From the amino alcohol **9**, the reaction sequence ($SOCl_2$; $SC(NH_2)_2$; NaOH) led to the amidine **41**. Thioethers were prepared by *S*-methylation (**31**→**39**, **37**→**40**), or by Cl/SR substitution (**23**→**42**), and the seven-membered cyclic *O*,*S*-acetals **43** and **44** were formed as single diastereoisomers from the sulfanyl alcohol **7** and acetaldehyde or benzaldehyde. The 2,2,2-trifluoroacetamides, **20** and **22**, and the corresponding trifluoromethanesulfanoamides, **19** and **21** [24b], were obtained *via* the silyloxy derivative **18** [24b].



41 **42** **43** R = Me, **44** R = Ph

Table 2. *Selected Physical Data of the Sulfanyl Derivatives of TADDOLs*

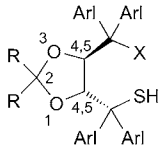


7, **31**, **32**, **34 – 38**, **45** Arl = Ph, R = Me
8 Arl = R = Ph
33 Arl = Naphthalen-2-yl, R = Me

Sulfanyl-TADDOL	X	M.p. [°]	$[\alpha]_D^{r.t.}$ (*c* in $CHCl_3$)	δ(H) [ppm] of S*H*
7	OH	128 – 129	– 36.2 (1.0)	2.34 or 2.35[a])
8	OH	118 – 119	+ 148.8 (1.0)	1.54 or 1.65[a])
31	Me_2N	162 – 163[b])	– 90.9 (1.0)[c])	9.51
32	MeO	182 – 183	+ 6.1 (1.2)	4.07
33	MeO	160 – 161	+ 63.0 (1.1)	3.92
34	^{i}PrO	177 – 179	– 43.2 (1.1)	5.45
35	BnO	93 – 96	– 60.0 (0.95)	4.60
36	4-^{t}Bu–C_6H_4O	105 – 108	– 64.5 (1.0)	2.27
37	CF_3SO_2NH	185 – 190	– 59.7 (1.6)	2.27[d])
38	CF_3CONH	159 – 161	– 97.4 (1.14)	2.05[e])
45	SH	148 – 149	– 32.4 (1.5)	2.03

[a]) Either S*H* or O*H*. [b]) Taken from [24b]. [c]) [24b]: $[\alpha]_D^{r.t.} = -54.1$ ($c = 0.98$, AcOEt). [d]) δ 8.75 ppm for N*H*. [e]) δ 8.66 ppm for N*H*.

Table 3. *Selected NMR Data of the Sulfanyl Derivatives of TADDOLs*

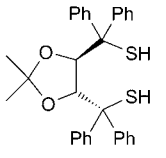


7, **31**, **32**, **34 – 38**, **45** Arl = Ph, R = Me
8 Arl = R = Ph
33 Arl = Naphthalen-2-yl, R = Me

Sulfanyl-TADDOL	δ(H)				δ(C)			
	CH_3–C(2)		H–C(4,5)		C(4,5)		Arl_2C–X	Arl_2C–S
7	0.86	1.05	4.97	5.14	82.2	83.2	78.1	60.6
8	–		5.56	5.75	84.1	85.7	79.8	60.8
31	0.60	1.14	4.48	4.99	76.5[a])	83.9[a])	73.8[a])	–
32	0.95	1.10	4.69[b])		80.6	82.7	84.2	59.7
33	1.07	1.29	4.94	5.09	81.1	83.1	84.2	60.7
34	0.86	0.92	4.41	4.58	81.3	82.8	85.3	57.8
35	0.97	1.02	4.46	4.58	81.0	83.1	85.0	57.9
36	0.98	1.06	4.57	4.75	83.2	83.4	87.2	58.8
37	0.81	1.08	4.33	4.70	82.6	82.7	70.1	58.0
38	0.71	0.90	4.80	4.90	82.4	82.9	67.0	58.0
45[c])	0.98		5.29		83.9		–	60.1

[a]) Taken from [24b]. [b]) H–C(4) and H–C(5) are isochronous. [c]) H–C(4), H–C(5), as well as CH_3–C(2) and C(4,5) are isochronous.

The isolation of the dithiol **45** was a problem; in previous attempts [24][25] the dichloro TADDOL derivative was treated with thiourea, NaSH, Na_2S, or LiS[13]) under various conditions to give mixtures of the dithiol **45**, the 1,2-dithiane **46**, and the thiolane **47**; the dithiol was readily oxidized to the disulfide[14]) in air, and the three compounds could not be separated by chromatography. By carrying out the reaction with thiourea in degassed DMF under an Ar atmosphere, a 9:1 mixture of dithiol and dithiane was isolated in 67% yield; a flash chromatography (10 l of pentane for a 200 mg sample!) led to further enrichment and eventually to crystalline dithiol **45**, the X-ray crystal structure of which could be determined (*vide infra*, *Sect. 3*). Subsequent reaction of the dithiol **45** was actually performed with the material containing *ca.* 10% of the dithiane **46** as an impurity. In this way, we prepared the Sn derivative **48** (50%)[15]) and the Pd^{II} complex **49** (79%), from which the dithiane could be readily separated.



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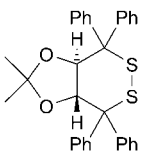

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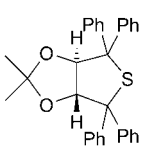

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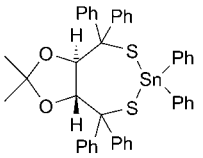

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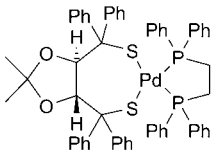

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3. X-Ray Crystal Structures. – The typical TADDOL structure is documented by well over 150 X-ray analyses: a propeller-type C_2-symmetric arrangement of the diarylmethanol units, in which the *quasi*-axial aryl groups are in a type of *edge-on*, the *quasi*-equatorial ones in a type of *face-on* conformation with respect to the C_2 axis (see **D** and **E**), with O–C–C–X and O–C–C–Y dihedral angles around the exocyclic C–C bond of *ca.* 180° (antiperiplanar heteroatoms!; see **G**), and with a H-bridge between the more acidic XH group on one of the two geminal diaryl-substituted C-atoms to a H-bond acceptor on the other one (see **F**) [6c][9]. Those characteristic features are confirmed in the crystal structures (deposited with the *Cambridge Crystallographic Data Centre* (CCDC)) of the monohydroxy compounds (*Fig. 1*) and of the sulfanyl derivatives (*Fig. 2*); the former ones contain OH···OR, or OH···N=CH–NMe_2, the latter ones SH···SH, SH···OR, SH···NR_2 or CF_3SO_2NH···SH H-bonds. The

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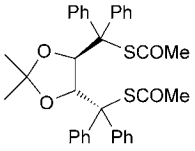
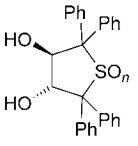
13) In an unsuccessful attempt to prepare the bis[sulfonic acid] derived from **45**, the dithioacetate **v** and, upon its oxidation with performic acid, the monocyclic sulfoxide and sulfone **vi** were isolated [26].



v



vi n = 1, 2

14) All attempts to open the cyclic disulfide **46**, reductively, back to the dithiol have been unsuccessful in our laboratory.

15) Attempted proto- and bromo-destannylations (Ph/H; Ph/Br) to acess chiral SnH and SnBr derivatives did not succeed: the Sn–S rather than the Sn–Ph bond was cleaved by HCl and Br_2.

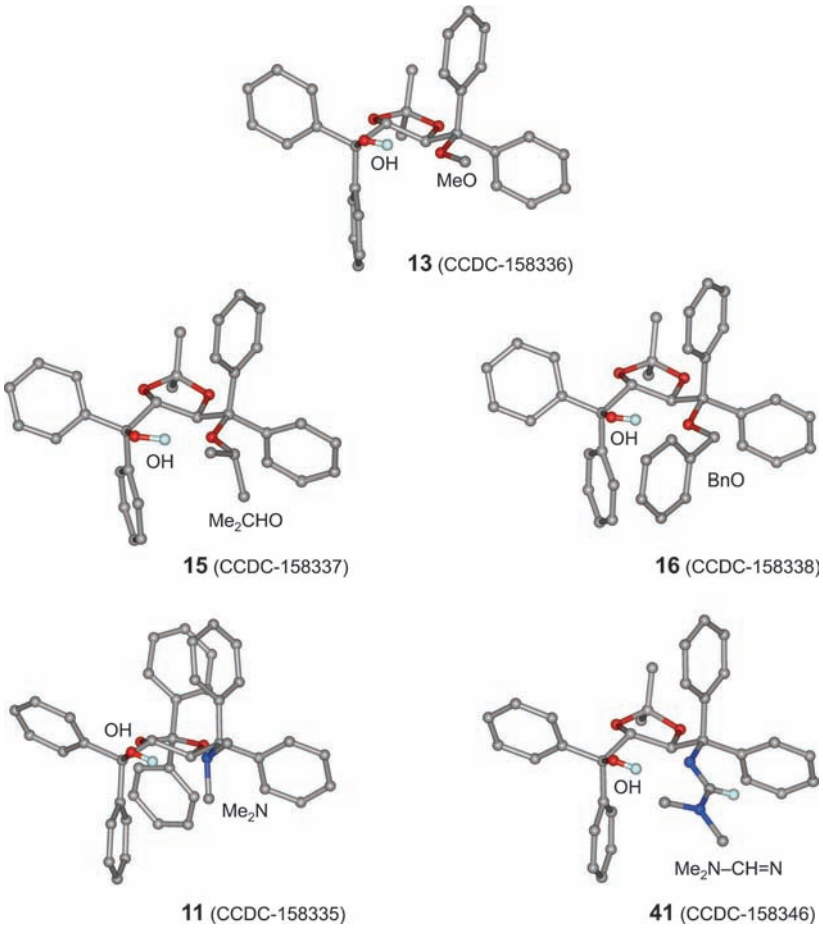
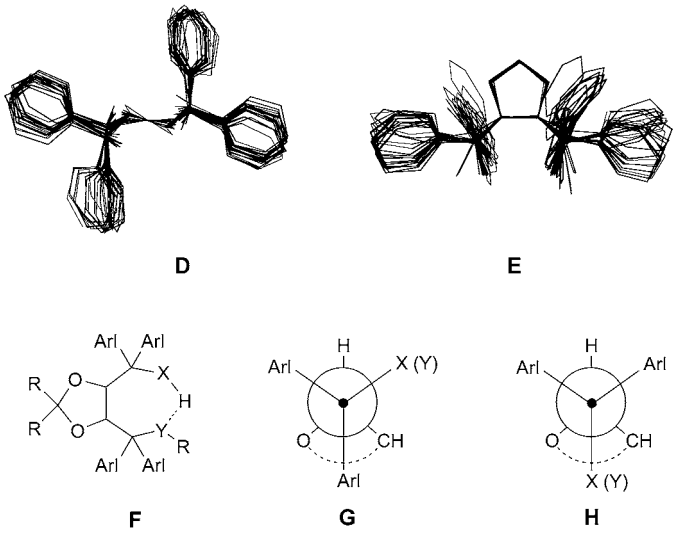


Fig. 1. *X-Ray crystal structures of the five monohydroxy derivatives* **11**, **13**, **15**, **16**, *and* **41** *with the CCDC* (*Cambridge Crystallographic Data Centre*) *codes.* The OH bonds have a H-bonding interaction with an O or N H-bond acceptor in seven-membered-ring arrangement. All exocyclic C,C bonds carry the heteroatoms in a stereoelectronically less favorable antiperiplanar (*ap*) conformation.

structures of the thiolane derivative **47**, with a *trans*-fused bicyclo[3.3.0]octane skeleton, of the Sn compound **48**, containing an almost perfectly planar five-membered ring, and of the chloro dimethylamino derivative **23** are shown in *Fig. 3*. The crystals of **23** have an unusually large unit cell ($19 \times 11 \times 41$ Å)[16]) containing three independent molecules, one of which has the rare structure with a heteroatom (see **H**), rather than a benzene ring (see **G**) above the dioxolane ring, and thus with the stereoelectronically

[16]) This is typical of TADDOL crystals not containing host molecules with H-bond-acceptor properties (see Sect. D in [6c]), see also TADDOL clathrates for enantiomer separation [21a][27] and 'destillative resolution' [28].



more favorable *gauche*-conformation of the exocyclic C,C bond (synclinal (*sc*) O–C–C–Cl dihedral angle)[17])[18]).

4. Enantioselective Conjugate Addition of *Grignard* Reagents to Cyclic Enones Catalyzed by TADDOL-Derived Thiolato-cuprates. – After the discovery by *Gilman et al.* [29], that organocopper compounds and Li-cuprates add to α,β-unsaturated carbonyl compounds in a 1,4-, rather than a 1,2-fashion (typical of Mg and Li derivatives), *Kharash* and *Tawney* [30] found that *Grignard* reagents, such as MeMgBr, can be induced to conjugatively add to cyclohexenone by the presence of *catalytic* amounts of CuCl. The first *enantioselective* variant of this 1,4-addition was reported by *Lippard* and co-workers [31]. In the past 20 years, numerous investigations about this useful reaction have been carried out with excellent regio-, diastereo-, and enantioselectivities; herein, we can only refer to selected review articles [32]. The chiral ligands used to complex the catalytically active Cu species vary widely, with sulfanes prevailing in the early phases [32f][33][34]. The employment of Zn rather than Mg reagents for Cu-catalyzed *Michael* additions can give superior results [32a,c,f].

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[17]) Other examples are the fluoro hydroxy (**C**; R = Me, Arl = Ph, X = F, Y = OH [18], CCDC-118716), the diazido (**C**; R = Me, Arl = Ph, X = Y = N_3 [24b], CCDC-NIBZIH), and the dichloro derivative (**C**; R = Me, Arl = Ph, X = Y = Cl [24b], CCDC-NICBUW), as well as the TADDOL **A**, R = Me, Arl = 2-MeO–C_6H_4 ([23], CCDC-POPJIN) and the hexaphenyl analog **A**, R = Arl = Ph ([21c], CCDC-VUSLEA; [23], CCDC-POPJOT). In these cases, the stereoelectronic *gauche*-effect (F, Cl, N_3 case) or steric repulsion (Ph_6 case) is structure determining – in the absence of H-bonding between the substituents of the dioxolane ring.

[18]) We have recently determined the crystal structure of the difluoro compound (**C**; R = Me, Arl = Ph, X = Y = F [1b], CCDC-858090; space group *P*1) which also has one of the F-atoms above the dioxolane ring.

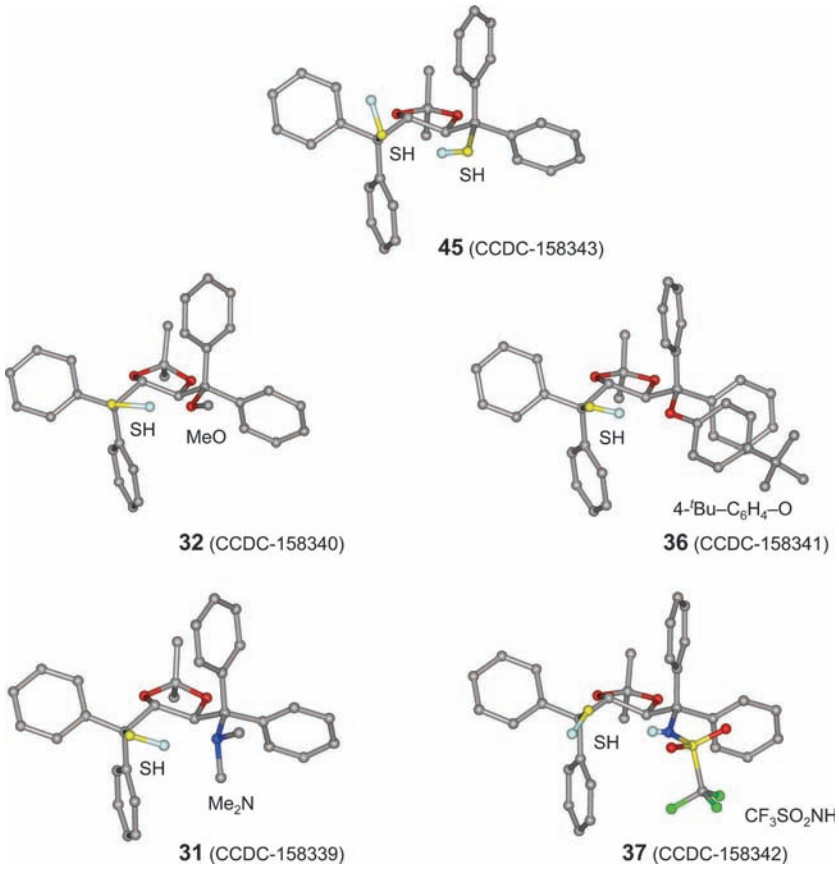


Fig. 2. *X-Ray crystal structures of the five sulfanyl derivatives* **31**, **32**, **36**, **37**, *and* **45** *with the CCDC codes.* There are H-bonds between the SH groups and a heteroatom S, O, or N, in seven-membered H-bonded rings. In **37**, the CF_3SO_2NH H-atom acts as the H-bond donor. The heteroatoms on all exocyclic C,C bonds are antiperiplanar to each other, *i.e.*, not in the stereoelectronically more favorable *gauche*-conformation.

We herein briefly present the results of an investigation, carried out more than ten years ago[2]), in which we tested the TADDOL-derived thiols in Cu-catalyzed 1,4-additions of *Grignard* reagents to cyclic enones (five- to eight-membered rings); furthermore, we discuss some mechanistic investigations, and describe the isolation and crystal structures of Cu complexes of some of these thiols.

First experiments were carried out by *G. Jaeschke* [1c][25] and *L. Audergon* [1c] in our group. The mode of preparing the reaction mixture turned out to be very critical, and there were severe reproducibility problems until we had optimized the procedure: for a 1-mmol batch, a suspension of the thiol (0.065 mmol) and CuCl (0.05 mmol) in 10 ml of THF was treated at $-75°$ with 0.08 mmol of BuLi (for the sulfanyl alcohols **7** and **8**, twice this amount was added), which led to a solution after 20 min at $0°$;

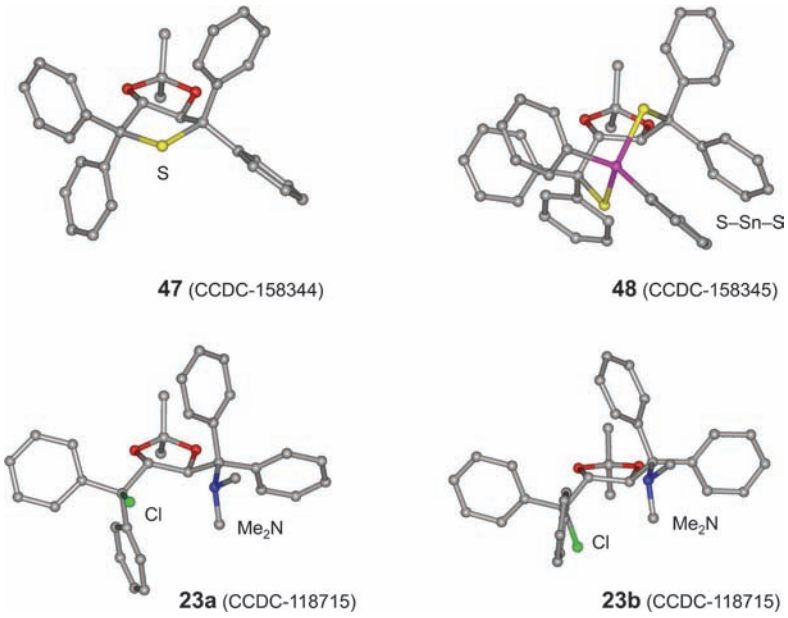


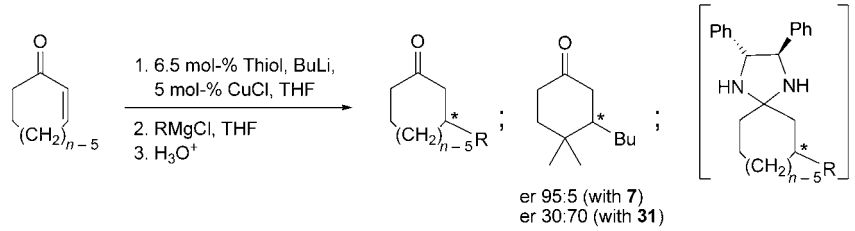
Fig. 3. *X-Ray crystal structures of the bicyclic derivatives* **47** *and* **48**, *and of the chloro dimethylamino compound* **23**, *of which three conformations were found in the unit cell of the crystal.* Two of the conformations have the familiar propeller-type structure (**23a** and a very similar form, **23a′**, not shown here); in the third one, **23b**, the chloro(diphenyl)methyl group is rotated by 120° to put the Cl-atom into a *gauche*-arrangement with the neighboring dioxolane O-atom.

following the addition of the cycloalkenone (1.0 mmol) at −75°, the *Grignard* reagent was added within 70–80 min with a syringe pump; it was very *important* that the reaction was carried out on an Ar line[19]) and *not* with an Ar balloon. The results obtained are compiled in *Table 4*. The following observations are noteworthy: *i*) The yields of 3-substituted cycloalkanones are generally in the range of 50–80%. *ii*) The enantioselectivities reach er values of up to 94:6 (*Entry 16* in *Table 4*). *iii*) The thiol **33** with naphthalen-2-yl groups is not superior to the Ph derivative[20]) (*Entries 9*/*10* and *30*/*31*); the thiol **8** with six Ph groups is inferior (*Entries 27*/*28*). *iv*) The dimethylamino thiol **31** and the methoxy thiol **32** give similar results (*cf. Entries 8*/*9*, *25*/*26*, *29*/*30*). *v*) Replacement of MeO with other RO groups in the thiol causes no improvement (*Entries 9*, *11–13*) or, rather, a decrease (*Entries 30*, *32–34* in *Table 4*) of the enantioselectivities. *vi*) Of the five-, six-, seven-, and eight-membered cycloalkenones, cycloheptenone generally reacts with highest enantioselectivities, and this is why we

[19]) Heating the flask before use with a heatgun under high vacuum, and using super-dry and O_2-free Ar gas, the conversions were poor, there was more 1,2-adduct formation, and the enantioselectivities dropped when we compared in-parallel Ar-line and Ar-balloon procedures! This comparison was carried out with the aminothiol **31**.

[20]) In many applications of TADDOL derivatives, the naphthalenyl-TADDOL gives higher enantioselectivities than the parent phenyl compound.

Table 4. *Enantioselective Conjugate Addition of* Grignard *Reagents to Cycloalkenones Catalyzed by Cu^{I} TADDOL-thiolates Derived from* **7**, **8**, *and* **31**–**36**. The absolute configurations of the products were assigned *a*) by comparison of the optical-rotation data with those reported in the literature, *b*) by comparison of the retention times (GC on chiral stationary phase; see *Exper. Part*) of major and minor isomer by analogy, or *c*) by NMR analysis of the (*R*,*R*)-1,2-diphenylethylenediamine derivatives [35].



Entry	*n*	R	Thiol	Yield [%]	er	Sense of optical rotation and absolute configuration
1	5	Bu	**7**	30	40 : 60	n.d.
2	5	Bu	**31**	50	70 : 30	n.d.
3	6	Me	**7**	60	20 : 80	(*S*)
4	6	Me	**32**	76	80 : 20	(*R*)
5	6	^{i}Pr	**7**	78	25 : 75	(*S*)
6	6	^{i}Pr	**32**	58	69 : 31	(*R*)
7	6	Bu	**7**	77	18 : 82	(−)-(*S*)
8	6	Bu	**31**	77	89 : 11	(+)-(*R*)
9	6	Bu	**32**	76	85 : 15	(+)-(*R*)
10	6	Bu	**33**	65	85 : 15	(+)-(*R*)
11	6	Bu	**34**	86	85 : 15	(+)-(*R*)
12	6	Bu	**35**	84	84 : 16	(+)-(*R*)
13	6	Bu	**36**	84	73 : 27	(+)-(*R*)
14	6	Ph	**7**	n.d.[a])	40 : 60	(*S*)
15	6	Ph	**32**	n.d.[a])	54 : 46	(*R*)
16	7	Me	**7**	51	6 : 94	(−)-(*S*)
17	7	Me	**31**	58	89 : 11	(+)-(*R*)
18	7	Me	**32**	76	89 : 11	(+)-(*R*)
19	7	Et	**7**	67	17 : 83	(*S*)
20	7	Et	**31**	69	76 : 24	(*R*)
21	7	Et	**32**	59	80 : 20	(*R*)
22	7	Pr	**7**	74	10 : 90	(−)-(*S*)
23	7	Pr	**31**	76	90 : 10	(+)-(*R*)
24	7	^{i}Pr	**7**	53	19 : 81	(−)-(*S*)
25	7	^{i}Pr	**31**	65	75 : 25	(+)-(*R*)
26	7	^{i}Pr	**32**	56	71 : 29	(+)-(*R*)
27	7	Bu	**7**	87	8 : 92	(−)-(*S*)
28	7	Bu	**8**	88	21 : 79	(−)-(*S*)
29	7	Bu	**31**	77	90 : 10	(+)-(*R*)
30	7	Bu	**32**	79	92.5 : 7.5	(+)-(*R*)
31	7	Bu	**33**	75	91 : 9	(+)-(*R*)
32	7	Bu	**34**	> 90[b])	85 : 15	(+)-(*R*)
33	7	Bu	**35**	> 90[b])	88 : 12	(+)-(*R*)
34	7	Bu	**36**	> 90[b])	82.5 : 17.5	(+)-(*R*)
35	8	Bu	**7**	81	20 : 80	(+)
36	8	Bu	**31**	78	76 : 24	(−)

[a]) Incomplete conversion and formation of side-products. [b]) Conversion (GC).

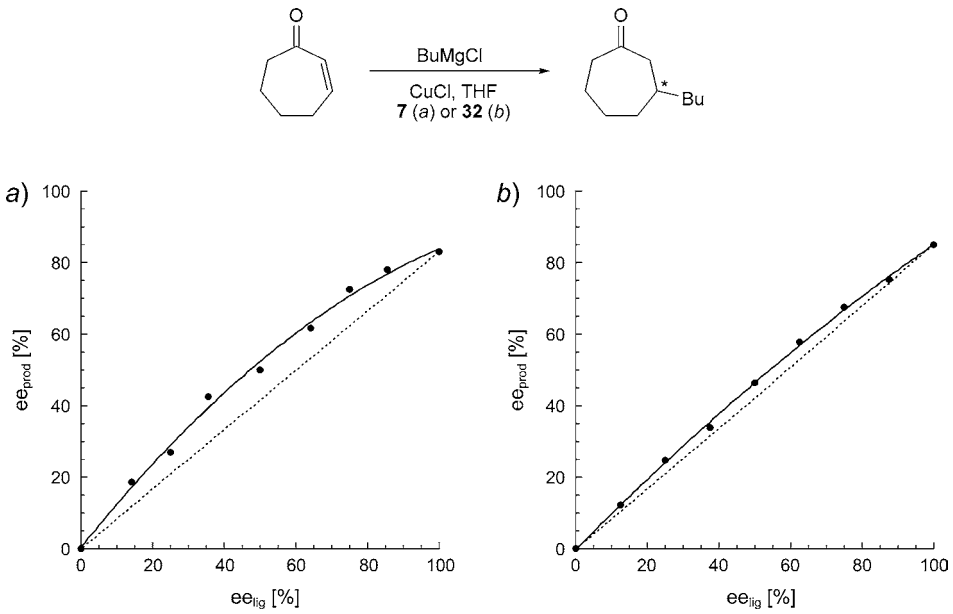


Fig. 4. *Positive nonlinear effect* (NLE) *for the Cu-catalyzed 1,4-addition of BuMgCl to cycloheptenone using ligand* **7** (*a*) *and ligand* **32** (*b*). The reactions were carried out under the conditions specified in *Table 4* and in the accompanying text.

conducted most experiments (*Entries 16–34*) with this enone. *vii*) Variation of the *Grignard* reagent gives rise to similar results for MeMgBr, PrMgBr, and BuMgCl (*cf. Entries 17*/*23*/*29*), while EtMgBr (*Entries 19–21*), ^{i}PrMgBr (*Entries 5*, *6*, *24–26*), and PhMgCl (*Entries 14*/*15*) undergo additions with poor selectivities. *viii*) We were surprised to see an almost complete reversal of selectivity when going from the dimethylamino or methoxy thiol to the sulfanyl alcohol (*Entries 1*/*2*; *3*/*4*; *5*/*6*; *7*/*8*, *9*; *14*/*15*; *16*/*17*, *18*; *19*/*20*, *21*; *22*/*23*; *24*/*25*, *26*; *27*/*29–34*; *35*/*36*; and the 4,4-dimethylcyclohexenone shown on top of *Table 4*). *ix*) Considering the fact that thiolato-Cu complexes may have tri- [36] or tetranuclear [37] structures, we were not surprised to find that there is a (positive) non-linear effect (NLE [32h][36][38]) of enantioselectivities in the addition of BuMgCl to cycloheptenone with the alkoxy-thiolato ligand (from **7**) and with the methoxy-thiolato ligand (from **32**; *Fig. 4*). *x*) The results obtained with other α,β-unsaturated carbonyl compounds, such as alkylidene malonates and cinnamoyl derivatives, indicate that the TADDOL-derived thiol ligands give rise to high enantioselectivities in this reaction only with cyclic enones (*cf.* similar differences between open-chain and cyclic *Michael* acceptors with other thiol ligands [32h][34]).

5. Structural Investigations of the Cu Complexes. – For isolation of the corresponding Cu complex, we treated the sulfanyl alkohol **7** with 1 equiv. CuCl and 1.1–1.5 equiv. Et_3N in MeOH under reflux or in CH_2Cl_2 at room temperature. Under both sets of conditions, the complex **50** was formed, which could be purified by flash chromatography, and which is stable in air and under weakly acidic aqueous conditions.

Similarly, the Cu complexes **51**–**53** and the Ag complex **54** were obtained[21]). Complex **50** was also formed from $Cu(OAc)_2$ and **7** in MeOH[22]). In an attempt to prepare an analogous complex of the dimethylamino thiol **31** (with excess CuCl in MeOH), we isolated the peculiar disulfide salt **55** (see the crystal structure in *Scheme 2*). The tetranuclear structure of the complexes **50**–**54** was established by X-ray crystal-structure analysis, by ESI-mass spectrometry, by vapor-pressure osmometry, and/or by NMR diffusion spectroscopy[1]).

In the crystal, the complex **50** has a structure with a C_2-symmetry axis[23]) through two of the Cu-atoms. The four Cu-atoms form a plane, above and below which the S-atoms are located alternatively, to form an eight-membered $(Cu\text{-}S)_4$ ring. The Cu-atoms are coordinatively unsaturated (no interaction with the HO groups!). According to the osmometry measurements, all complexes **50**–**52** and **54** are tetranuclear in CH_2Cl_2, and this is in line with the ESI mass spectra showing $[M+K]^+$ peaks for the tetramers (see *Table 5* and *Exper. Part*). *van Koten* and co-workers have reported that their Cu-

Table 5. *Molecular-Weight Determination of the Cuprates* **50**–**52** *and of* **54** *by Osmometry and Electrospray-Ionization Mass Spectrometry*

Cuprate complexes	M_r calc.	Osmometry (CH_2Cl_2) found	ESI-MS $[M+K]^+$ found
50	2180.7	2195.8	2219
51	2677.9		2717
52	2236.8	2211.7	2275
54	2358.0	2329.6	2398

thiolate complex is trinuclear in the non-polar solvent toluene and mononuclear in coordinating solvents such as THF [36a–c]. Since all our conjugate *Grignard* additions were carried out in THF (*Table 4*), we have determined the structures of the complexes **50** and **52**, as well as of the *in situ* generated complex from dimethylamino thiol **31** by ^{1}H-NMR pulsed-gradient diffusion measurements[24]) in (D_8)THF at 20°. All three complexes turned out to be tetranuclear in this solvent, and even when we added excess ^{t}BuNC there was no deaggregation. Thus, the tetranuclear structures of the Cu complexes of TADDOL-derived thiols are *very* stable. NOE Measurements of the three complexes 'garnished' with ^{t}BuNC show distinct differences between the OH/SH

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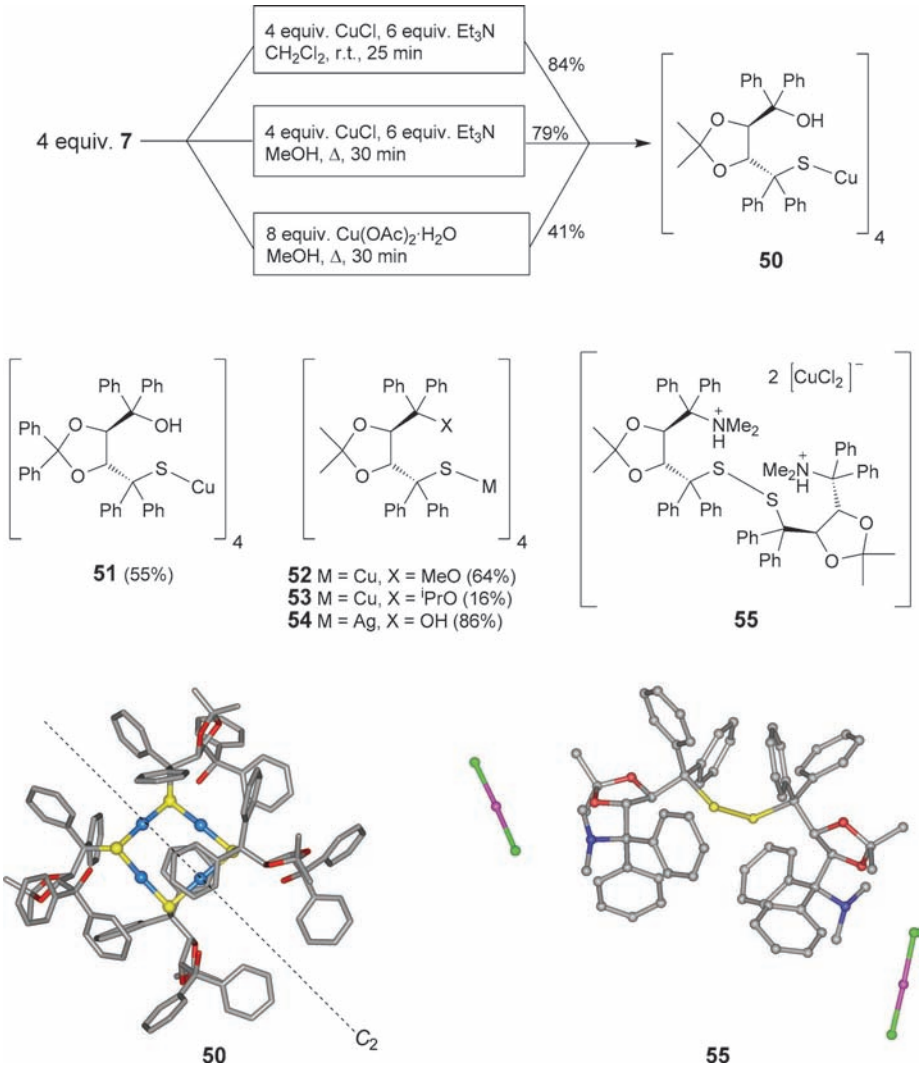
21) The alkoxy-thiolate complexes **52** and **53** are less stable than **50**, and the corresponding benzyloxy derivative could not be isolated at all.

22) With Cu^{II}-acetate, a 2:1 reaction must have taken place, in which Cu^{II} was reduced to Cu^{I} by the thiol **7**, probably with disulfide formation (*cf.* **55**).

23) Actually, two crystals grown from different solvent mixtures were analyzed. One has the space group $C222_1$ (with an approximate C_2 axis), the other has the space group $P2_12_12$ (with a crystallographic C_2 axis; CCDC-CUPQEJ). For a 'non-crystallographer', the differences between the two dimorphic structures are minor.

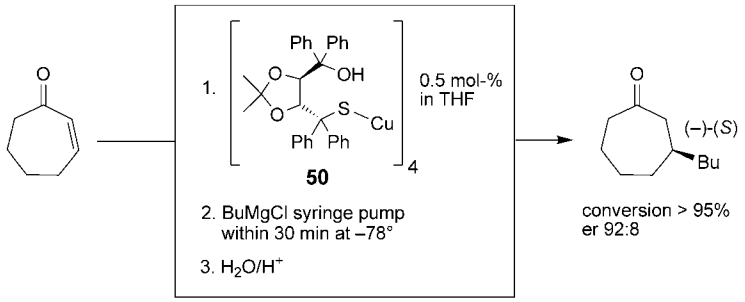
24) This method was first applied for the determination of aggregation of transition-metal complexes (in independent investigations) by the groups of *Pregosin* [1a] and *Brintzinger* [39]. For details of the measurements with our thiolato-Cu complexes, we refer to [1a] and the ETH Dissertation No. 14323 of *M. Valentini* (2001).

Scheme 2. *Preparation of TADDOL-Derived Thiolato-Cu and -Ag Complexes* **50** – **54**, *a Bis-Ammonium Dichloro Cuprate Salt,* **55**, *Derived from the Amino Thiol* **31**, *and X-Ray Crystal Structures of* **50** *and* **55**



derivative on the one hand, and the MeO/SH and Me_2N/SH derivatives on the other hand, including cross-peaks between the *t*Bu H-atoms and H-atoms of the ligands [1a][2]). We herein refrain from discussing details of the NMR spectra, which may not be relevant to the mechanism of the conjugate addition of *Grignard* reagents (*Table 4* and *Scheme 3*). The fact is that the TADDOL-derived Cu^I-thiolato complexes are present as tetranuclear species in the gas phase (*cf.* MS), in solution (*cf.* NMR), and in the solid state (*cf.* X-ray).

Scheme 3. *Conjugate Addition of BuMgCl to Cycloheptenone, with 0.5 mol-% of the Pure Cu Complex* **50** *as Catalyst.* The yield of the product of 1,2-addition is <5%. The enantioselectivities with cyclohexenone and cyclooctenone are 82:18 and 80:20 (*cf. Entries 7*, *27*, and *35* in *Table 4*), respectively. For a comparison with the *in situ* procedure (*Table 4*), note that 0.5 mol-% of the tetranuclear complex corresponds to 2 mol-% of the monomer.



The complex **50** derived from the sulfanyl alcohol **7** turned out to be a highly active catalyst for conjugate additions to cycloalkenones, and its use is very simple: rather than treating a mixture of CuCl and **7** with BuLi (*ca.* 6 mol-% each), then adding the enone, and finally the *Grignard* reagent (within 70–80 min; *Table 4*), the enone and the complex **50** (0.5 mol-%) are dissolved in THF, and the Mg compound is added (within 30 min; *Scheme 3*). The enantioselectivities with the six-, seven-, and eight-membered cyclic enones are identical within experimental error for the two procedures. In contrast, use of the isolated Cu complexes **52** and **53**, prepared from the methoxy and isopropoxy thiols **32** and **34** (*Scheme 2*), gave much poorer results according to the new procedure (up to 40% 1,2-adduct and low enantioselectivities in the range of 2:1 with cycloheptenone; *cf. Entries 30* and *32* of *Table 4*)[25]).

We are unable to discuss possible mechanistic models for these reactions, which would be compatible with the observed results: in the original procedure (*Table 4*), there are LiX derivatives involved, and in both procedures there is an increasing amount of Mg salts with proceeding addition of the *Grignard* reagent. The LiO or XMgO groups, which must be present when the sulfanyl alcohol **7** is employed, may become ligands at the Cu center, which, in turn, could lead to deaggregation. On the other hand, the poor selectivities observed with the isolated MeO- and ^{i}PrO-substituted tetranuclear Cu complexes **52** and **53**, as compared to the *in situ* procedure, might be considered as a hint as to a less highly aggregated catalytic species in the presence of Li ions with the two alkoxy ligands, and also with the Me_2N-substituted ligand (*cf. Table 4*, *Entry 30*), which all give rise to preferred formation of the (*R*)-enantiomers, while the sulfanyl-alcohol-derived ligand leads to the (*S*)-3-alkylcycloalkanones.

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[25]) The Ag complex **54** gave a racemic product with cycloheptenone; Ag derivatives generally do not add to α,β-unsaturated carbonyl compounds in a 1,4-fashion.

weights); and Dr. *W. B. Schweizer*, *M. Solar* (X-ray, see *Footnote 18*). We also acknowledge the generous financial support by *ETH Zürich* and *Novartis* AG, Basel.

Experimental Part

1. *General. Abbreviations:* FC, flash chromatography; h.v., high vacuum, 0.01 – 0.1 Torr. THF was freshly distilled over K before use. Et_3N was distilled over CaH_2. CH_2Cl_2 was used in *puriss.* quality. Solvents for workup and chromatography: pentane and hexane were distilled over P_4O_{10} or *Sikkon* (anh. $CaSO_4$; *Fluka*), AcOEt over *Sikkon*, Et_2O over KOH/$FeSO_4$, and CH_2Cl_2 over P_4O_{10}. PCl_3 was distilled before use. All indicated reaction temp. were monitored with an internal thermometer (*Ebro-TTX-690* digital thermometer). Autoclave used for reactions under high pressure: 80 ml (home-made, ETH Zürich); the pressure was monitored with a *Haenni-ED-510* apparatus (Piezoresistiver Druckmessumformer). TLC: *Macherey-Nagel Alugram SIL G/UV$_{254}$* or *Merck 60 F$_{254}$* silica gel plates; detection by $UV_{254\,nm}$ light or I_2 or by dipping in/spraying with phosphomolybdic acid soln. (phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot 4\,H_2O$ (10 g), H_2SO_4 (60 ml), H_2O (940 ml)), followed by heating. FC: *Fluka* silica gel *60* (0.040 – 0.063 mm), at *ca.* 0.3 bar. GC: *Carlo Erba Fractovap 4160* with *Carlo Erba DP 700 CE.* M.p.: *Büchi-510* apparatus; uncorrected. Optical rotations: *Perkin-Elmer 241* polarimeter (10-cm, 1-ml cell), at r.t. IR spectra: *Perkin-Elmer 1620* FT-IR spectrometer, in cm^{-1}. NMR Spectra: *Bruker AMX-500* (^1H: 500 and ^{13}C: 125 MHz), *AMX-400* (^1H: 400 and ^{13}C: 100 MHz), *Varian Gemini-300* (^1H: 300, ^{13}C: 75, and ^{19}F: 282 MHz), *Mercury-300* (^1H: 300, ^{13}C: 75, ^{19}F: 282 MHz), or *Gemini-200* (^1H: 200 and ^{13}C: 50 MHz); chemical shifts (δ) in ppm downfield from TMS (δ 0.0 ppm) as internal standard; *J* values in Hz. MS: *VG Tribrid* (EI; 70 eV), *VG ZAB-2 SEQ* (FAB; 3-nitrobenzyl alcohol matrix), *IonSpec Ultima* (FT-ICR-MALDI; 4.7 T; 2,5-dihydroxybenzoic acid matrix), *Bruker REFLEX* (TOF-MALDI; N_2 laser), or *Finnigan MAT TSQ 7000* (ESI) spectrometer; in *m/z* (% of basic peak). HR-MS: *IonSpec Ultima* (FT-ICR-MALDI; 4.7 T; 2,5-dihydroxybenzoic acid matrix). Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie, ETH Zürich.

2. *General Procedures. Preparation of Monochloro TADDOL Derivatives by* Apple *Reaction. General Procedure 1* (*GP 1*). To a soln. of the appropriate TADDOL derivative (1 equiv.) in CH_2Cl_2 (0.3 – 0.65M), Ph_3P (2 equiv.), pyridine (2 – 6 equiv.), and CCl_4 (10 equiv.) were added at r.t. After stirring for 2 – 5 d at ambient temp., the solvent was removed under reduced pressure, and the crude product was purified as indicated.

Preparation of Monochloro TADDOL Derivatives with SOCl$_2$. General Procedure 2 (*GP 2*). To a soln. of the appropriate mono-ether (1 equiv.) in CH_2Cl_2 (0.1 – 0.3M), Et_3N (1.3 – 1.5 equiv.) and $SOCl_2$ (1.2 – 1.3 equiv.) were added. The mixture was stirred at reflux for 1.5 h where upon the color of the mixture changed from yellow to black. After cooling to r.t., the mixture was carefully poured into sat. aq. $NaHCO_3$ soln. and stirred for 5 min. The org. layer was separated, and the aq. layer was extracted with CH_2Cl_2 (2 ×). The combined org. layers were washed with H_2O, sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the crude product was used without further purification.

Preparation of Monochloro TADDOL Derivatives with SOCl$_2$ in the Presence of LiCl. General Procedure 3 (*GP 3*). The appropriate mono-ether (1 equiv.) and LiCl (10 equiv.) were dissolved (some LiCl may remain undissolved) in THF (0.1M), $SOCl_2$ (3 – 5 equiv.) was added, and the mixture was refluxed for 6 h (TLC control) where upon a colorless precipitate (LiCl) was formed, which partially disappeared by cooling to r.t. The mixture was then carefully poured into sat. aq. $NaHCO_3$ soln. and stirred for 5 min. Et_2O was added, the org. layer was separated, and the aq. layer was extracted with Et_2O (2 ×). The combined org. layers were washed with sat. aq. NaCl soln. and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the crude product was used either without further purification or purified as indicated.

Preparation of TADDOL Monoether Derivatives. General Procedure 4 (*GP 4*). The appropriate monochloro TADDOL derivative (1 equiv.) was suspended in the appropriate alcohol (0.1 – 0.2 M), Et_3N (1.2 equiv.) was added, and the mixture was heated. After cooling to r.t., the suspension was filtered, and the residue was purified as indicated.

Preparation of TADDOL Monothiol Derivatives. General Procedure 5 (*GP 5*). The appropriate monochloro TADDOL derivative was dissolved in DMF (0.1–0.3M), thiourea (20–30 equiv.) was added, and the mixture was stirred at r.t. for 3 d. NaOH soln. (1 or 2N) and Et_2O (*ca.* 20 ml) were added, and the mixture was stirred for 1 h. The org. layer was separated, and the aq. layer was extracted with Et_2O (3 × 25 ml). The combined org. layers were washed with H_2O (2 × 25 ml) and sat. aq. NaCl soln. (15 ml), and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by FC.

Methylation of Thiols. General Procedure 6 (*GP 6*). The appropriate thiol (1 equiv.) was dissolved in $MeCN/CH_2Cl_2$ (0.08 M) and treated with K_2CO_3 (1 or 2 equiv.). The mixture was cooled to −10°, treated with MeI (1 equiv.), and stirred at r.t. until completion (TLC control). The mixture was washed with H_2O (2×) and sat. NaCl soln., and the org. phase was dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by FC.

Preparation of S,O-*Acetals. General Procedure 7* (*GP 7*). A soln. of **7** (1 equiv.) in CH_2Cl_2 (0.12M) was cooled to −25°, and the appropriate aldehyde (1 or 6 equiv.) was added. The mixture was stirred for 30 min, $BF_3 \cdot Et_2O$ (1 equiv.) was added, and stirring was continued for 45 min at −25° and then for 30 min at 0°. A 5% Na_2CO_3 soln. was added, the mixture was stirred for 15 min, and the phases were separated. The aq. phase was extracted with CH_2Cl_2, and the combined org. layers were washed with H_2O and sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by FC.

3. *Preparation of Monochloro TADDOLs* **4**, *ent*-**4**, **24**, *ent*-**24**, **25**–**30**. *(4*R,5R*)- and (4*S,5S*)-5-[(Chloro)(diphenyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanol* (**4** and ent-**4**, resp.). *Compound* **4**. A soln. of TADDOL **1** (10.0 g, 21.4 mmol) in CH_2Cl_2 (38 ml) was treated with Ph_3P (11.3 g, 43.0 mmol), pyridine (3.5 ml, 43.0 mmol), and CCl_4 (4.5 ml, 47.0 mmol) according to *GP 1* for 3 d. The soln. was concentrated under reduced pressure to *ca.* 20 ml, and the residue was purified by flash filtration (pentane/Et_2O 8:2; 350 g of SiO_2). The filtrate was concentrated under reduced pressure to *ca.* 30–40 ml. Colorless crystals were formed upon standing for 6 h, which were isolated and identified as **4** (7.80 g, 76%). M.p. 133–135° ([24b]: 135–137°). $[\alpha]_D^{r.t.} = -17.8$ ($c = 1.0$, $CHCl_3$) ([24b]: −18.1 ($c = 0.4$, $CHCl_3$)). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.91 (*s*, Me); 1.07 (*s*, Me); 1.82 (*s*, OH); 5.12 (*d*, $J = 5.9$, CH); 5.35 (*d*, $J = 5.9$, CH); 7.15–7.42 (*m*, 20 arom. H). The anal. data matched those of [24b].

Compound ent-**4**. A soln. of TADDOL *ent*-**1** (5.0 g, 10.7 mmol) in CH_2Cl_2 (20 ml) was treated with Ph_3P (5.60 g, 21.4 mmol), pyridine (1.7 ml, 21.4 mmol), and CCl_4 (2.5 ml, 25 mmol) according to *GP 1*. Purification by FC afforded *ent*-**4** (3.05 g, 60 %). $[\alpha]_D^{r.t.} = +17.5$ ($c = 1.3$, $CHCl_3$).

*(4*R,5R*)-5-[(Chloro)(diphenyl)methyl]-α,α,2,2-tetraphenyl-1,3-dioxolane-4-methanol* (**5**). A soln. of **2** (7.70 g, 13.0 mmol) in CH_2Cl_2 (20 ml) was treated with Ph_3P (6.80 g, 26.0 mmol), CCl_4 (13.0 ml, 134 mmol), and pyridine (2.1 ml, 26.0 mmol) according to *GP 1* for 5 d. FC (2×) (1. pentane/Et_2O 9:1; 80 g of SiO_2; 2. pentane/Et_2O 95:5; 80 g of SiO_2) and crystallization from pentane/Et_2O (95:5; 40 ml) yielded **5** (4.45 g, 56%). Colorless solid. M.p. 165–166°. $[\alpha]_D^{r.t.} = +118.9$ ($c = 1.04$, $CHCl_3$). IR ($CHCl_3$): 3539*m*, 3089*w*, 3062*w*, 3007*w*, 1948*w*, 1892*w*, 1810*w*, 1599*w*, 1492*m*, 1449*s*, 1324*w*, 1165*w*, 1107*s*, 1064*m*, 1029*m*, 960*w*, 640*m*, 617*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.61 (*s*, OH); 5.57 (*d*, $J = 3.4$, CH); 5.80 (*d*, $J = 3.4$, CH); 6.94–7.38 (*m*, 28 arom. H); 7.45–7.52 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 77.23, 79.96 (C); 82.98, 85.51 (CH); 112.60 (C); 124.73, 125.04, 126.34, 126.59, 126.76, 126.82, 126.97, 127.05, 127.24, 127.43, 127.57, 127.84, 127.88, 127.97, 128.11, 128.70, 129.61 (CH); 141.24, 142.18, 143.72, 144.08, 145.66, 146.49 (C). FAB-MS: 425 (11, $[M-184]^+$), 391 (9, $[M-218]^+$), 361 (100, $[M-248]^+$), 183 (58), 179 (27), 167 (41) 105 (37). Anal. calc. for $C_{41}H_{33}ClO_3$ (609.16): C 80.84, H 5.46, Cl 5.82; found: C 80.70, H 5.65, Cl 5.90.

*(4*R,5R*)-5-[(Chloro)[di(naphthalen-2-yl)]methyl]-2,2-dimethyl-α,α-di(naphthalen-2-yl)-1,3-dioxolane-4-methanol* (**6**). A soln. of **3** (6.10 g, 9.15 mmol) in CH_2Cl_2 (30 ml) was treated with Ph_3P (4.80 g, 18.30 mmol), pyridine (5.0 ml, 62 mmol), and CCl_4 (9.0 ml, 93.0 mmol) according to *GP 1* for 2 d. FC (pentane/Et_2O 8:2 → 1:1; 80 g of SiO_2) yielded **6** (4.00 g, 64%), which was used without further purification (*caution:* very prone to hydrolysis on silica gel). Solid foam. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.34 (*s*, Me); 1.38 (*s*, Me); 5.60 (*d*, $J = 5.3$, CH); 5.76 (*d*, $J = 5.3$, CH); 6.75–6.90 (*m*, 4 arom. H); 7.36–7.53 (*m*, 12 arom. H); 7.64–7.90 (*m*, 8 arom. H); 8.00–8.05 (*m*, 2 arom. H); 8.16–8.18 (*m*, 2 arom. H).

*(4*R,5R*)- and (4*S,5S*)-4-[(Chloro)(diphenyl)methyl]-5-[(methoxy)(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolane* (**24** and *ent*-**24**, resp.). A soln. of **13** (2.50 g, 5.20 mmol) in CH_2Cl_2 (25 ml) was treated with Et_3N (1.10 ml, 7.80 mmol) and $SOCl_2$ (0.50 ml, 6.87 mmol) according to *GP 2*. Workup yielded **24** (2.78 g, quant.) as a brown solid foam, which was used without further purification. For anal. purposes, a sample was purified by FC (pentane/Et_2O). Colorless foam. M.p. 115–117°. $[\alpha]_D^{rt} = +50.9$ ($c = 1.07$, $CHCl_3$). IR ($CHCl_3$): 3059*w*, 3007*m*, 2936*w*, 2827*w*, 1598*w*, 1492*m*, 1445*m*, 1380*m*, 1370*m*, 1318*w*, 1166*m*, 1093*s*, 1034*w*, 980*w*, 893*m*, 865*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.97 (*s*, Me); 1.29 (*s*, Me); 2.30 (*s*, MeO); 4.85 (*d*, $J = 6.6$, CH); 5.16 (*d*, $J = 6.9$, CH); 7.18–7.50 (*m*, 20 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 27.69, 27.80, 51.71 (Me); 79.52 (C); 80.83, 82.50 (CH); 83.80, 109.87 (C); 126.93, 127.10, 127.30, 127.41, 127.44, 127.52, 127.59, 128.79, 129.47, 130.02, 130.63 (CH); 139.32, 140.87, 144.01, 144.80 (C). FAB-MS: 431 (4, $[M - MeO - Cl - 1]^+$), 318 (32), 237 (70), 197 (100), 167 (49), 136 (38), 105 (65).

Compound ent-**24**: A soln. of *ent*-**13** (0.70 g, 1.50 mmol) in CH_2Cl_2 (10 ml) was treated with Et_3N (0.31 ml, 2.25 mmol) and $SOCl_2$ (0.14 ml, 1.90 mmol) according to *GP 2*. Workup yielded *ent*-**24** (745 mg, 99%), which was used without further purification.

*(4*R,5R*)-4-[(Chloro)[di(naphthalen-2-yl)]methyl]-5-[(methoxy)[di(naphthalen-2-yl]methyl]-2,2-dimethyl-1,3-dioxolane* (**25**). A soln. of **14** (2.10 g, 3.10 mmol) in CH_2Cl_2 (25 ml) was treated with Et_3N (0.64 ml, 4.60 mmol) and $SOCl_2$ (0.30 ml, 4.13 mmol) according to *GP 2*. Workup yielded **25** (2.10 g, 97%) as a beige solid foam, which was used without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.14 (*s*, Me); 1.46 (*s*, Me); 2.12 (*s*, MeO); 5.10 (*d*, $J = 6.5$, CH); 5.48 (*d*, $J = 6.8$, CH); 7.27–7.31 (*m*, 2 arom. H); 7.39–7.93 (*m*, 24 arom. H); 8.06 (*d*, $J = 1.9$, 1 arom. H); 8.20 (*d*, $J = 1.9$, 1 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 27.82, 28.05, 51.99 (Me); 81.42, 82.78 (CH); 83.92, 109.86 (C); 125.87, 125.97, 126.05, 126.12, 126.20, 126.28, 126.34, 126.76, 127.23, 127.28, 127.39, 127.51, 128.06, 128.54, 128.70, 128.79, 129.17, 129.20 (CH); 132.34, 132.44, 132.62, 132.76, 137.25, 138.18, 140.32 (C).

*(4*R,5R*)-4-[(Chloro)(diphenyl)methyl]-2,2-dimethyl-5-[(1-methylethoxy)(diphenyl)methyl]-1,3-dioxolane* (**26**). A soln. of **15** (2.90 g, 5.70 mmol) in CH_2Cl_2 (50 ml) was treated with Et_3N (1.20 ml, 8.55 mmol) and $SOCl_2$ (0.58 ml, 8.00 mmol) according to *GP 2*. Workup yielded a mixture (3.15 g) of **26** (73%) and **15** (27%; according to ^{1}H-NMR) as a brown solid foam, which was used without further purification. ^{1}H-NMR (300 MHz): 0.31 (*d*, $J = 5.8$, Me); 0.95 (2*s*, 2 Me); 1.06 (*d*, $J = 5.9$, Me); 3.50–3.58 (*m*, CH); 4.71 (*d*, $J = 6.8$, CH); 4.84 (*d*, $J = 6.8$, CH); 7.20–7.41 (*m*, 16 arom. H); 7.61–7.66 (*m*, 4 arom. H). ^{13}C-NMR (75 MHz): 23.38, 24.11, 27.25, 27.56 (Me); 66.82 (CH); 76.16 (C); 81.72, 81.79 (CH); 84.79, 108.68 (C); 126.67, 126.93, 127.09, 127.30, 127.38, 127.54, 127.59, 128.61, 130.29, 130.76, 131.05 (CH); 140.21, 141.59, 141.75, 145.92 (C).

*(4*R,5R*)-4-[(Chloro)(diphenyl)methyl]-5-[(diphenyl)(phenylmethoxy)methyl]-2,2-dimethyl-1,3-dioxolane* (**27**). A soln. of **16** (3.00 g, 5.40 mmol) in CH_2Cl_2 (25 ml) was treated with Et_3N (1.05 ml, 7.60 mmol) and $SOCl_2$ (0.47 ml, 6.40 mmol) according to *GP* 2. Workup yielded **27** (3.08 g, 99%) as a brown solid foam, which was used without further purification. ^{1}H-NMR (300 MHz): 0.99 (*s*, Me); 1.08 (*s*, Me); 3.97 (*d*, $^2J = 11.8$, 1 H, CH_2); 4.09 (*d*, $^2J = 11.8$, 1 H, CH_2); 4.78 (*d*, $J = 7.2$, CH); 4.97 (*d*, $J = 7.2$, CH); 6.94–7.41 (*m*, 21 arom. H); 7.45–7.54 (*m*, 2 arom. H); 7.55–7.65 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz): 27.14, 27.65 (Me); 66.13 (CH_2); 75.93 (C); 80.88, 82.00 (CH); 84.56, 108.57 (C); 126.77, 126.98, 127.09, 127.30, 127.38, 127.46, 127.52, 127.80, 128.24, 129.84, 130.36 (CH); 139.09, 139.95, 141.70, 141.78, 145.39 (C).

*(4*R,5R*)-4-[(Chloro)(diphenyl)methyl]-5-{[4-(1,1-dimethylethyl)phenoxy](diphenyl)methyl}-2,2-dimethyl-1,3-dioxolane* (**28**). A soln. of **17** (2.25 g, 3.75 mmol) in THF (50 ml) was cooled to −75°, and BuLi (2.70 ml, 4.30 mmol; 1.6M soln. in hexane) was added dropwise over 5 min. After warming to 0°, the mixture was stirred for 30 min at this temp. Then, $SOCl_2$ (0.31 ml, 4.30 mmol) was added dropwise over 10 min, the mixture was allowed to warm to r.t. and refluxed for 2 h (TLC control is not possible due to complete hydrolysis of **28** on the silica plate). Workup according to *GP 2* yielded **28** (2.50 g, quant.) as a yellow solid, which was used without further purification. ^{1}H-NMR (300 MHz): 0.99 (*s*, Me); 1.10 (*s*, Me) 1.15 (*s*, ^{t}Bu); 4.89 (*d*, $J = 6.9$, CH); 4.93 (*d*, $J = 6.9$, CH); 6.37–6.44 (*m*, 2 arom. H); 6.85–6.92 (*m*, 2 arom. H); 7.04–7.22 (*m*, 6 arom. H); 7.27–7.39 (*m*, 10 arom. H); 7.56–7.63 (*m*, 2 arom. H); 7.64–7.70 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz): 27.27, 27.62, 31.39 (Me); 33.85, 76.30 (C); 82.10, 83.71 (CH); 86.47, 109.15 (C); 119.92, 124.74, 126.90, 127.12, 127.32, 127.38, 127.51, 127.58, 128.30, 129.65, 130.42, 130.65 (CH); 138.66, 140.41, 141.72, 143.35, 145.28, 153.04 (C). ESI-MS (pos.): 1248 (22, $[2\,M + 16]^+$), 667 (28, $[M -$

$Cl-1+2\,MeOH+Na]^+$), 651 (32, $[M-Cl-1+MeOH+K]^+$), 635 (70, $[M-Cl-1+MeOH+Na]^+$), 616 (28, M^+), 391 (100).

N-*{[(4*S*,5*R*)-5-[(Chloro)(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}diphenylmethyl)-1,1,1-trifluoromethanesulfonamide* (**29**). A soln. of **21** (4.80 g, 8.00 mmol) in THF (95 ml) was treated with LiCl (3.39 g, 80.0 mmol) and $SOCl_2$ (3.00 ml, 41.2 mmol) according to *GP 3*. Trituration of the crude product with hexane (30 ml) under reflux for 30 min yielded **29** (4.00 g, 81%). For anal. purposes, a sample was triturated with Et_2O. Colorless solid. M.p. 193–194° (dec.). $[\alpha]_D^{r.t.} = -47.5$ ($c = 0.45$, $CHCl_3$). IR ($CHCl_3$): 3240*m*, 3067*w*, 3008*w*, 2916*w*, 1496*w*, 1445*m*, 1373*s*, 1177*m*, 1138*m*, 1082*m*, 1054*m*, 1029*w*, 931*w*, 893*w*, 833*w*, 600*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.00 (*s*, Me); 1.04 (*s*, Me); 4.61 (*d*, $J = 7.3$, CH); 4.75 (*d*, $J = 7.3$, CH); 6.81 (br. *s*, NH); 7.16–7.21 (*m*, 1 arom. H); 7.23–7.46 (*m*, 15 arom. H); 7.55–7.63 (*m*, 4 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.89, 27.15 (Me); 70.65, 76.92 (C); 81.73, 82.50 (CH); 109.01, 118.82 (*q*, ^1J(C,F) = 322, CF_3) (C); 127.07, 127.52, 127.71, 128.07, 128.30, 128.49, 128.54, 128.60, 130.00, 130.12, 130.90 (CH); 137.36, 137.61, 139.14, 143.97 (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −76.91. ESI-MS (pos.): 671 (17, $[M + MeOH + Na + 1]^+$), 666 (24, $[M + MeOH + NH_4 + 1]^+$), 638 (16, $[M + Na]^+$), 634 (48, $[M + NH_4 + 1]^+$), 629 (29, $[M + 14]^+$), 602 (15, $[M - Cl - 1 + Na]^+$), 580 (9, $[M - Cl]^+$), 512 (76, $[M - Cl - CF_3 + 1]^+$), 508 (100, $[M - 107]^+$). ESI-MS (neg.): 614 (100, $[M - 1]^-$). Anal. calc. for $C_{32}H_{29}ClF_3NO_4S$ (616.10): C 62.38, H 4.74, Cl 5.75, N 2.27; found: C 62.26, H 4.83, Cl 6.00, N 2.21.

N-*{[(4*S*,5*R*)-5-[(Chloro)(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}diphenylmethyl)-2,2,2-trifluoroacetamide* (**30**). A soln. of **22** (2.20 g, 3.92 mmol) in THF (50 ml) was teated with LiCl (1.60 g, 37.7 mmol) and $SOCl_2$ (1.20 ml, 16.5 mmol) according to *GP 3*. Workup yielded **30** (2.56 g, quant.) as a beige solid foam, which was used without further purification. M.p. 150–152° (dec.). $[\alpha]_D^{r.t.} = -112.6$ ($c = 1.05$, $CHCl_3$). IR ($CHCl_3$): 3360*w*, 3063*w*, 3007*w*, 2938*w*, 1739*s*, 1538*m*, 1520*m*, 1496*m*, 1445*m*, 1382*m*, 1372*m*, 1326*w*, 1176*s*, 1070*m*, 896*w*, 855*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.74 (*s*, Me); 0.82 (*s*, Me); 4.97 (*d*, $J = 6.8$, CH); 5.11 (*d*, $J = 6.8$, CH); 7.22–7.45 (*m*, 18 arom. H); 7.51–7.55 (*m*, 2 arom. H); 7.75 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.88, 27.16 (Me); 67.10, 75.67 (C); 80.72, 81.74 (CH); 109.97, 115.75 (*q*, ^1J(C,F) = 290, CF_3) (C); 127.52, 127.55, 127.62, 127.78, 128.03, 128.07, 128.30, 128.35, 128.53, 129.51, 129.68, 130.82 (CH); 137.57, 139.30, 140.82, 145.47, 155.33 (*q*, ^2J(CF) = 37, CO) (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −75.72. ESI-MS (pos.): 680 (16, $[M + 101]^+$), 639 (46, $[M + 60]^+$), 635 (42, $[M + MeOH + Na + 1]^+$), 618 (16, $[M + K]^+$), 602 (100, $[M + Na]^+$), 598 (67, $[M - Cl - 1 + Na + MeOH]^+$), 593 (25, $[M - Cl - 1 + NH_4 + MeOH]^+$), 566 (29, $[M - Cl - 1 + Na]^+$), 544 (66, $[M - Cl]^+$), 431 (22, $[M - 148]^+$). ESI-MS (neg.): 614 (50, $[M + Cl]^-$), 578 (100, $[M - 1]^-$), 560 (22, $[M - 19]^-$), 542 (26, $[M - 37]^-$).

4. *Preparation of the TADDOL Mono-ethers* **13**, ent-**13**, **14**–**17**. *(4*R*,5*R*)- and (4*S*,5*S*)-5-[(Methoxy)(diphenyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanol* (**13** and *ent*-**13**, resp.). *Compound* **13**. Monochloride **4** (3.86 g, 7.96 mmol) in MeOH (60 ml) was treated with Et_3N (1.20 ml, 8.61 mmol) according to *GP 4* under reflux for 1.5 h. Filtration yielded anal. pure **13** (3.16 g, 83%). Colorless solid. M.p. 165–166° ([24b]: 169.8–170.4°). $[\alpha]_D^{r.t.} = -30.1$ ($c = 1.35$, $CHCl_3$) ([24b]: $[\alpha]_D^{r.t.} = -27.0$ ($c = 1.00$, $CHCl_3$)). IR ($CHCl_3$): 3321br., 3059*m*, 2941*m*, 1957*w*, 1817*w*, 1600*w*, 1495*s*, 1447*s*, 1381*m*, 1372*m*, 1168*s*, 1087*s*,1048*s*, 882*s*, 641*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 (*s*, Me); 1.03 (*s*, Me); 2.97 (*s*, MeO); 4.25 (*d*, $J = 8.1$, CH); 4.59 (*d*, $J = 8.1$, CH); 6.35 (*s*, OH); 7.20–7.50 (*m*, 18 arom. H); 7.62–7.65 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.85, 27.06, 52.41 (Me); 77.24 (C); 79.30, 81.51 (CH); 84.75, 108.87 (C); 126.91, 127.07, 127.20, 127.64, 127.70, 127.88, 128.40, 128.66, 129.98 (CH); 137.11, 138.86, 143.85, 146.43 (C). MALDI-FT-ICR-MS: 503.2 (72, $[M + Na]^+$), 413.2 (20, $[M - MeO - OCMe_2 - 1 + Na]^+$), 273.0 (100). HR-MS: 503.2191 ($[M + Na]^+$, $C_{32}H_{32}NaO_4$; calc. 503.2193 (−0.4 ppm)). Anal. calc. for $C_{32}H_{32}O_4$ (480.60): C 79.97, H 6.71; found: C 79.94, H 6.63.

Compound ent-**13**. Monochloride *ent*-**4** (0.95 g, 1.96 mmol) in MeOH (15 ml) was treated with Et_3N (0.30 ml, 2.15 mmol) according to *GP 4* to yield *ent*-**13** (0.79 g, 84%). $[\alpha]_D^{r.t.} = +25.0$ ($c = 1.15$, $CHCl_3$).

*(4*R*,5*R*)-5-{(Methoxy)[di(naphthalen-2-yl]methyl}-2,2-dimethyl-α,α-di(naphthalen-2-yl)-1,3-dioxolane-4-methanol* (**14**). The crude monochloride **6** (4.00 g, 5.84 mmol) in MeOH (60 ml) was treated (without Et_3N) according to *GP 5* under reflux for 3 h and subsequent stirred at r.t. overnight. The residue was purified by FC (SiO_2 (200 g); pentane/Et_2O 95:5) to yield **14** (2.23 g, 57%). Colorless solid. M.p. 155–156°. R_f (hexane/AcOEt 8:2) 0.40. $[\alpha]_D^{r.t.} = -52.8$ ($c = 1.15$, $CHCl_3$). IR ($CHCl_3$): 3318br., 3061*s*, 2940*w*, 1951*w*, 1631*w*, 1599*m*, 1505*s*, 1381*s*, 1372*s*, 1273*m*, 1168*s*, 1086*s*, 952*w*. ^{1}H-NMR (400 MHz,

$CDCl_3$): 0.99 (*s*, Me); 1.14 (*s*, Me); 3.07 (*s*, MeO); 4.52 (*d*, $J = 8.2$, CH); 4.90 (*d*, $J = 8.2$, CH); 6.67 (*s*, OH); 7.28–7.94 (*m*, 26 arom. H); 8.12 (*s*, 1 arom. H); 8.33 (*s*, 1 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.03, 27.27, 53.03 (Me); 77.59 (C); 79.65, 82.27 (CH); 85.02, 109.20 (C); 125.52, 125.73, 125.86, 125.92, 126.06, 126.11, 126.18, 126.33, 126.39, 126.59, 126.67, 126.78, 126.92, 127.17, 127.31, 127.36, 127.47, 127.49, 127.53, 127.55, 127.84, 127.98, 128.53, 128.60, 128.69, 128.70, 128.85, 130.03 (CH); 132.44, 132.52, 132.53, 132.68, 132.80, 132.81, 132.85, 132.99, 135.47, 136.31, 141.64, 143.40 (C). ESI-MS (pos.): 735 (34, $[M + MeOH + Na]^+$), 719 (17, $[M + K]^+$), 703 (100, $[M + Na]^+$). ESI-MS (neg.): 680 (60, M^-), 679 (100, $[M - 1]^-$). Anal. calc. for $C_{48}H_{40}O_4$ (680.84): C 84.68, H 5.92; found: C 84.70, H 6.19.

*(4*R*,5*R*)-2,2-Dimethyl-5-[(1-methylethoxy)(diphenyl)methyl]-α,α-diphenyl-1,3-dioxolane-4-methanol* (**15**). Monochloride **4** (4.00 g, 8.25 mmol) in ^{i}PrOH (40 ml) was treated with Et_3N (1.72 ml, 12.35 mmol) according to *GP 5* at 50° for 15 h. To remove NH_4Cl, the residue was dissolved in CH_2Cl_2 and washed with H_2O. The org. layer was separated and dried (Na_2SO_4), and the solvent was removed under reduced pressure to yield **15** (3.08 g, 73%). Colorless solid. M.p. 203–205°. R_f (hexane/AcOEt 95:5) 0.42. $[\alpha]_D^{rt.} = -16.3$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3310*s* (br.), 3059*w*, 3007*s*, 2934*w*, 1600*w*, 1495*m*, 1446*s*, 1382*m*, 1372*s*, 1332*w*, 1170*m*, 1130*w*, 1110*m*, 1082*s*, 1050*s*, 1033*s*, 1016*s*, 918*w*, 885*m*, 835*w*. ^{1}H-NMR (400 MHz): 0.45 (*d*, $J = 5.9$, Me); 0.89 (*s*, Me); 1.05 (*s*, Me); 1.39 (*d*, $J = 6.2$, Me); 3.73–3.82 (*m*, CH); 4.25 (*d*, $J = 8.2$, CH); 4.54 (*d*, $J = 8.2$, CH); 6.61 (*s*, OH); 7.17–7.39 (*m*, 16 arom. H); 7.52–7.55 (*m*, 2 arom. H); 7.64–7.67 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz): 23.32, 24.26, 26.77, 27.10 (Me); 68.71 (CH); 77.34 (C); 79.95, 81.27 (CH); 85.40, 108.60 (C); 126.88, 126.94, 127.67, 127.76, 127.80, 127.86, 128.48, 128.87, 130.41, 130.47 (CH); 138.68, 139.77, 143.84, 146.37 (C). ESI-MS (pos.): 1055 (35, $[2M + K]^+$), 1039 (40, $[2M + Na]^+$), 1034 (100, $[2M + NH_4]^+$), 563 (29, $[M + MeOH + Na]^+$), 554 (12, $[M + 46]^+$), 547 (35, $[M + K]^+$), 531 (43, $[M + Na]^+$), 526 (56, $[M + NH_4]^+$), 522 (13, $[M + 14]^+$), 449 (74, $[M - {}^i$PrO$]^+$), 391 (90, $[M - {}^i$PrO $- Me_2CO]^+$). Anal. calc. for $C_{34}H_{36}O_4$ (508.66): C 80.28, H 7.13; found: C 80.42, H 7.15.

*(4*R*,5*R*)-5-[(Diphenyl)(phenylmethoxy)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanol* (**16**). Monochloride **4** (4.00 g, 8.25 mmol) in BnOH (40 ml) was treated with Et_3N (1.72 ml, 12.35 mmol) according to *GP 5* at 50° for 12 h. The residue was purified by FC (SiO_2 (60 g); pentane/Et_2O) to yield **16** (3.50 g, 76%). Colorless solid. M.p. 211–213°. R_f (hexane/AcOEt 9:1) 0.48. $[\alpha]_D^{rt.} = -26.1$ ($c = 1.1$; $CHCl_3$). IR ($CHCl_3$): 3370*s*, 3091*w*, 3061*m*, 3007*s*, 2934*w*, 1600*w*, 1495*s*, 1447*s*, 1381*m*, 1372*s*, 1332*m*, 1169*s*, 1082*s*, 1056*s*, 1020*s*, 920*w*, 881*m*, 643*m*. ^{1}H-NMR (400 MHz): 0.95 (*s*, Me); 1.14 (*s*, Me); 3.79 (*d*, $^2J = 10.5$, 1 H, CH_2); 4.16 (*d*, $J = 8.3$, CH); 4.30 (*d*, $^2J = 10.5$, 1 H, CH_2); 4.56 (*d*, $J = 8.3$, CH); 5.84 (*s*, OH); 7.10–7.25 (*m*, 7 arom. H); 7.27–7.37 (*m*, 11 arom. H); 7.38–7.50 (*m*, 5 arom. H); 7.60–7.64 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz): 26.74, 27.13 (Me); 67.16 (CH_2); 76.92 (C); 79.95, 82.09 (CH); 85.30, 108.41 (C); 126.88, 126.92, 127.04, 127.31, 127.63, 127.71, 127.79, 127.97, 128.27, 128.48, 128.55, 128.59, 130.02, 130.05 (CH); 136.49, 137.31, 139.41, 143.47, 145.89 (C). ESI-MS (pos.): 616 (10, $[M + 60]^+$), 602 (13, $[M + 46]^+$), 595 (28, $[M + K]^+$), 579 (24, $[M + Na]^+$), 574 (100, $[M + NH_4]^+$), 449 (14, $[M - BnO]^+$), 391 (17, $[M - BnO - Me_2CO]^+$). Anal. calc. for $C_{38}H_{36}O_4$ (556.70): C 81.99, H 6.52; found: C 81.92, H 6.50.

*(4*R*,5*R*)-5-{[4-(1,1-Dimethylethyl)phenoxy](diphenyl)methyl}-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanol* (**17**). To a soln. of **4** (2.00 g, 4.10 mmol) in CH_2Cl_2 (40 ml) was added Et_3N (1.14 ml, 8.20 mmol) and 4-(*tert*-butyl)phenol (3.08 g, 20.5 mmol) at r.t. After stirring for 3 d at ambient temp., the mixture was washed with 2N NaOH soln. The org. layer was separated, and the aq. layer was extracted with CH_2Cl_2. The combined org. layers were washed with H_2O and sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the crude product was purified by FC (pentane/Et_2O 97:3; 80 g SiO_2). Subsequent trituration with pentane afforded **17** (1.37 g, 56%). Colorless solid. M.p. 148–149° ([1b]: 154–155°). $[\alpha]_D^{rt.} = -54.2$ ($c = 0.88$, $CHCl_3$) ([1b]: $[\alpha]_D^{rt.} = -50.5$ ($c = 0.65$, $CHCl_3$)). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.98 (*s*, Me); 1.09 (*s*, Me); 1.15 (*s*, ^{t}Bu); 4.40 (*d*, $J = 8.1$, CH); 4.77 (*d*, $J = 8.1$, CH); 5.92 (*s*, OH); 6.48–6.54 (*m*, 2 arom. H); 6.89–6.96 (*m*, 2 arom. H); 7.02–7.12 (*m*, 3 arom. H); 7.13–7.26 (*m*, 5 arom. H); 7.30–7.47 (*m*, 8 arom. H); 7.69–7.77 (*m*, 4 arom. H). ESI-MS (pos.): 1236 (8, $[2M + K + 1]^+$), 1215 (44, $[2M + NH_4 + 1]^+$], 653 (18, $[M + MeOH + Na]^+$), 637 (32, $[M + K]^+$), 621 (58, $[M + Na]^+$), 616 (100, $[M + NH_4]^+$). ESI-MS (neg.): 657 (100, $[M + AcO]^-$), 633 (74, $[M + Cl]^-$), 597 (64, $[M - 1]^-$). The anal. data matched those of [1b].

5. *Preparation of the TADDAMIN* **11**. *(4*R,5S*)-5-[(Dimethylamino)(diphenyl)methyl]-α,α,2,2-tetraphenyl-1,3-dioxolane-4-methanol* (**11**). Monochloride **4** (2.40 g, 4.00 mmol) and Me_2NH (*ca.* 35 g, 776 mmol) were placed in an autoclave (80 ml) and heated at 80° for 3 d (4.5 bar). After cooling to r.t., excess Me_2NH was vented, and the crude product was dissolved in CH_2Cl_2. The soln. was washed with 1N NaOH soln. and sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by FC (SiO_2 (80 g); pentane/Et_2O) to yield **11** (337 mg, 14%). Colorless solid foam. For anal. purposes, **11** was recrystallized from EtOH. Colorless crystals. M.p. 225–227°. $[\alpha]_D^{r.t.} = +108.8$ ($c = 1.10$, $CHCl_3$). IR ($CHCl_3$): 3062*m*, 3007*s*, 2950*w*, 2798*w*, 1599*w*, 1492*m*, 1448*s*, 1349*w*, 1096*s*, 1048*w*, 1031*s*, 1004*w*, 988*w*, 944*w*, 905*w*, 642*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.48 (*s*, MeN); 2.25 (*s*, MeN); 4.23 (*d*, $J = 8.7$, CH); 5.18 (*d*, $J = 8.7$, CH); 6.41–6.55 (*m*, 1 arom. H); 6.57–6.63 (*m*, 2 arom. H); 6.70–7.00 (*m*, 6 arom. H); 7.11–7.54 (*m*, 16 arom. H); 7.58–7.68 (*m*, 1 arom. H); 7.83–7.90 (*m*, 2 arom. H); 7.95–8.06 (*m*, 1 arom. H); 8.71 (*s*, OH). ^{13}C-NMR (100 MHz, $CDCl_3$): 40.45, 41.19 (Me); 73.45, 74.97 (C); 78.10, 86.15 (CH); 108.09 (C); 125.20, 125.62, 126.58, 126.75, 126.77, 126.95, 126.99, 127.20, 127.40, 127.59, 127.62, 127.78, 128.06, 128.16, 129.48, 130.75, 131.21, 134.42 (CH); 135.67, 136.80, 142.75, 143.82, 144.01, 146.62 (C). FAB-MS: 1236 (6, $[2M + 1]^+$), 618 (65, $[M + 1]^+$), 540 (6), 391 (17), 381 (15), 361 (71), 307 (14), 210 (100), 183 (23), 167 (42). Anal. calc. for $C_{43}H_{39}NO_3$ (617.79): C 83.60, H 6.36, N 2.27; found: C 83.58, H 6.49, N 2.27.

6. *Preparation of the Trifluoroacetamides* **20** *and* **22**. N-*[((4*S,5R*)-5-{(Diphenyl)[(trimethylsilyl)oxy]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl)(diphenyl)methyl]-2,2,2-trifluoroacetamide* (**20**). According to [24b], amino alcohol **9** (6.00 g, 12.89 mmol) was TMS-protected to afford **18** (7.0 g, quant.). To a soln. of **18** in CH_2Cl_2 (100 ml) at −75° was added dropwise over 30 min (temp. ≤ −70°) a soln. of $(CF_3CO)_2O$ (2.77 ml, 19.95 mmol) in CH_2Cl_2 (15 ml). The mixture was stirred for 15 min at −75°, then a soln. of Et_3N (1.80 ml, 12.90 mmol) in CH_2Cl_2 (8 ml) was added dropwise over 30 min (temp. ≤ −70°). After warming up slowly to r.t. and stirring overnight at ambient temp., the mixture was washed with H_2O. The org. layer was separated, washed with sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford **20** (7.95 g, 97% from **9**). Colorless solid. M.p. 145–148° (dec.). $[\alpha]_D^{r.t.} = -41.9$ ($c = 1.04$, $CHCl_3$). IR ($CHCl_3$): 3338*w*, 3064*w*, 2992*w*, 1731*s*, 1533*m*, 1496*m*, 1446*m*, 1372*w*, 1254*m*, 1177*s*, 1080*m*, 1053*m*, 893*m*, 866*m*, 846*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): −0.26 (*s*, Me_3Si); 1.10 (*s*, Me); 1.25 (*s*, Me); 4.14 (*d*, $J = 8.2$, CH); 4.38 (*d*, $J = 8.2$, CH); 7.03–7.10 (*m*, 4 arom. H); 7.15–7.28 (*m*, 6 arom. H); 7.42–7.49 (*m*, 6 arom. H); 7.63–7.72 (*m*, 4 arom. H); 8.04 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 2.18, 26.75, 26.99 (Me); 66.18 (C); 81.48 (CH); 81.68 (C); 83.17 (CH); 107.05, 115.63 (*q*, ^1J(C,F) = 289, CF_3) (C); 127.13, 127.33, 127.48, 127.75, 127.94, 127.99, 128.05, 128.55, 129.34, 130.63 (CH); 135.93, 141.02, 142.11, 142.29, 155.49 (*q*, ^2J(C,F) = 37, CO) (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −74.39. MALDI-FT-ICR-MS: 656.2 (25, $[M + Na]^+$), 566.2 (10), 486.3 (5), 431.2 (5), 395.1 (10), 301.1 (100), 273.0 (62), 255.1 (44). HR-MS: 656.2419 ($[M + Na]^+$, $C_{36}H_{38}F_3NNaO_4Si$; calc. 656.2414 (+0.76 ppm)).

*2,2,2-Trifluoro-*N*-[{(4*S,5R*)-5-[(hydroxy)(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}(diphenyl)methyl]acetamide* (**22**). To a soln. of **20** (7.26 g, 11.45 mmol) in THF (60 ml) was added $(Bu)_4NF \cdot 3\,H_2O$ (5.40 g, 17.20 mmol) at r.t. After stirring for 30 min (TLC control) at ambient temp., Et_2O (30 ml) was added, and the mixture was washed with 1N HCl soln. The org. layer was separated, and the aq. layer was extracted with Et_2O (2×). The combined org. layers were washed with H_2O and sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the crude product was purified by FC (pentane/Et_2O 8:2; 150 g SiO_2). Subsequent trituration with hexane under reflux for 2 h yielded **22** (5.75 g, 89%). Colorless solid. M.p. 196–199°. $[\alpha]_D^{r.t.} = -103.1$ ($c = 1.07$, $CHCl_3$). IR ($CHCl_3$): 3584*w*, 3254*m*, 3065*m*, 2994*w*, 2936*w*, 1957*w*, 1892*w*, 1735*s*, 1572*m*, 1496*m*, 1447*m*, 1382*m*, 1372*m*, 1337*w*, 1322*w*, 1177*s*, 1163*s*, 1098*m*, 1030*m*, 885*m*, 637*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.60 (*s*, Me); 1.03 (*s*, Me); 2.90 (*s*, OH); 4.35 (*d*, $J = 7.6$, CH); 4.88 (*d*, $J = 7.6$, CH); 7.22–7.50 (*m*, 20 arom. H); 9.85 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.80, 27.27 (Me); 65.78, 79.20 (C); 79.88, 81.82 (CH); 110.15, 116.09 (*q*, ^1J(C,F) = 290, CF_3) (C); 127.35, 127.37, 127.46, 127.50, 127.57, 127.95, 128.02, 128.46, 128.74, 129.08, 129.15, 129.72 (CH); 135.40, 140.72, 141.12, 145.88, 155.32 (*q*, ^2J(C,F) = 36, CO) (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −75.44. ESI-MS (pos.): 616 (6, $[M + MeOH + Na]^+$), 600 (32, $[M + K]^+$), 584 (33, $[M + Na]^+$), 579 (100, $[M + NH_4]^+$), 544 (18, $[M - OH]^+$), 431 (18, $[M - OH - NHCOCF_3 - 1]^+$). ESI-MS (neg.): 560 (100, $[M - 1]^-$). Anal. calc. for $C_{33}H_{30}F_3NO_4$ (561.60): C 70.58, H 5.38, N 2.49; found: C 70.40, H 5.56, N 2.47.

7. *Preparation of the TADDOL-Derived thiols* **7**, ent-**7**, **8**, **31**, **32**, ent-**32**, **33**–**38** *and* **45**. *(4*R,*5*R*)- and (4*S,*5*S*)-5-[(Diphenyl)(sulfanyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanol* (**7** and *ent*-**7**, resp.). *Compound* **7**[26]). Monochloride **4** (7.00 g, 14.40 mmol) was treated with thiourea (22.0 g, 290 mmol) in DMF (45 ml) according to *GP 5*. FC (SiO_2 (450 g); hexane/AcOEt 98:2 → 95:5) and subsequent trituration with boiling pentane (20 ml) for 1 h yielded **7** (4.50 g). After partially removing the solvent from the mother liquor, further **7** (750 mg) were obtained. Total yield: 5.25 g (75%). Colorless powder. M.p. 128–129° ([40a]: 120–121°). R_f (hexane/AcOEt 98:2) 0.29. $[\alpha]_D^{r.t.} = -36.2$ ($c = 1.0$, $CHCl_3$) ([40a]: $[\alpha]_D^{r.t.} = -31.8$ ($c = 1$, $CHCl_3$)). IR ($CHCl_3$): 3566*m*, 3365*w*, 3061*m*, 3008*s*, 2936*w*, 2561*w*, 1954*w*, 1892*w*, 1599*w*, 1494*s*, 1446*s*, 1380*s*, 1370*s*, 1165*s*, 1064*s*, 1036*m*, 1016*m*, 972*w*, 886*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.86 (*s*, Me); 1.05 (*s*, Me); 2.34, 2.35 (2*s*, OH, SH); 4.97 (*d*, $J = 6.7$, CH); 5.14 (*d*, $J = 6.7$, CH); 7.18–7.49 (*m*, 20 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 27.69, 27.80 (Me); 60.58, 78.12 (C); 82.16, 83.18 (CH); 110.83 (C); 127.02, 127.10, 127.13, 127.25, 127.35, 127.49, 127.60, 127.93, 128.02, 128.66, 130.18 (CH); 143.51, 144.67, 146.32, 146.61 (C). ESI-MS (pos.): 537 (6, $[M + MeOH + Na]^+$), 521 (7, $[M + K]^+$), 505 (12, $[M + Na]^+$), 500 (100, $[M + NH_4]^+$). ESI-MS (neg.): 481 (100, $[M - 1]^-$), 423 (6, $[M - 58]^-$). Anal. calc for $C_{31}H_{30}O_3S$ (482.64): C 77.15, H 6.26, S 6.64; found: C 77.25, H 6.28, S 6.58. The NMR data matched those of [40a].

Compound ent-**7**. Compound *ent*-**4** (2.0 g, 4.1 mmol) was treated with thiourea (6.3 g, 82 mmol) in DMF (20 ml) according to *GP 5*. FC (250 g of SiO_2) and tritutarion with pentane (15 ml) yielded *ent*-**7** (1.25 g, 63%). $[\alpha]_D^{r.t.} = +36.7$ ($c = 1.0$, $CHCl_3$).

*(4*R,*5*R*)-5-[(Diphenyl)(sulfanyl)methyl]-α,α,2,2-tetraphenyl-1,3-dioxolane-4-methanol* (**8**). Monochloride **5** (3.00 g, 4.90 mmol) was treated with thiourea (9.4 g, 123 mmol) in DMF (35 ml) according to *GP 5*. FC (SiO_2 (200 g); pentane/Et_2O 95:5) yielded **8** (1.9 g, 63%). For anal. purposes, a sample was recrystallized (pentane, −20°). Colorless solid. M.p. 118–119°. R_f (hexane/dioxane 9:1) 0.27. $[\alpha]_D^{r.t.} = +148.8$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3542*s*, 3062*m*, 3007*m*, 2582*w*, 1949*w*, 1889*w*, 1810*w*, 1598*w*, 1492*s*, 1449*s*, 1323*w*, 1103*s*, 1062*s*, 1028*s*, 962*m*, 942*m*, 639*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.54, 1.66 (2*s*, OH, SH); 5.56 (*d*, $J = 3.7$, CH); 5.76 (*d*, $J = 3.7$, CH); 6.95–7.46 (*m*, 30 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 60.82, 79.82 (C); 84.13, 85.71 (CH); 112.15 (C); 124.80, 125.10, 126.48, 126.52, 126.65, 126.72, 127.03, 127.10, 127.75, 127.85, 127.88, 127.96, 128.11, 128.67, 129.58 (CH); 142.62, 144.42, 144.65, 144.92, 145.61, 146.33 (C). MALDI-FT-ICR-MS: 629.2 (100, $[M + Na]^+$), 413.2 (24, $[M - SH - Ph_2CO - 1 + Na]^+$), 273.0 (35). HR-MS: 629.2104 ($[M + Na]^+$, $C_{41}H_{34}NaO_3S$; calc. 629.2121 (−2.70 ppm)). Anal. calc. for $C_{41}H_{34}O_3S$ (606.78): C 81.16, H 5.65, S 5.28; found: C 81.28, H 5.91, S 5.13.

*(4*R,*5*S*)-5-[(Dimethylamino)(diphenyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanethiol* (**31**). Monochloride **23** (1.87 g, 3.65 mmol) was treated with thiourea (8.4 g, 111 mmol) in DMF (30 ml) according to *GP 5*. FC (SiO_2 (80 g); pentane/Et_2O 8:2) yielded **31** (1.56 g, 84%). For anal. purposes, a sample was recrystallized (pentane). Colorless crystals. $[\alpha]_D^{r.t.} = -90.9$ ($c = 1.0$, $CHCl_3$), −60.9 ($c = 1.0$, AcOEt) ([24b]: −54.1 ($c = 0.98$, AcOEt)). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.60 (*s*, Me); 1.14 (*s*, Me); 1.70 (*s*, MeN); 2.20 (*s*, NMe); 4.48 (*d*, $J = 8.1$, CH); 4.99 (*d*, $J = 8.1$, CH); 6.85–7.39 (*m*, 16 arom. H); 7.50–7.57 (*m*, 1 arom. H); 8.10–8.14 (*m*, 2 arom. H); 8.21–8.26 (*m*, 1 arom. H); 9.51 (br. *s*, SH). The anal. data match those of [24b].

*(4*R,*5*R*)- and (4*S,*5*S*)-5-[(Methoxy)(diphenyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanethiol* (**32** and *ent*-**32**). Compound **32**. Monochloride **24** (4.00 g, 8.02 mmol) was treated with thiourea (6.0 g, 79 mmol) in DMF (35 ml) according to *GP 5*. FC (hexane/AcOEt 95:5; 200 g SiO_2) yielded **32** (2.65 g, 66%). For anal. purposes, a sample was recrystallized (pentane/CH_2Cl_2). Colorless powder. M.p. 182–183°. R_f (hexane/AcOEt 95:5) 0.39. $[\alpha]_D^{r.t.} = +6.5$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3059*m*, 2990*s*, 2937*m*, 2831*w*, 2512*m*, 1958*w*, 1599*m*, 1493*s*, 1445*s*, 1380*s*, 1370*s*, 1318*m*, 1177*s*, 1081*s*, 1033*s*, 1020*m*, 893*s*, 867*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.95 (*s*, Me); 1.10 (*s*, Me); 2.62 (*s*, MeO); 4.07 (*s*, SH); 4.69 (*s*, 2 CH); 7.11–7.31 (*m*, 13 arom. H); 7.35–7.40 (*m*, 3 arom. H); 7.45–7.49 (*m*, 2 arom. H); 7.64–7.66 (*m*, 2 arom. H). ^{13}C-NMR (125 MHz, $CDCl_3$): 27.37, 27.50, 51.81 (Me); 59.68 (C); 80.57, 82.68 (CH); 84.18, 108.07 (C); 126.39, 126.72, 126.91, 126.98, 127.43, 127.54, 127.68, 128.62, 129.87, 130.60, 130.88 (CH);

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[26]) The sulfanyl alcohol **7** has first been prepared in 30% yield by treatment of **1** with *Lawesson* reagent, and the preparation of the corresponding *O*,*S*-acetal of CH_2O (*cf.* **43** and **44**) was described in the same report [40a].

138.26, 140.47, 144.91, 146.23 (C). FAB-MS: 495 (9, $[M-1]^+$), 463 (43, $[M-SH]^+$), 447 (21, $[M-SH-Me-1]^+$), 431 (96, $[M-SH-MeO-1]^+$), 407 (35, $[M-MeO-Me_2CO]^+$), 389 (28), 373 (25), 237 (91, $[M-MeO-OCHCPh_2SH]^+$), 197 (100), 179 (70). Anal. calc. for $C_{32}H_{32}O_3S$ (496.67): C 77.39, H 6.49, S 6.46; found: C 77.28, H 6.31, S 6.34.

Compound ent-**32**. Compound *ent*-**24** (745 mg, 1.50 mmol) was treated with thiourea (1.1 g, 15 mmol) in DMF (10 ml) according to *GP* 5. FC (80 g SiO_2) yielded *ent*-**32** (490 mg, 67%). $[\alpha]_D^{rt.} = -6.1$ ($c = 1.0$, $CHCl_3$).

*(4*R*,5*R*)-5-[(Methoxy)[di(naphthalen-2-yl]methyl]-2,2-dimethyl-α,α-di(naphthalen-2-yl)-1,3-dioxolane-4-methanethiol* (**33**). Monochloride **25** (2.10 g, 3.00 mmol) was treated with thiourea (12.0 g, 158 mmol) in DMF (30 ml) according to *GP 5*. FC (2 ×; 1. SiO_2 (70 g); pentane/Et_2O 95:5; 2. SiO_2 (210 g); hexane/toluene 1:1) yielded **33** (0.95 g, 47%). For anal. purposes, a sample was purified by further FC (SiO_2 (10 g); pentane/Et_2O 95:5). Colorless solid. M.p. 160–161°. R_f (pentane/Et_2O 95:5) 0.25. $[\alpha]_D^{rt.} = +63.0$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): 3060*s*, 2958*s*, 2935*m*, 2512*w*, 1950*w*, 1922*w*, 1631*w*, 1599*m*, 1504*s*, 1463*w*, 1433*w*, 1380*s*, 1370*s*, 1274*m*, 1170*s*, 1126*s*, 1084*s*, 1064*s*, 1019*w*, 951*w*, 891*s*, 860*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.07 (*s*, Me); 1.29 (*s*, Me); 2.41 (*s*, MeO); 3.92 (*s*, SH); 4.94 (*d*, $J = 7.5$, CH); 5.09 (*d*, $J = 7.5$); 7.24–7.30 (*m*, 2 arom. H); 7.37–7.58 (*m*, 8 arom. H); 7.63–7.83 (*m*, 15 arom. H); 7.85–7.94 (*m*, 2 arom. H); 8.20 (*s*, 1 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.57, 27.73, 52.17 (Me); 60.67 (C); 81.04, 83.05 (CH); 84.16, 108.29 (C); 125.83, 125.90, 125.97, 126.07, 126.14, 126.23, 126.35, 126.63, 126.84, 127.15, 127.23, 127.27, 127.28, 127.33, 127.35, 127.53, 127.65, 128.35, 128.42, 128.59, 128.63, 128.67, 129.40, 129.44, 129.51 (CH); 132.18, 132.22, 132.41, 132.44, 132.46, 132.67, 132.80, 132.82, 136.63, 138.03, 142.47, 143.12 (C). ESI-MS (pos.): 751 (42, $[M + MeOH + Na]^+$), 735 (22, $[M + K]^+$), 719 (100, $[M + Na]^+$). ESI-MS (neg.): 696 (56, M^-), 695 (100, $[M-1]^-$). Anal. calc. for $C_{48}H_{40}O_3S$ (696.91): C 82.73, H 5.78, S 4.60; found: C 82.62, H 5.86, S 4.57.

*(4*R*,5*R*)-2,2-Dimethyl-5-[(1-methylethoxy)(diphenyl)methyl]-α,α-diphenyl-1,3-dioxolane-4-methanethiol* (**34**). A *ca.* 7:3 mixture (3.10 g) of **26** (2.24 g, 4.25 mmol) and **15** was treated with thiourea (9.0 g, 118 mmol) in DMF (38 ml) according to *GP 5*. FC (SiO_2 (100 g); pentane/Et_2O 97:3) and subsequent trituration with MeOH (8 ml) for 30 min yielded **33** (1.65 g, 74%). Colorless solid. M.p. 177–179°. R_f (pentane/Et_2O 9:1) 0.69. $[\alpha]_D^{rt.} = -43.2$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): 3059*m*, 2987*m*, 2935*m*, 2508*m*, 1599*w*, 1492*m*, 1444*s*, 1381*s*, 1370*s*, 1316*w*, 1177*s*, 1113*m*, 1074*s*, 1060*s*, 1038*s*, 1019*s*, 919*w*, 898*m*, 870*w*, 832*w*, 651*w*, 633*w*. ^{1}H-NMR (400 MHz): 0.43 (*d*, $J = 5.9$, Me); 0.86 (*s*, Me); 0.92 (*s*, Me); 1.29 (*d*, $J = 6.2$, Me); 3.59–3.69 (*m*, CH); 4.41 (*d*, $J = 7.7$, CH); 4.58 (*d*, $J = 7.7$, CH); 5.45 (*s*, SH); 7.12–7.30 (*m*, 10 arom. H); 7.32–7.43 (*m*, 6 arom. H); 7.65–7.70 (*m*, 2 arom. H); 7.72–7.77 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz): 23.66, 24.38, 27.07, 27.19 (Me); 57.84 (C); 68.32, 81.33, 82.75 (CH); 85.34, 107.37 (C); 126.33, 126.64, 126.74, 126.98, 127.44, 127.52, 127.56, 127.84, 128.43, 130.39, 130.89, 131.97 (CH); 139.11, 141.06, 142.62, 147.08 (C). ESI-MS (pos.): 579 (98, $[M + MeOH + Na]^+$), 563 (74, $[M + K]^+$), 547 (100, $[M + Na]^+$). ESI-MS (neg.): 523 (88, $[M-1]^-$), 265 (100), 255 (74). Anal. calc. for $C_{34}H_{36}O_3S$ (524.72): C 77.83, H 6.91, S 6.11; found: C 77.71, H 7.01, S 6.10.

*(4*R*,5*R*)-5-[(Diphenyl)(phenylmethoxy)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanethiol* (**35**). Monochloride **27** (3.05 g, 5.30 mmol) was treated with thiourea (8.1 g, 106 mmol) in DMF (32 ml) according to *GP 5*. FC (SiO_2 (80 g); pentane/Et_2O 95:5) yielded **35** (2.52 g, 83%). Colorless solid foam. Subsequent trituration with MeOH yielded **35** (1.98 g, 65%). Colorless solid. M.p. 93–96°. R_f (pentane/Et_2O 95:5) 0.50. $[\alpha]_D^{rt.} = -60.0$ ($c = 0.95$, $CHCl_3$). IR ($CHCl_3$): 3062*m*, 3008*s*, 2932*w*, 2880*w*, 2527*m*, 1597*w*, 1494*s*, 1445*s*, 1380*m*, 1371*m*, 1318*w*, 1171*m*, 1065*s*, 1023*s*, 922*m*, 900*m*, 866*w*, 656*w*, 628*w*. ^{1}H-NMR (400 MHz): 0.97 (*s*, Me); 1.02 (*s*, Me); 3.80 (*d*, $^2J = 10.7$, 1 H, CH_2); 4.21 (*d*, $^2J = 10.7$, 1 H, CH_2); 4.46 (*d*, $J = 7.8$, CH); 4.58 (*d*, $J = 7.8$, CH); 4.60 (*s*, SH); 7.05–7.14 (*m*, 5 arom. H); 7.20–7.33 (*m*, 13 arom. H); 7.35–7.48 (*m*, 3 arom. H); 7.55–7.61 (*m*, 2 arom. H); 7.67–7.73 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz): 27.09, 27.17 (Me); 57.91 (C); 66.88 (CH_2); 80.95, 83.10 (CH); 84.99, 107.35 (C); 126.31, 126.74, 126.99, 127.07, 127.44, 127.64, 127.67, 127.82, 127.85, 128.29, 128.35, 128.45, 129.81, 130.58, 131.57 (CH); 137.61, 137.88, 140.78, 142.66, 146.69 (C). ESI-MS (pos.): 627 (15, $[M + MeOH + Na]^+$), 611 (86, $[M + K]^+$), 595 (78, $[M + Na]^+$), 590 (100, $[M + NH_4]^+$). ESI-MS (neg.): 571 (100, $[M-1]^-$). Anal. calc. for $C_{38}H_{36}O_3S$ (572.77): C 79.69, H 6.33, S 5.60; found: C 79.65, H 6.27, S 5.48.

*(4*R*,5*R*)-5-[[4-(1,1-Dimethylethyl)phenoxy](diphenyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanethiol* (**36**). Monochloride **28** (2.40 g, 3.75 mmol) was treated with thiourea (5.7 g,

75 mmol) in DMF (50 ml) according to *GP 5*. FC (pentane/Et_2O 98:2; 250 g SiO_2) yielded **36** (980 mg, 43%). Colorless powder. M.p. 105–108°. R_f (pentane/Et_2O 9:1) 0.72. $[\alpha]_D^{r.t.} = -64.5$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3061*w*, 3007*m*, 2984*m*, 2554w, 1604*w*, 1508*s*, 1445*m*, 1380*m*, 1370*m*, 1177*s*, 1062*m*, 1033*w*, 1015*m*, 924*w*, 896*m*. ^{1}H-NMR (400 MHz): 0.98 (*s*, Me); 1.06 (*s*, Me); 1.16 (*s*, ^{t}Bu); 3.93 (*s*, SH); 4.57 (*d*, $J = 7.65$, CH); 4.75 (*d*, $J = 7.65$, CH); 6.48–6.51 (*m*, 2 arom. H); 6.89–6.96 (*m*, 2 arom. H); 7.04–7.24 (*m*, 10 arom. H); 7.31–7.47 (*m*, 6 arom. H); 7.74–7.84 (*m*, 4 arom. H). ^{13}C-NMR (100 MHz): 27.15, 27.21, 31.36 (Me); 33.94, 58.83 (C); 83.15, 83.40 (CH); 87.25, 107.65 (C); 120.60, 125.01, 126.36, 126.90, 126.95, 127.08, 127.32, 127.47, 127.53, 127.70, 128.41, 129.72, 130.80, 131.36 (CH); 137.94, 139.87, 143.04, 144.36, 147.04, 152.37 (C). ESI-MS (pos.): 669 (46, $[M + MeOH + Na]^+$), 653 (44, $[M + K]^+$), 637 (100, $[M + Na]^+$). ESI-MS (neg.): 613 (100, $[M - 1]^-$). Anal. calc. for $C_{41}H_{42}O_3S$ (614.85): C 80.09, H 6.88, S 5.22; found: C 80.08, H 7.03, S 5.31.

N-*[{(4*S*,5*R*)-5-[(Diphenyl)(sulfanyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}(diphenyl)methyl]-1,1,1-trifluoromethanesulfonamide* (**37**). A soln. of **29** (3.90 g, 6.30 mmol) in CH_2Cl_2 (8 ml) was treated with thiourea (12.0 g, 158 mmol) in DMF (60 ml) according to *GP 5*. After purification by FC (SiO_2 (60 g); pentane/Et_2O 9:1), the resulting solid foam was dissolved in CH_2Cl_2 and precipitated with hexane. Further trituration with hexane under reflux yielded **37** (2.90 g, 74%). Colorless solid. M.p. 185–190° (dec.). R_f (hexane/AcOEt 8:2) 0.42. $[\alpha]_D^{r.t.} = -59.7$ ($c = 1.16$, $CHCl_3$). IR ($CHCl_3$): 3274*m*, 3064*m*, 2886*m*, 2825*w*, 1598*w*, 1496*m*, 1445*m*, 1373*s*, 1177*m*, 1139*m*, 1080*m*, 1055*m*, 1033*m*, 897*w*, 858*w*, 600*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*s*, Me); 1.08 (*s*, Me); 2.27 (*s*, SH); 4.33 (*d*, $J = 7.5$, CH); 4.70 (*d*, $J = 7.5$, CH); 7.10–7.31 (*m*, 10 arom. H); 7.37–7.50 (*m*, 8 arom. H); 7.67–7.70 (*m*, 2 arom. H); 8.75 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.78, 27.19 (Me); 57.98, 70.06 (C); 82.59, 82.68 (CH); 108.36, 118.96 (*q*, ^1J(C,F) = 322, CF_3) (C); 126.96, 127.14, 127.67, 127.72, 128.15, 128.17, 128.54, 129.82, 130.51, 130.88 (CH); 137.96, 138.12, 139.78, 147.99 (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −76.80. ESI-MS (pos.): 668 (17, $[M + MeOH + Na]^+$), 658 (16, $[M + 45]^+$), 652 (5, $[M + K]^+$), 636 (100, $[M + Na]^+$), 631 (16, $[M + NH_4]^+$). ESI-MS (neg.): 612 (100, $[M - 1]^-$). Anal. calc. for $C_{32}H_{30}F_3NO_4S_2$ (613.72): C 62.63, H 4.93, N 2.28, S 10.45; found: C 62.40, H 5.05, N 2.20, S 10.49.

N-*[{(4*S*,5*R*)-5-[(Diphenyl)(sulfanyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}(diphenyl)methyl]-2,2,2-trifluoroacetamide* (**38**). A soln. of crude **30** (2.56 g, ca. 3.90 mmol) in CH_2Cl_2 (5 ml) was treated with thiourea (7.4 g, 97 mmol) in DMF (20 ml) according to *GP 5*. FC (pentane/Et_2O 95:5; 120 g SiO_2) yielded **38** (1.70 g, 75% from **22**). Colorless foam. Trituration with hexane (35 ml) yielded anal. pure **38** (1.28 g, 56% from **22**). Colorless solid. M.p. 159–161°. $[\alpha]_D^{r.t.} = -97.4$ ($c = 1.14$, $CHCl_3$). IR ($CHCl_3$): 3399*w*, 3230*w*, 3062*w*, 2936*w*, 1736*s*, 1540*m*, 1496*m*, 1444*m*, 1381*m*, 1372*w*, 1327*w*, 1177*s*, 1060*m*, 897*w*, 865*w*, 657*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.71 (*s*, Me); 0.90 (*s*, Me); 2.05 (*s*, SH); 4.80 (*d*, $J = 7.1$, CH); 4.90 (*d*, $J = 7.1$, CH); 7.13–7.51 (*m*, 20 arom. H); 8.66 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.92, 27.23 (Me); 57.96, 66.94 (C); 82.39, 82.87 (CH); 109.21, 115.80 (*q*, ^1J(C,F) = 290, CF_3) (C); 127.45, 127.52, 127.65, 127.85, 127.88, 127.92, 128.00, 128.35, 129.37, 129.61, 130.72 (CH); 136.75, 139.84, 140.78, 148.10, 155.11 (*q*, ^2J(CF) = 37, CO) (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −75.19. MALDI-FT-ICR-MS: 600.2 (100, $[M + Na]^+$), 566.2 (10), 487.2 (4), 431.2 (7), 301.1 (11), 200.1 (10). Anal. calc. for $C_{33}H_{30}F_3NO_3S$ (577.67): C 68.61, H 5.23, N 2.42, S 5.55; found: C 68.71, H 5.34, N 2.42, S 5.45.

*(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanethiol* (**45**). A soln. of dichloro-TADDOL [24] (3.00 g, 5.96 mmol) in DMF (30 ml, degassed by three freeze-thaw cycles) was treated with thiourea (15.0 g, 197 mmol) according to *GP 5*. Purification by FC (SiO_2 (80 g); pentane/Et_2O 95:5 → 9:1) yielded a 9:1 mixture (^{1}H-NMR) **45**/**46** (total yield: 2.00 g, 67%). A sample (600 mg) was purified by FC (SiO_2 (80 g); pentane (10 l) → pentane/Et_2O 95:5) to yield pure (> 96% according to ^{1}H-NMR) **45** (250 mg). For anal. purposes, a sample was recrystallized from pentane. Colorless solid. M.p. 148.5–149.5°. R_f (pentane; 10 runs) 0.30 (**46**: 0.49). $[\alpha]_D^{r.t.} = -32.4$ ($c = 1.5$, $CHCl_3$). IR ($CHCl_3$): 3061*m*, 3008*s*, 2936*w*, 2569*w*, 1597*w*, 1493*s*, 1444*s*, 1380*m*, 1370*m*, 1162*m*, 1084*m*, 1055*s*, 1038*m* . ^{1}H-NMR (300 MHz, $CDCl_3$): 0.98 (*s*, 2 Me); 2.03 (*s*, 2 SH); 5.29 (*s*, 2 CH); 7.14–7.37 (*m*, 16 arom. H); 7.48–7.52 (*m*, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 28.01 (Me); 60.11 (C); 83.92 (CH); 110.50 (C); 126.97, 127.09, 127.54, 127.99, 129.27, 130.48 (CH); 145.16, 146.97 (C). ESI-MS (neg.): 497.2 (100, $[M - 1]^-$). Anal. calc. for $C_{31}H_{30}O_2S_2$ (498.71): C 74.66, H 6.06, S 12.86; found: C 74.69, H 6.17, S 12.71. A 6:4 mixture **45**/**46** has already been reported in the literature [24b].

8. *Preparation of Thioether* **39**, *Trifluoromethanesulfonamide* **40**, *Formamidine* **41**, *Oxathiepines* **43** *and* **44**, *Thiophene* **47**, *Sn Complex* **48**, *and Pd Complex* **49**. *(4*S,*5*R*)*-N,N,*2,2-Tetramethyl-5-[(methylsulfanyl)(diphenyl)methyl]-α,α-diphenyl-1,3-dioxolane-4-methanamine (**39**). A soln. of **31** (100 mg, 0.20 mmol) in MeCN/CH_2Cl_2 2:1 (3 ml) was treated with K_2CO_3 (28 mg, 0.20 mmol) and MeI (14 ml, 0.22 mmol) according to *GP 6* at r.t. After stirring overnight, purification by FC (SiO_2 (15 g); pentane/Et_2O 96:4) yielded **39** (90 mg, 85%). Colorless solid foam. M.p. 148–154°. R_f (hexane/AcOEt 8:2) 0.52. $[\alpha]_D^{r.t.} = -40.8$ ($c = 1.3$, $CHCl_3$). IR ($CHCl_3$): 3089*w*, 3058*w*, 2935*w*, 2867*w*, 2831*w*, 2788*w*, 1597*w*, 1491*m*, 1443*m*, 1379*w*, 1359*w*, 1173*m*, 1054*m*, 1034*m*, 1011*w*, 928*w*, 886*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.49 (*s*, Me); 1.04 (*s*, Me); 1.52 (*s*, Me); 1.75 (br. *s*, Me); 1.95 (br. *s*, Me); 4.77 (br. *s*, CH); 5.02 (br. *s*, CH); 6.70–7.60 (*m*, 17 arom. H); 7.85–7.90 (*m*, 2 arom. H); 7.95–8.25 (br. *s*, 1 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.75, 26.63, 27.50, 41.28 (br.) (Me); 62.68, 74.18 (C); 77.45, 83.58 (CH); 106.87 (C); 125.85, 126.04, 126.84, 127.00, 127.19, 127.23, 129.28, 131.94 (CH); 137.57, 139.48, 144.61 (C). ESI-MS (pos.): 546 (4, $[M + Na]^+$], 524 (100, $[M + 1]^+$), 479 (18, $[M - Me_2N]^+$), 431 (27, $[M - Me_2N - MeS - 1]^+$). Anal. calc. for $C_{34}H_{37}NO_2S$ (523.74): C 77.97, H 7.12, N 2.67, S 6.12; found: C 77.91, H 7.30, N 2.59, S 6.12.

N-*[(4*S,*5*R*)-2,2-Dimethyl-5-[(methylsulfanyl)(diphenyl)methyl]-1,3-dioxolan-4-yl](diphenyl)methyl]-1,1,1-trifluoromethanesulfonamide* (**40**). A soln. of **37** (250 mg, 0.41 mmol) in MeCN/CH_2Cl_2 3:2 (5 ml) was treated with K_2CO_3 (113 mg, 0.82 mmol) and MeI (26 ml, 0.42 mmol) according to *GP 6* at r.t. After stirring for 7 h, purification by FC (SiO_2 (20 g); pentane/Et_2O 95:5) yielded **40** (226 mg, 87%). Colorless solid. M.p. 181–183°. R_f (hexane/AcOEt 8:2) 0.50. $[\alpha]_D^{r.t.} = -107.6$ ($c = 1.23$, $CHCl_3$). IR ($CHCl_3$): 3008*m*, 2871*m*, 2801*m*, 1598*w*, 1496*m*, 1444*m*, 1373*s*, 1177*m*, 1139*m*, 1081*m*, 1057*m*, 1032*m*, 966*w*, 938*w*, 896*w*, 853*w*, 600*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.61 (*s*, Me); 1.09 (*s*, Me); 1.58 (*s*, Me); 4.25 (*d*, $J = 7.4$, CH); 4.77 (*d*, $J = 7.4$, CH); 7.14–7.29 (*m*, 10 arom. H); 7.37–7.50 (*m*, 8 arom. H); 7.72–7.77 (*m*, 2 arom. H); 10.11 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 13.37, 26.78, 27.41 (Me); 59.67, 69.50 (C); 78.70, 82.55 (CH); 108.41, 119.08 (*q*, ^1J(C,F) = 322, CF_3) (C); 126.82, 126.98, 127.50, 127.54, 128.06, 128.09, 128.40, 129.80, 130.65 (CH); 138.53, 138.60, 140.24, 142.80 (C). ^{19}F-NMR (282 MHz, $CDCl_3$): –76.93. ESI-MS (pos.): 663 (8, $[M + K]^+$), 650 (14, $[M + Na]^+$), 645 (100, $[M + NH_4]^+$). ESI-MS (neg.): 626 (100, $[M - 1]^-$). Anal. calc. for $C_{33}H_{32}F_3NO_4S_2$ (627.75): C 63.14, H 5.14, N 2.23, S 10.22; found: C 63.24, H 5.15, N 2.19, S 10.16.

N′-*[[(4*S,*5*R*)-5-[(Hydroxy)(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl](diphenyl)methyl]*-N,N-*dimethylmethanimidamide* (**41**). A soln. of **9** (1.40 g, 3.01 mmol) in CH_2Cl_2 (20 ml) was treated with Et_3N (0.40 ml, 2.86 mmol) and $SOCl_2$ (0.40 ml, 5.50 mmol) according to *GP 2*. The residue was dissolved in DMF (50 ml) and treated with thiourea (19.0 g, 250 mmol) according to *GP 5*. Purification by FC (SiO_2 (80 g); pentane/Et_2O 9:1 → Et_2O) yielded **41** (310 mg, 20%). Colorless crystals. M.p. 212–215°. R_f (hexane/AcOEt 4:1) 0.04. $[\alpha]_D^{r.t.} = -27.0$ ($c = 1.2$, $CHCl_3$). IR ($CHCl_3$): 3056*w*, 3007*m*, 1637*s*, 1493*m*, 1444*m*, 1380*m*, 1370*m*, 1077*m*, 1050*m*, 901*w*, 886*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.05 (*s*, Me); 1.06 (*s*, Me); 2.74 (br. *s*, MeN); 3.18 (br. *s*, MeN); 4.23 (*d*, $J = 8.4$, CH); 4.37 (*d*, $J = 8.4$, CH); 6.42 (*s*, OH); 7.02–7.06 (*m*, 2 arom. H); 7.11–7.34 (*m*, 14 arom. H); 7.59–7.64 (*m*, 4 arom. H); 9.46 (*s*, NCH). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.09, 27.12, 35.52 (br.), 40.96 (br.) (Me); 69.74, 76.88 (C); 81.83, 82.06 (CH); 107.88 (C); 126.46, 126.56, 126.65, 126.88, 126.91, 127.64, 127.78, 127.80, 129.12, 129.72, 130.56 (CH); 143.02, 144.14, 144.90, 147.48 (C); 156.26 (CH). FAB-MS: 1041.4 (16.5, $[2M + H]^+$), 521.2 (100, $[M + H]^+$), 443.1 (8.8), 338.1 (8.1), 237.1 (61.2), 179.1 (27.5), 167.1 (23.2), 104.9 (19.6). Anal. calc. for $C_{34}H_{36}N_2O_3$ (520.67): C 78.43, H 6.97, N 5.38; found: C 78.41, H 6.78, N 5.45.

*(3a*R,*8a*R*)-Tetrahydro-2,2,6-trimethyl-4,4,8,8-tetraphenyl-1,3-dioxolo[4,5-*e*][1,3]oxathiepin* (**43**). A soln. of **7** (718 mg, 1.49 mmol) in CH_2Cl_2 (12 ml) was treated with MeCHO (0.50 ml, 8.85 mmol) and $BF_3 \cdot Et_2O$ (0.20 ml, 1.60 mmol) according to *GP 7*. FC (SiO_2 (80 g); hexane/AcOEt 9:1) yielded **43** (623 mg, 82%). Colorless solid. M.p. 255–257°. R_f (hexane/AcOEt 9:1) 0.50. $[\alpha]_D^{r.t.} = -125.5$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): 3062*m*, 3007*s*, 2931*m*, 1950br., 1900br., 1810br., 1711*s*, 1598*m*, 1492*s*, 1445*s*, 1382*m*, 1373*s*, 1248*s*, 1164*s*, 1074*s*, 1035*s*, 1001*s*, 967*m*, 924*m*, 896*m*, 877*m*, 857*m*, 832*w*, 658*w*, 635*m*, 615*w*, 607*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.10 (*s*, Me); 1.50 (*d*, $J = 7.2$, *Me*CH); 1.52 (*s*, Me); 4.71 (*d*, $J = 8.6$, CH); 5.11 (*q*, $J = 6.3$, MeC*H*); 5.50 (*d*, $J = 8.6$, CH); 7.12–7.29 (*m*, 10 arom. H); 7.32–7.38 (*m*, 4 arom. H); 7.40–7.42 (*m*, 2 arom. H); 7.49–7.51 (*m*, 2 arom. H); 7.59–7.61 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 23.67, 24.55, 27.89 (Me); 60.31 (C); 73.74, 80.64 (CH); 83.02 (C); 83.16 (CH); 109.16 (C); 126.39, 127.07, 127.16, 127.19, 127.42, 127.65, 127.79, 127.84, 128.23, 128.77, 128.80, 132.49 (CH); 140.81, 141.54,

145.97, 149.60 (C). ESI-MS (pos.): 563 (8, $[M + MeOH + Na]^+$), 547 (35, $[M + K]^+$), 526 (100, $[M + NH_4]^+$). Anal. calc. for $C_{33}H_{32}O_3S$ (508.21): C 77.92, H 6.34, S 6.30; found: C 77.86, H 6.32, S 6.39.

*(3a*R*,8a*R*)-Tetrahydro-2,2-dimethyl-4,4,6,8,8-pentaphenyl-1,3-dioxolo[4,5-*e*][1,3]oxathiepin* (**44**). A soln. of **7** (519 mg, 1.08 mmol) in CH_2Cl_2 (10 ml) was treated with PhCHO (0.11 ml, 1.08 mmol) and $BF_3 \cdot Et_2O$ (0.14 ml, 1.08 mmol) according to *GP 7*. Purification by FC (2 ×) (SiO_2 (50 g); hexane/AcOEt 95 : 5) yielded **44** (324 mg, 53%). Colorless solid. M.p. 208–210°. R_f (hexane/AcOEt 9 : 1) 0.40. $[\alpha]_D^{r.t.} = -300.2$ ($c = 0.5$, $CHCl_3$). IR ($CHCl_3$): 3065*m*, 3007*m*, 2934*m*, 1963br., 1800br., 1598*m*, 1493*s*, 1446*s*, 1392*m*, 1371*m*, 1316*w*, 1164*s*, 1067*s*, 1032*s*, 988*m*, 928*s*, 886*m*, 845*m*, 816*w*, 654*w*, 648*w*, 620*m*, 609*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.38 (*s*, Me); 1.16 (*s*, Me); 4.65 (*d*, $J = 8.1$, CH); 5.81 (*d*, $J = 8.1$, CH); 6.03 (*s*, PhC*H*); 7.13–7.39 (*m*, 19 arom. H); 7.50–7.53 (*m*, 4 arom. H); 7.73–7.93 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 25.55, 27.59 (Me); 62.87 (C); 80.32, 81.02, 82.38 (CH); 84.01 (C); 111.14 (C); 126.09, 127.12, 127.19, 127.24, 127.37, 127.56, 127.67, 127.84, 128.08, 128.28, 128.33, 128.38, 129.49, 131.48 (CH); 139.01, 140.88, 141.71, 144.01, 144.65 (C). ESI-MS (pos.): 630 (22, $[M + 60]^+$), 616 (18, $[M + 46]^+$), 588 (100, $[M + NH_4]^+$), 571 (12, $[M + 1]^+$). Anal. calc. for $C_{33}H_{32}O_3S$ (570.75): C 79.97, H 6.00, S 5.62; found: C 79.91, H 6.23, S 5.60.

*(3a*R*,6a*R*)-Tetrahydro-2,2-dimethyl-4,4,6,6-tetraphenylthieno[3,4-*d*]-1,3-dioxole* (**47**). In analogy to [40b], to a soln. of hexamethyldisilathiane (0.27 ml, 1.30 mmol) in THF (10 ml) was added MeLi (1.60 ml, 2.55 mmol; 1.6M soln. in hexane), and the mixture was refluxed for 2 h. A soln. of dichloro-TADDOL [24] (621 mg, 1.23 mmol) in THF (5 ml) was added, and the purple mixture was stirred under reflux for 44 h. After cooling to r.t., H_2O (10 ml), Et_2O (10 ml), and sat. NaCl soln. (10 ml) were added, the phases were separated, and the aq. phase was extracted with Et_2O (3 × 10 ml). The combined org. layers were washed with H_2O (10 ml) and sat. NaCl soln., and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by FC (SiO_2 (70 g); hexane/AcOEt 9 : 1) to yield **47** (334 mg, 58%). Beige solid foam. M.p. 174–176° ([24a]: 179°). R_f (hexane/AcOEt 9 : 1) 0.60. $[\alpha]_D^{r.t.} = -389.8$ ($c = 0.5$, $CHCl_3$) ([24a]: $[\alpha]_D^{r.t.} = -428.3$ ($c = 1$, $CHCl_3$)). ^{1}H-NMR (300 MHz): 1.20 (*s*, 6 H, Me); 4.97 (*s*, 2 H, CH); 7.18–7.34 (*m*, 16 arom. H); 7.58–7.61 (*m*, 4 arom. H). The anal. data matched those of [24a].

*(3a*R*,8a*R*)-Tetrahydro-2,2-dimethyl-4,4,6,6,8,8-hexaphenyl[1,3,2]dithiastannepino[5,6-*d*]-1,3-dioxole* (**48**). A 9 : 1 mixture **45**/**46** (1.20 g, 2.40 mmol), dissolved in CH_2Cl_2 (20 ml), was treated with Ph_2SnCl_2 (830 mg, 2.40 mmol) and Et_3N (0.70 ml, 5.02 mmol). The mixture was stirred for 12 h at r.t., washed with 0.5N NaOH soln. (10 ml), and the aq. phase was extracted with CH_2Cl_2. The combined org. layers were dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residue was dissolved in a small amount of CCl_4 and purified by FC (SiO_2 (80 g); pentane/Et_2O 95 : 5; R_f (**48**) < R_f (**45**/**46**)). *Caution*: **48** is prone to hydrolysis on SiO_2. Trituration with MeOH under reflux for 5 min yielded **48** (950 mg, 51%). Colorless powder. M.p. 179–180°. R_f (hexane/AcOEt 8 : 2) 0.50. $[\alpha]_D^{r.t.} = -333.0$ ($c = 1.95$, $CHCl_3$). IR ($CHCl_3$): 3056*m*, 3007*s*, 2938*w*, 1951*w*, 1896*w*, 1813*w*, 1597*w*, 1578*w*, 1492*s*, 1443*s*, 1431*s*, 1380*s*, 1370*m*, 1332*w*, 1071*s*, 1060*s*, 1045*s*, 1021*w*, 996*m*, 870*w*, 842*m*, 835*m*, 644*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.60 (*s*, 2 Me); 6.05 (*s*, 2 CH); 7.07–7.34 (*m*, 22 arom. H); 7.53–7.57 (*m*, 8 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.06 (Me); 64.32 (*t*, ^2J(C,Sn) = 8.9) (C); 85.34 (*t*, ^2J(C,Sn) = 5.7) (CH); 109.12, 111.61 (C); 126.52, 126.84, 126.98, 127.67, 128.71 (*t*, ^3J(C,Sn) = 33.8), 129.17, 129.84 (*t*, ^2J(C,Sn) = 7.2), 131.13, 135.88 (*t*, J(C,Sn) = 24.5) (CH); 137.62, 145.00 (*t*, ^1J(C,Sn) = 12.4), 148.79 (C). ^{119}Sn-NMR (149 MHz, $CDCl_3$): −27.04. EI-MS: 532 (9), 500 (7), 383 (5), 351 (8), 265 (10), 237 (8), 229 (6), 211 (11), 207 (58), 198 (100), 179 (42). Anal. calc. for $C_{43}H_{38}O_2S_2Sn$ (769.61): C 67.11, H 4.98, S 8.33; found: C 67.10, H 4.98, S 8.10.

*[(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanethiolato(2−)-κS^4,κS^5][1,1′-(1,2-ethanediyl)bis[1,1-diphenylphosphine-κP]]palladium* (**49**). A 9 : 1 mixture **45**/**46** (500 mg, 1.00 mmol), dissolved in CH_2Cl_2 (10 ml), was treated with [Pd(dppe)Cl_2] (518 mg, 0.90 mmol) and Et_3N (250 ml, 1.80 mmol). The mixture was stirred for 15 min at r.t., during which the color of the suspension changed from yellow to orange-red. After filtration the solvent was removed under reduced pressure to *ca.* 2–3 ml, and, after FC (SiO_2 (15 g); CH_2Cl_2; R_f (**49**) < R_f (**45**/**46**)), **49** (672 mg, 79%) was isolated. For anal. purposes, a sample of **49** was recrystallized (CH_2Cl_2). Orange-yellow crystals. M.p. 150–160° (dec.). R_f (CH_2Cl_2) 0.41. $[\alpha]_D^{r.t.}$ n.d. (0% transmission). IR ($CHCl_3$): 3054*m*, 3006*s*, 2933*w*, 1595*w*, 1486*s*, 1436*s*, 1412*w*, 1378*w*, 1368*w*, 1308*w*, 1175*w*, 1103*s*, 1044*s*, 999*w*, 877*m*. ^{1}H-NMR (400 MHz,

$CDCl_3$): 0.82 (*s*, 2 Me); 2.04–2.24 (*m*, 2 H); 2.29–2.45 (*m*, 2 H); 5.70 (*s*, 2 CH); 6.89–6.97 (*m*, 6 arom. H); 7.06–7.13 (*m*, 10 arom. H); 7.23–7.29 (*m*, 4 arom. H); 7.34–7.38 (*m*, 6 arom. H); 7.43–7.48 (*m*, 6 arom. H); 7.62–7.67 (*m*, 4 arom. H); 7.91–7.96 (*m*, 4 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.33 (*dd*, ^1J(C,P) = ^2J(C,P) = 22.5) (CH_2); 62.84 (C); 85.31 (CH); 108.38 (C); 124.35, 125.31, 125.69, 126.46, 128.27, 128.32, 128.38, 128.80, 128.86, 128.93, 129.07, 129.29, 129.55, 129.77, 129.99, 130.22, 130.43, 130.71, 131.25, 132.93, 133.04, 133.09, 133.14, 134.30, 134.36, 134.42, 146.35, 152.54, 152.56 (C,P coupling!). ^{31}P-NMR (162 MHz, $CDCl_3$): 48.13. ESI-MS (pos.): 1039 (60, $[M + K-1]^+$), 1023 (100, $[M + Na-1]^+$), 1001 (58, M^+), 569 (21), 537 (16). Anal. calc. for $C_{57}H_{52}O_2P_2PdS_2$ (1001.54): C 68.36, H 5.23, S 6.40, P 6.19; found: C 68.21, H 5.46, S 6.32, P 6.24.

9. *Preparation of the Cu and Ag complexes* **50**–**54**. *Tetrakis{μ-(4*R,*5*R*)-5-[(Diphenyl)(sulfanyl–*κ*S,*κ*S)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanolato(1−)}tetracopper(1)* (**50**). To a stirred soln. of **7** (750 mg, 1.55 mmol) in CH_2Cl_2 (12 ml) at r.t. were added Et_3N (325 μl, 2.33 mmol) and CuCl (153 mg, 1.55 mmol). After 25 min, the heterogeneous mixture was concentrated to *ca.* 2 ml on a rotovap, and the residue was purified by FC (SiO_2 (10 g); pentane/Et_2O 1:1). To the combined fractions containing **50** was added hexane (10 ml), and subsequent concentration on a rotovap led to precipitation of **50** (710 mg, 84%). Colorless solid. M.p. 192–195° (dec.). R_f (hexane/AcOEt 8:2) 0.45. $[\alpha]_D^{r.t.} = -71.6$ ($c = 1.04$, $CHCl_3$). IR ($CHCl_3$): 3360*s*, 3058*w*, 3007*m*, 2936*w*, 1597*w*, 1493*m*, 1446*m*, 1380*m*, 1370*m*, 1169*m*, 1060*s*, 1033*w*, 901*w*, 882*w*. ^{1}H-NMR (400 MHz): 0.60 (*s*, 2 Me); 0.68 (*s*, 2 Me); 0.82 (*s*, 2 Me); 1.32 (*s*, 2 Me); 4.20 (*d*, $J = 8.0$, 2 CH); 4.42 (*d*, $J = 8.0$, 2 CH); 4.47 (*d*, $J = 6.5$, 2 CH); 4.79 (*s*, 2 OH); 5.35 (*d*, $J = 6.5$, 2 CH); 5.38 (*s*, 2 OH); 5.92 (br., 2 arom. H); 6.43 (br., 2 arom. H); 6.50–7.95 (*m*, 76 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.55, 27.17, 27.53 (Me); 60.95, 61.37, 77.19, 77.76 (C); 81.40, 82.79, 84.62 (CH); 107.35, 111.20 (C); 124.53, 126.31, 126.76, 127.06, 127.21, 127.39, 127.49, 127.64, 127.79, 127.94, 128.26, 128.41, 128.73, 129.01, 129.37, 130.98, 131.81, 133.84 (CH); 140.64, 142.36, 142.76, 143.48, 146.01, 148.67, 153.82, 154.15 (C). ESI-MS (pos.): 2219 (100, $[M + K]^+$), 2204 (20, $[M + Na]^+$). Anal. calc. for $C_{124}H_{116}O_{12}S_4Cu_4$ (2180.72): C 68.30, H 5.36, S 5.88; found: C 68.12, H 5.43, S 5.80.

*Tetrakis{μ-(4*R,*5*R*)-5-[(Diphenyl)(sulfanyl–*κ*S,*κ*S)methyl]-α,α,2,2-tetraphenyl-1,3-dioxolane-4-methanolato(1−)}tetracopper(1)* (**51**). A stirred suspension of **8** (270 mg, 0.44 mmol) in MeOH (5 ml) at r.t. was added Et_3N (100 μl, 0.72 mmol). The mixture became a clear soln., which turned turbid again after a few min. After addition of CuCl (44 mg, 0.44 mmol), the mixture was heated to reflux for *ca.* 10 min (TLC: R_f (hexane/AcOEt 4:1) 0.16 (**51**), 0.51 (**8**)). Removal of the solvent to *ca.* 2 ml in a rotovap, filtration, dissolution in CH_2Cl_2, and FC (SiO_2 (6 g); pentane/Et_2O 1:1) gave **51** (160 mg, 55%). Colorless solid. M.p. 172–174° (dec.). R_f (hexane/AcOEt 4:1) 0.16. $[\alpha]_D^{r.t.} = +241.6$ ($c = 1.05$, $CHCl_3$). IR ($CHCl_3$): 3691*w*, 3542*m*, 3353*s*, 3086*w*, 3061*m*, 3007*m*, 2958*w*, 2928*w*, 1952*w*, 1896*w*, 1810*w*, 1599*m*, 1492*s*, 1448*s*, 1317*w*, 1170*m*, 1096*s*, 1089*s*, 1058*s*, 1030*s*, 943*m*. ^{1}H-NMR (400 MHz): 3.21 (br., 2 H); 4.24 (*d*, $J =$ 8.1, 2 CH); 4.57 (*d*, $J = 8.1$, 2 CH); 4.66 (*d*, $J = 5.2$, 2 CH); 5.39 (*d*, $J = 5.2$, 2 CH); 5.44 (*s*, 2 H); 5.54 (*d*, $J = 3.8$, 2 H); 6.12–6.25 (*m,* 2 arom. H); 6.24 (*t*, $J = 7.1$, 2 arom H); 6.42 (*d*, $J = 8.3$, 2 arom. H); 6.54 (br., 4 arom. H) 6.68–7.76 (*m*, 110 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 60.75, 61.11, 77.43, 78.64 (C); 83.44, 84.80, 85.41. 85.94 (CH); 108.48, 109.78 (C); 124.03, 124.81, 125.02, 125.05, 125.59, 126.21, 126.26, 126.42, 126.51, 126.68, 126.89, 127.04, 127.16, 127.38, 127.46, 127.60, 127.68, 127.78, 127.82, 127.90, 127.95, 128.07, 128.32, 128.49, 129.70, 129.93, 130.03, 1333.09 (CH); 139.60, 141.12, 141.60, 143.15, 143.72, 143.86, 144.55, 145.35, 145.69, 152.57, 154.67 (C). ESI-MS (pos.): 2717 (100, $[M + K]^+$), 2701 (58, $[M + Na]^+$).

*Tetrakis{μ-(4*R,*5*R*)-5-[(methoxy)(diphenyl)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanethiolato–*κ*S,*κ*S(1−)}tetracopper(1)* (**52**). To a soln. of **32** (180 mg, 0.36 mmol) in CH_2Cl_2 (8 ml) at r.t. were added Et_3N (90 μl, 0.65 mmol) and CuCl (36 mg, 0.36 mmol). After stirring for *ca.* 15 min (TLC: R_f (hexane/AcOEt 4:1) 0.58 (**52**), 0.72 (**32**)), evaporating to a volume of 2 ml, and FC (SiO_2 (6 g); pentane/Et_2O 4:1), the product-containing fractions were combined. After adding MeOH (5 ml), the solvent was evaporated to afford **52** (130 mg, 64%). Colorless solid. M.p. 144–146° (dec.). R_f (hexane/AcOEt 8:2) 0.58. $[\alpha]_D^{r.t.} = +63.0$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3058*m*, 2987*m*, 2936*m*, 2900*w*, 2825*w*, 1597*w*, 1493*m*, 1444*m*, 1379*m*, 1369*m*, 1318*w*, 1177*m*, 1094*s*, 1080*s*, 1054*s*, 1032*m*, 892*m*. ^{1}H-NMR (400 MHz): 0.65–1.10 (br., 24 H); 2.98 (br., 2 MeO); 3.10 (br., 2 MeO); 4.25 (br., 4 CH); 4.63 (br., 2 CH); 4.73 (br., 2 CH); 6.18 (br., 2 arom. H); 6.40–7.95 (*m*, 76 arom. H); 8.50 (br., 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.37, 51.72 (Me); 61.22 (C); 81.19, 82.46, 83.21, 84.17; 107.24 (C); 126.35, 127.09, 127.46, 129.51, 129.99, 131.24, 131.83. ESI-MS (pos.): 2275 (99, $[M + K]^+$), 2259 (60, $[M + Na]^+$,

1741 (100, $[M-106+1]^+$). Anal. calc. for $C_{128}H_{124}O_{12}S_4Cu_4$ (2236.83): C 68.73, H 5.59, S 5.73; found: C 68.62, H 5.77, S 5.58.

*Tetrakis{μ-(4*R,*5*R*)-2,2-dimethyl-5-[(1-methylethoxy)(diphenyl)methyl]-α,α-diphenyl-1,3-dioxolane-4-methanethiolato–κ*S,*κ*S*(1−)}tetracopper(I)* (**53**). To a stirred soln. of **34** (411 mg, 0.78 mmol) in CH_2Cl_2 (5 ml) at r.t. were added Et_3N (163 μl, 1.17 mmol) and CuCl (77.5 mg, 0.78 mmol). After 25 min, the mixture was concentrated to *ca.* 2 ml on a rotovap, followed by FC (SiO_2 (8 g); pentane/Et_2O 8:2). The residues of the product-containing fractions were subjected to further FC (2×) (pentane/Et_2O 95:5; 1. 12 g of SiO_2, 2. 16 g of SiO_2). The obtained product was triturated with MeOH to afford **53** (72 mg, 16%). Colorless solid. M.p. 142–143° (dec.). R_f (pentane/Et_2O 8:2) 0.64. $[\alpha]_D^{r.t.} = -20.0$ ($c = 0.85$, $CHCl_3$). ESI-MS (pos.): 2388 (38, $[M+K]^+$), 2372 (15, $[M+Na]^+$), 1825 (30, $[M-108+1]^+$, 1799 (43, $[M-108+1-Cu+K]^+$, 1784 (36, $[M-108+1-Cu+Na]^+$, 1238 (100, $[M-(2\times108)+2-Cu]^+$).

*Tetrakis{μ-(4*R,*5*R*)-5-[(Diphenyl)(sulfanyl–κ*S,*κ*S)methyl]-2,2-dimethyl-α,α-diphenyl-1,3-dioxolane-4-methanolato(1−)}tetrasilver(I)* (**54**). A stirred suspension of **7** (500 mg, 1.04 mmol) in MeOH (10 ml) at r.t. was converted to a clear soln. within 10 min by adding Et_3N (160 μl, 1.14 mmol). Addition of AcOAg (173 mg, 1.04 mmol) and heating at reflux for 15 min led to a grey precipitate (627 mg), which was filtered off, dissolved in CH_2Cl_2 and subjected to FC (SiO_2 (6 g); pentane/Et_2O 1:1). To the combined product fractions was added MeOH (*ca.* 6 ml), and concentration in a rotovap led to precipitation of **54** (525 mg, 86%). Colorless solid. M.p. 195–196° (dec.). $[\alpha]_D^{r.t.} = -5.8$ ($c = 1.0$, $CHCl_3$). R_f (pentane/Et_2O 1:2) 0.70. IR ($CHCl_3$): 3328*s*, 3060*m*, 3008*s*, 2937*w*, 1599*w*, 1493*m*, 1446*m*, 1381*m*, 1371*m*, 1170*s*, 1058*s*, 900*m*, 882*m*, 852*w*, 658*w*. ^{1}H-NMR (500 MHz): 0.81 (*s*, 2 Me); 0.87 (*s*, 2 Me); 1.05 (*s*, 2 Me); 1.38 (*s*, 2 Me); 4.06 (*d*, $J = 8.1$, 2 CH); 4.37 (*d*, $J = 7.0$, 2 CH); 4.45 (*d*, $J = 8.1$, 2 CH); 5.14 (*d*, $J = 7.0$, 2 CH); 5.19 (*s*, 2 OH); 5.77 (*s*, 2 OH); 6.09 (br., 2 arom. H); 6.19 (br., 2 arom. H); 6.51 (br., 4 arom. H); 6.97 (*t*, $J = 7.3$, 2 arom. H); 7.03–7.41 (*m*, 42 arom. H); 7.45–7.70 (*m*, 20 arom. H); 7.87 (*d*, $J = 7.4$, 4 arom. H); 8.01 (*m*, $J = 7.5$, 4 arom. H). ^{13}C-NMR (125 MHz): 26.58, 27.27, 27.46, 27.62 (CH_3); 59.80, 59.98, 76.93, 77.57 (C); 81.51 (*d*, ^3J(C,Ag) = 11.1), 83.10, 83.75 (*d*, ^3J(C,Ag) = 8.0), 84.01 (CH); 107.37, 109.67 (C); 124.18, 126.20, 126.64, 126.78, 127.11, 127.42, 127.46, 127.54, 127.72, 127.75, 127.82, 128.14, 128.48, 128.74, 128.86, 129.49, 130.26, 131.51, 134.02 (CH); 140.87, 142.71, 142.98, 144.08, 146.07, 147.25, 156.22, 156.87 (C). ESI-MS (pos.): 2398 (12, $[M+K]^+$), 2382 (12, $[M+Na]^+$). Anal. calc. for $C_{124}H_{116}Ag_4O_{12}S_4$ (2358.01): C 63.16, H 4.96, S 5.44. found: C 62.98, H 5.25, S 5.25.

10. *Enantioselective Cu^I-Catalyzed Addition of* Grignard *Reagents to Cyclic Enones Using the Thiol Ligands* **7**, **8**, **31**–**36** *and the Cu complexes* **50**–**53**. a) In situ *Procedure.* Under an Ar atmosphere, the thiol ligand (0.065 mmol) and CuCl (0.05 mmol) are suspended in 10 ml of THF and combined at −78° with BuLi (0.08 mmol for **31**–**36**, 0.16 mmol for **7** and **8**). The stirred mixture is allowed to warm to 0°, whereupon a clear soln. is formed (*ca.* 20 min). After cooling back to −78°, 1.0 mmol enone is added, and the RMgCl soln. (0.5M in THF) is introduced, within 70–80 min, using a syringe pump. After stirring for another 30–45 min, a sat. NH_4Cl soln. is added, and, after warming to r.t., the mixture is combined with Et_2O and H_2O. The phases are separated, the aq. layer is extracted with Et_2O (2×), and the combined org. phases are washed with sat. NaCl and dried (Na_2SO_4). After careful evaporation of the solvent under reduced pressure, the residue is purified by bulb-to-bulb distillation. For yields and selectivities, see *Table 4*.

b) *With the Isolated Cu Complex.* The enone (1.0 mmol) and the Cu complex (0.5 mmol **50**–**53**) are dissolved in 10 ml of THF, and the soln. is combined (within 30 min) with the *Grignard* reagent at −78° as described above.

c) *Derivatization of the 3-Alkyl- and 3-Phenylcycloalkanones with (*R,R*)-1,2-Diphenylethylenediamine for the er Determination.* Following the procedure of *Alexakis et al.* [41], 0.2 mmol of the ketone in 2 ml of CH_2Cl_2 was combined with 2 equiv. of the enantiomerically pure diamine and a bead of 4-Å molecular sieve (MS). After stirring for 1 h at r.t., the MS was removed, the solvent was evaporated, and the residue was dissolved in 0.6 ml of $CDCl_3$. The signals of the diastereoisomeric aminals in the ^{13}C-NMR spectra used for configurational assignments are specified in the procedures (*vide infra*).

d) *er Determination by Other Methods.* In one case, 3-butylcyclooctanone, the er was determined by derivatization with (*R*,*R*)-butane-2,3-diol; in another case, 3-butyl-4,4-dimethylcyclohexanone, by derivatization with (*R*,*R*)-pentane-2,4-diol in analogy to literature procedures [33][42][43]. For the

Table 6. *Crystallographic Data for Compounds* **11**, **13**, **15**, **16**, **31**, **32**, **36**, **37**, *and* **41**

	11	**13**	**15**	**16**
Formula	$C_{43}H_{39}NO_3$	$C_{32}H_{32}O_4$	$C_{34}H_{36}O_4$	$C_{38}H_{36}O_4$
Formula weight [g/mol]	617.75	480.61	508.63	556.67
T [K]	293(2)	293(2)	293(2)	293(2)
Wavelength [Å]	0.71073	0.71073	1.54178	1.54178
Source	MoK_α	MoK_α	CuK_α	CuK_α
Crystal dimensions [mm]	$0.3 \times 0.2 \times 0.1$	$0.4 \times 0.3 \times 0.2$	$0.3 \times 0.1 \times 0.1$	$0.3 \times 0.2 \times 0.2$
Crystal system	monoclinic	orthorhombic	orthorhombic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
θ Range [°]	$4.4 < \theta < 50.0$	$1.6 < \theta < 20.0$	$3.7 < \theta < 50.0$	$3.5 < \theta < 50.0$
a [Å]	9.778(5)	8.129(5)	9.64(1)	9.574(7)
b [Å]	17.473(2)	16.011(9)	15.23(2)	16.79(1)
c [Å]	10.578(5)	20.43(1)	19.34(2)	19.34(1)
α [°]	90	90	90	90
β [°]	106.00(4)	90	90	90
γ [°]	90	90	90	90
V [Å^3]	1737(2)	2659(3)	2838(5)	3109(4)
Z	2	4	4	4
ρ_{calc} [g cm^{-3}]	1.181	1.200	1.191	1.189
μ [mm^{-1}]	0.573	0.078	0.606	0.599
Total reflections measured	1855	1463	1694	1849
Independent reflections	1855	1463	1694	1849
Reflections observed	1803	1105	1416	1752
No. of variables	425	330	344	380
Criterion	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
Final R [%]	3.57	2.88	3.71	4.25
wR_2 [%]	9.37	6.18	10.43	10.91
Goodness-of-fit	1.092	0.801	0.979	1.141
$\Delta\rho$ (max, min) [e Å^{-3}]	0.123, −0.147	0.088, −0.097	0.128, −0.129	0.173, −0.188
CCDC No.	158335	158336	158337	158338

GC determination of er values, a *β-DEX 120* (30 m × 0.25-mm inner diameter) column by *Supelco* was used. Details are given with the product specifications, below.

3-Butylcyclopentanone. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.87–0.97 (*m*, Me); 1.29–2.54 (*m*, 13 H).

(*2*R,*3*R)*-7-Butyl-2,3-diphenyl-1,4-diazaspiro[4.4]nonane).* ^{13}C-NMR (50 MHz, $CDCl_3$): 48.2 (3*R*)/47.5 (3*S*); 41.1 (3*R*); 40.2 (3*S*) [41].

3-Butylcyclohexanone. $[\alpha]_D^{r.t.} = +12.8$ ($c = 0.9$, $CHCl_3$), er(*R*/*S*) 89:11 ([34]: $[\alpha]_D^{r.t.} = +9.4$ ($c = 2.78$, $CHCl_3$), er(*R*/*S*) 80:20). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82–0.93 (*m*, Me); 1.22–1.40 (*m*, 7 H); 1.55–2.47 (*m*, 8 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.87; 22.60; 25.20; 28.75; 31.23; 36.21; 38.97; 41.45; 48.18; 212.32.

*(2*R,*3*R)*-7-Butyl-2,3-diphenyl-1,4-diazaspiro[4.5]decane.* ^{13}C-NMR (75 MHz, $CDCl_3$): 46.9 (3*S*)/46.1 (3*R*); 40.0 (3*R*); 38.8 (3*S*); 35.4 (3*R*); 34.5 (3*S*) [41].

3-Butyl-4,4-dimethylcyclohexanone. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89 (*t*, $J = 7.1$, Me); 0.99 (*s*, Me); 1.03 (*s*, Me); 1.05–1.76 (*m*, 9 H); 1.99–2.09 (*m*, 1 H); 2.25–2.47 (*m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.99; 19.45; 22.74; 28.71; 29.70; 30.23; 32.83; 38.30; 40.49; 42.91; 46.76; 212.43. GC: *p*, 100 kPa; *T*, 120°, t_{R1}(3*R*) 28.8, t_{R2} (3*S*) 31.2 min.

rac-*Ketal from 3-Butyl-4,4-dimethylcyclohexanone and (*R,R*)-Pentane-2,4-diol.* ^{1}H-NMR (200 MHz, $CDCl_3$): 0.76 (*s*, Me); 0.77 (*s*, Me); 0.85–0.93 (*m*, 16 H); 1.02–1.62 (*m*, 34 H); 1.79–2.08 (*m*, 4 H); 3.86–4.13 (*m*, 4 H).

Table 6 (cont.)

31	**32**	**36**	**37**	**41**
$C_{33}H_{35}NO_2S$	$C_{32}H_{32}O_3S$	$C_{41}H_{42}O_3S + C_{4.5}H_{10.5}$	$C_{32}H_{30}F_3NO_4S_2$	$C_{34}H_{36}N_2O_3$
509.71	496.64	679.43	613.69	520.65
293(2)	293(2)	293(2)	293(2)	293(2)
1.54184	1.54178	1.54178	0.71073	1.54178
CuK_α	CuK_α	CuK_α	MoK_α	CuK_α
n.d.	$0.3 \times 0.3 \times 0.3$	$0.3 \times 0.2 \times 0.1$	$0.3 \times 0.2 \times 0.1$	$0.6 \times 0.3 \times 0.3$
monoclinic	monoclinic	orthorhombic	orthorhombic	trigonal
$P2_1$	$C2$	$P2_12_12_1$	$P2_12_12_1$	$P3_1$
$3.7 < \theta < 50.0$	$3.0 < \theta < 50.0$	$2.8 < \theta < 47.5$	$1.3 < \theta < 20.8$	$2.6 < \theta < 20.0$
9.400(5)	22.32(2)	8.067(8)	11.6(1)	9.299(4)
12.934(7)	8.202(5)	19.63(2)	21.1(1)	9.299(4)
12.146(8)	16.85(2)	26.58(2)	24.7(2)	27.77(1)
90	90	90	90	90
102.18(5)	119.20(4)	90	90	90
90	90	90	90	120
1444(2)	2693(5)	4209(7)	6066(82)	2080(2)
2	4	4	8	3
1.173	1.225	1.072	1.344	1.247
1.211	1.304	0.951	0.231	0.079
1568	1347	2235	3540	1469
1568	1347	2235	3540	1318
1551	1208	1922	2696	1183
369	319	462	770	353
$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
4.28	5.18	4.56	3.89	2.57
10.43	13.54	12.15	10.25	5.80
1.117	1.091	1.060	1.039	0.907
0.213, −0.303	0.251, −0.222	0.175, −0.128	0.186, −0.185	0.103, −0.102
158339	158340	158341	158342	158346

3-Butylcycloheptanone. $[\alpha]_D^{r.t.} = +37.7$ ($c = 1.0$, $CHCl_3$), er(R/S) 91:9 ([34]: +44.2 ($c = 2.3$, $CHCl_3$), er(R/S) 91.5:8.5). GC: *p*, 100 kPa; *T*, 110°; $t_{R1}(S)$ 28.9, $t_{R2}(R)$ 29.8 min. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.84–0.94 (*m*, Me); 1.20–1.48 (*m*, 8 H); 1.54–1.72 (*m*, 2 H); 1.81–1.97 (*m*, 3 H); 2.32–2.52 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.86; 22.59; 24.26; 28.39; 28.98; 35.89; 36.75; 36.85; 43.79; 48.87; 214.93.

3-Butylcyclooctanone. $[\alpha]_D^{r.t.} = +8.9$ ($c = 1.4$, $CHCl_3$), er 82:18. GC: *p*, 100 kPa; *T*, 130° (20 min) → 0.5°/min; t_{R1}((−)-enantiomer) 26.8, t_{R2}((+)-enantiomer) 28.6 min. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.84–0.94 (*m*, Me); 1.10–2.04 (*m*, 15 H); 2.25–2.52 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.91; 22.68; 23.71; 24.65; 27.61; 29.24; 33.37; 36.91; 37.85; 42.85; 47.35; 217.68.

rac-*Ketal from 3-Butylcyclooctanone and (*R,R*)-Butane-2,3-diol.* ^{1}H-NMR (300 MHz, $CDCl_3$): 0.84–0.94 (*m*, 6 H); 1.16–1.38 (*m*, 26 H); 1.42–1.98 (*m*, 24 H); 3.46–3.68 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.15; 16.51; 16.69; 16.68; 16.94; 21.93; 22.15; 22.85; 23.32; 23.64; 27.56; 27.78; 29.21; 29.31; 29.68; 32.35; 32.91; 35.19; 35.89; 36.46; 39.03; 39.08; 41.88; 42.35; 77.52; 78.02; 78.12; 110.94; 111.23.

3-Methylcyclohexanone. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.02 (*d*, $J = 6.2$, Me); 1.24–1.42 (*m*, 1 H); 1.58–1.75 (*m*, 1 H); 1.81–2.09 (*m*, 4 H); 1.96–2.46 (*m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.85; 25.09; 33.11; 34.90; 40.94; 49.82; 212.09.

(2R,3R*)-7-Methyl-2,3-diphenyl-1,4-diazaspiro[4.5]decane*). ^{13}C-NMR (75 MHz, $CDCl_3$): 49.0 (3*S*)/47.8 (3*R*); 49.8 (3*R*); 38.5 (3*S*); 30.6 (3*R*); 29.7 (3*S*) [41].

3-Methylcycloheptanone. $[\alpha]_D^{r.t.} = +51.0$ ($c = 0.4$, $CHCl_3$), er(R/S) 89:11 ([44]: $[\alpha]_D^{r.t.} = +64$ (MeOH; (*R*)-enantiomer). GC: *p*, 100 kPa; *T*, 100°; $t_{R1}(S)$ 9.4 min, $t_{R2}(R)$ 9.7 min. ^{1}H-NMR (300 MHz, $CDCl_3$):

1.00 (*d*, *J* = 6.9, Me); 1.20–1.98 (*m*, 7 H); 2.39–2.51 (*m*, 4 H); 1.81–1.97 (*m*, 3 H); 2.32–2.52 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 23.49; 24.15; 28.52; 31.20; 39.14; 44.00; 51.73; 214.40.

3-Ethylcycloheptanone. GC: *p*, 100 kPa; *T*, 100°; $t_{R1}(S)$ 16.9, $t_{R2}(R)$ 17.4. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.90 (*t*, *J* = 7.3, Me); 1.20–1.48 (*m*, 4 H); 1.50–1.71 (*m*, 2 H); 1.78–1.98 (*m*, 3 H); 2.32–2.52 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.19; 24.26; 28.40; 29.89; 36.33; 37.54; 43.77; 49.48; 214.90.

3-Propylcycloheptanone. $[\alpha]_D^{r.t.} = +42.4$ (*c* = 0.9, $CHCl_3$), er(*R*/*S*) 90:10. GC: *p*, 100 kPa; *T*, 100°; $t_{R1}(S)$ 27.4, $t_{R2}(R) = 28.3$. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89 (*t*, *J* = 7.0, Me); 1.99–1.48 (*m*, 6 H); 1.54–1.74 (*m*, 2 H); 1.80–1.96 (*m*, 3 H); 2.32–2.52 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.10; 19.97; 24.39; 28.51; 35.71; 36.81; 39.47; 43.88; 49.92; 214.81.

3-Isopropylcyclohexanone. GC: *p*, 100 kPa; *T*, 80°; $t_{R1}(S)$ 41.0, $t_{R2}(R)$ 42.6 min. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.90 (*d*, *J* = 6.5, Me); 0.91 (*d*, *J* = 6.5, Me); 1.29–1.44 (*m*, 1 H); 1.50–1.69 (*m*, 3 H); 1.81–1.92 (*m*, 1 H); 2.01–2.13 (*m*, 2 H); 2.18–2.43 (*m*, 1 H).

3-Isopropylcycloheptanone. $[\alpha]_D^{r.t.} = +27.6$ (*c* = 1.8, $CHCl_3$), er(*R*/*S*) 75:25 ([34]: $[\alpha]_D^{r.t.} = +61.4$ (*c* = 1.92, $CHCl_3$), er(*R*/*S*) 93.5:7.5). GC: *p*, 100 kPa; *T*, 90°; $t_{R1}(S)$ 43.3, $t_{R2}(R)$ 44.2 min. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.86 (*d*, *J* = 6.9, Me); 0.87 (*d*, *J* = 6.8, Me); 1.20–2.04 (*m*, 8 H); 2.32–2.52 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.68; 19.06; 24.49; 28.94; 33.45; 35.54; 41.76; 43.67; 46.94; 215.16.

3-Phenylcyclohexanone. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.66–1.86 (*m*, 2 H); 2.03–2.17 (*m*, 2 H); 2.31–2.62 (*m*, 4 H); 2.95–3.06 (*m*, 1 H); 7.19–7.38 (*m*, 5 H). The NMR data are in agreement with those in [45], but they were partly overlapping with some starting- and by-product signals.

(*2*R,*3*R*)-2,3,7-Triphenyl-1,4-diazaspiro[4.5]decane*). ^{13}C-NMR (75 MHz, $CDCl_3$): 47.3 (3*S*)/46.2 (3*R*); 42.0 (3*R*); 41.0 (3*S*); 39.8 (3*R*); 38.5 (3*S*); 24.1 (3*S*)/23.4 (3*R*) [41].

10. *X-Ray Crystallographic Data*. See *Table 6*.

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