phosphatase efficiently and selectively, thereby displaying the fundamental requirements for turnover-based enzyme inactivation.

We wondered whether a catalyst with low turnover rates, which would be expected to initially arise from selection experiments with a "first-generation" non-enzyme protein library (e.g. catalytic antibodies),[19] can also be identified by means of this screening procedure. As a model for such a case, we investigated a mutant of alkaline phosphatase, S102A, which lacks the primary nucleophile at the active site. Even though the turnover rate for the S102A enzyme is about four orders of magnitude lower than for the wild-type, it is still substantially faster than the uncatalyzed reaction ($k_{cat}/k_{uncat} \cong 10^5$).[20] Briefly, the mutant enzyme was injected in the BIAcore instrument in the same way as the wild-type enzyme to bind to the suicide substrate, and noncovalent bound protein was washed off with guanidinium chloride. More than 30% of the total bound enzyme remained after this step, demonstrating significant covalent coupling. The covalently coupled protein could be removed by reductive cleavage of the disulfide-containing linker that connects the suicide substrate to the surface. Thus, poorly active protein can still be identified by means of this turnover-based screening procedure. This strongly suggests that the rate of covalent inactivation depends on the successful reaction of a second nucleophile with the quinone methide rather than on the primary hydrolysis. However, under the same conditions, less enzyme is trapped than in the case of wildtype enzyme, thus suggesting that the suicide inhibitor may be potentially selective for catalytic efficiency. BSA does not show any covalent binding when used as a control in these reactions, excluding the possibility that the covalent binding might simply be a result of random reactivity of surface nucleophiles on the protein.

The synthesis and successful deployment of **3** is now being applied to the selection of catalysts from large protein libraries. Moreover, BIAcore analysis is demonstrated herein to represent a useful approach for the direct screening of library members and enables real-time analysis of the sequence of steps necessary for catalyst selection from a library of proteins. The relative advantages of *o*-trifluoro, *o*-difluoro, and *o*-monofluoromethylphenyl phosphate suicide substrates[11] are currently under investigation.

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[1] S. Halazy, V. Berges, A. Ehrhard, C. Danzin, *Bioorg. Chem*. **1990**, *18*, 330–344.
[2] Q. Wang, U. Dechert, F. Jirik, S. G. Withers, *Biochem. Biophys. Res. Commun*. **1994**, *200*, 577–583.
[3] J. K. Myers, T. S. Widlanski, *Science* **1993**, *262*, 1451–1453.
[4] K. D. Janda, L.-C. Lo, C.-H. L. Lo, M.-M. Sim, R. Wang, C.-H. Wong, R. A. Lerner, *Science* **1997**, *275*, 945–948; K. D. Janda, US 5571681, **1996**.
[5] M. Wakselman, *New J. Chem.* **1983**, *7*, 439–447.
[6] J. R. Betley, PhD thesis, University of Sheffield (UK), **1997**.
[7] W. J. Middleton, *J. Org. Chem.* **1975**, *40*, 574–578.
[8] S. Pinitglang, PhD thesis, University of London (UK), **1996**.
[9] G. M. Blackburn, *Chem. Ind*. **1981**, 834; G. M. Blackburn, D. E. Kent, *Chem. Commun.* **1981**, 134–138; C. E. McKenna, J. Schmidhauser, *Chem. Commun.* **1979**, 739–740.
[10] All new compounds were fully characterized by means of ^{1}H, ^{19}F, and ^{32}P NMR spectroscopy and by HR-MS.
[11] J. H. Rickard, PhD thesis, University of Sheffield (UK), **2000**.
[12] R. L. Jue, J. M. Lambert, L. R. Pierce, R. R. Traut, *Biochemistry* **1978**, *17*, 5399–5406; R. Singh, L. Kats, W. A. Blättler, J. M. Lambert, *Anal. Biochem*. **1996**, *236*, 114–125.
[13] H. Denham, PhD thesis, University of Sheffield (UK), **1998**.
[14] L.-C. Lo, C.-H. L. Lo, K. D. Janda, D. B. Kassel, F. M. Raushel, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2117–2200.
[15] When the alkaline phosphatase was preincubated with 10 mM EDTA (which inhibits 95% of phosphatase activity), binding to the trapping agent was halved.
[16] Alkaline phosphatase incubated for 3 d at 37 °C in an ELISA plate coated with untreated BSA still cleaved *p*-nitrophenyl phosphate.
[17] K. M. Müller, K. M. Arndt, A. Plückthun, *Anal. Biochem*. **1998**, *261*, 149–158.
[18] The Michaelis constant K_M for **3** was found to be 250 μM, measured by phosphate release from uncoupled inhibitor **3** by alkaline phosphatase in solution. An affinity of this magnitude will lead, at best, to a tiny plateau since, because of the fast off-rate, equilibration with the surface is instantaneous.
[19] "Catalytic Antibodies": G. M. Blackburn, A. Datta, H. Denham, P. Wentworth, *Adv. Phys. Org. Chem.* **1998**, *31*, 249–391.
[20] B. Stec, M. J. Hehir, C. Brennan, M. Nolte, E. R. Kantrowitz, *J. Mol. Biol.* **1998**, *277*, 647–662; "Chemistry and enzymology of phosphatases": T. S. Widlanski, W. Taylor, *Compr. Nat. Prod. Chem*. **1999**, *5*, 139–162.

The Inhibiting Influence of Aromatic Solvents on the Activity of Asymmetric Hydrogenations**

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Dedicated to Franz Hein (1892–1976)

Complexes of ruthenium, iridium, and especially rhodium have been used in the homogeneously catalyzed asymmetric hydrogenation of prochiral olefins, ketones, and imines.[1] Hydrogenations are usually carried out in simple alcohols, but aromatic solvents, water, or alcohol/aromatic solvent mixtures can also be used. It has been reported that aromatic solvents such as benzene can inhibit asymmetric hydrogena-

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[**] We would like to thank the Deutsche Forschungsgemeinschaft as well as the Fonds der Chemischen Industrie for their generous support of this work. We are also indebted to Prof. Dr. U. Rosenthal and Dr. D. Selent for helpful discussions. Franz Hein prepared bis(η^6-arene)-chromium(0)-complex cations already in 1919; their true structure as hexahapto complexes was only realized more than 35 years later.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

tion. For example, Burk et al. recently showed that the hydrogenation of ethyl α-benzoyloxycrotonate with the very active Et-DuPHOS–Rh system (Et-DuPHOS = 2′,5′,2″,5″-tetraethyl-1,2-bis(phospholanyl)benzene) does not work in benzene, whereas high selectivity and activity are observed in other solvents. The formation of inactive [Rh(Et-DuPHOS)(benzene)]$^+$ complex, which was characterized by means of ^{31}P NMR spectroscopy, was postulated to be the cause.[2]

The stability of such Rh^{I}–η^6-arene complexes with chelating bisphosphanes has already been reported by Halpern et al.[3] To our knowledge, only one crystal structure with a chiral bisphosphane is described: the benzene complex of (1*R*,2*R*)-*trans*-1,2-bis((diphenylphosphanyl)methyl)cyclobutane rhodium(I).[4]

Bargon and co-workers used the PHIP method (PHIP = *para*-hydrogen-induced polarization) to investigate arene complexes of styrene derivatives.[5] Likewise, Gridnev, Imamoto, and co-workers provided NMR spectroscopic evidence for the formation of Rh–arene complexes after the hydrogenation of phenyl-substituted enamides, preferably at lower temperatures.[6] Herein we report detailed spectroscopic and kinetic investigations and quantitatively describe the inhibiting influence of η^6-arene–Rh^{I} complexes on catalytic activity, for example, in the homogeneously catalyzed asymmetric hydrogenation. The crystal structures of arene complexes [Rh((*R*,*R*)-Et-DuPHOS)(benzene)]BF_4 (**1**) and [Rh((*S*,*S*)-Me-DuPHOS)(toluene)]BF_4 (**2**) are presented.

The addition of benzene or toluene (0.2 mL) to a solution of either [Rh(Et-DuPHOS)$(MeOH)_2$]BF_4 (**3**) or [Rh(Me-DuPHOS)$(MeOH)_2$]BF_4 (**4**)[7] (0.01 mmol) in methanol (0.8 mL) already leads quantitatively to the corresponding arene complexes **1** and **2**, respectively. The formation of **1** and **2** was unequivocally confirmed by means of ^{31}P or ^{103}Rh NMR spectroscopy (Table 1). The molecular structures are shown in Figure 1.[8]

Although the ^{31}P NMR data of the arene and of the methanol complexes are very similar (Table 1), the two complexes can be distinguished by means of ^{103}Rh NMR spectroscopy (Table 1).[9] The signals for the arene complexes are clearly shifted upfield, and the established dependence of the rhodium shift on the size of the chelate ring is observed.[10] The ^{1}H and ^{13}C NMR spectra unambiguously confirm the presence of π-arene complexes. The signals for the coordinated benzene ring in **1** are shifted by −0.75 ppm in the ^{1}H NMR spectrum and by −27.8 ppm in the ^{13}C NMR spectrum. A coupling constant of 2 Hz was found for $^1J(^{13}C,^{103}Rh)$, and the observed $^1J(^{13}C,^1H)$ value of 174 Hz is typical for π-arene complexes.[11] Although a scalar ^{1}H,^{103}Rh coupling could not be resolved in the ^{1}H NMR signals of the coordinated arenes, its existence follows from the observation of crosspeaks in ^{1}H,^{103}Rh-HMQC experiments (HMQC = heteronuclear multiple quantum coherence), particularly for the methyl groups of π-coordinated toluene or xylene.

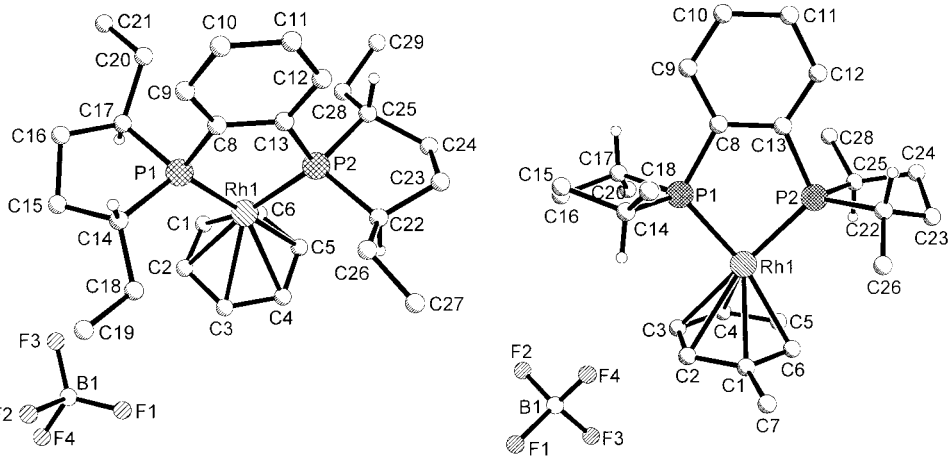

Figure 1. Molecular structures of **1** (left) and **2** (right) in the crystal (only hydrogen atoms at the asymmetric carbon atoms are represented). For disordered toluene, the atoms with highest probability of occupation (60 %) are shown. Selected bond lengths (Å) and angles (°) for **1**/**2**: Rh1–P1 2.211(2)/2.212(3), Rh1–P2 2.213(2)/2.214(3); P1-Rh1-P2 84.54(7)/84.88(10).

The stability of η^6-arene complexes must be considered in asymmetric hydrogenations. The formation of stable Rh–π-arene complexes in the presence of aromatic solvents means that the rhodium catalyst is only partly available for the actual catalytic process.[12]

The hydrogenation of dimethyl itaconate (**5**) with [Rh(Ph-β-glup-OH)$(MeOH)_2$]BF_4 (**6**)[7c] (Ph-β-glup-OH = phenyl-2,3-bis(*O*-diphenylphosphanyl-β-D-glucopyranoside) is a pseudo-first-order reaction in methanol. Mechanistically,[13] this means that during the asymmetric hydrogenation, the equilibrium (solvent complex/prochiral olefin ⇄ diastereomeric substrate complexes) is shifted toward the solvent complex. This is proven by UV/Vis spectroscopy.[14] For such systems characterized by the low stability of the substrate complexes, it is to be expected that already small amounts of arene derivatives in the solvent (usually alcohol) lead to a decrease in the activity. Essentially, only the weakly coordinating solvent (present in a large excess) and the strongly coordinating arene derivative compete for the rhodium atom to form stable complexes. Thus, the addition of toluene (0.28 mmol, 0.03 mL) to a solution of **6** (0.02 mmol) and **5** (1.0 mmol) in methanol (15.0 mL) causes a reproducible decrease in the activity (Figure 2). It follows from the ratio of

Table 1. ^{31}P and ^{103}Rh NMR data for solvent-stabilized cations of the type [Rh(P–P)(solvent)]BF_4 in [D_4]methanol at 298 K.[a]

Chelate ligand	Solvent	$\delta(^{31}P)$	$^1J(^{31}P,^{103}Rh)$ [Hz]	$\delta(^{103}Rh)$
Et-DuPHOS	η^6-benzene	93.0	202	−1116
	methanol	95.7	205	−149
DIPAMP	η^6-benzene	72.2	207	−1006
	η^6-*p*-xylene	75.7	207	−956
	methanol	81.2	208	−38
Ph-β-glup-OH	η^6-toluene	136.4, 134.8	228, 228	−762
	methanol	147.6, 142.9	229, 226	−28

[a] Further data and experimental details are to be found in the Supporting Information.

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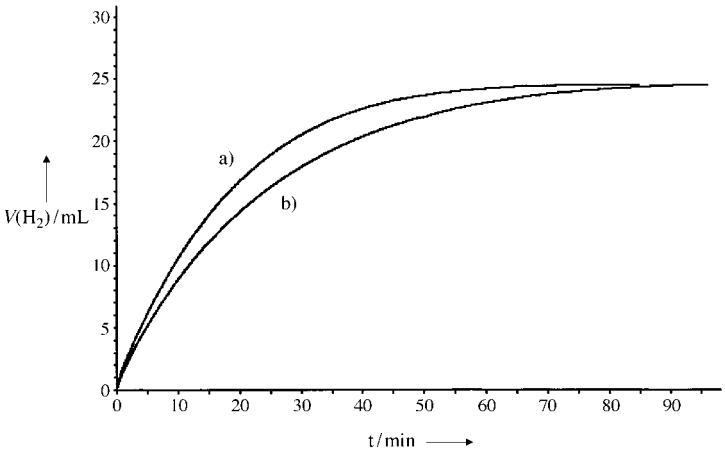

Figure 2. Hydrogenation of **5** in a) pure methanol ($k = 0.055\ min^{-1}$) and b) after the addition of 0.28 mmol toluene ($k = 0.041\ min^{-1}$); molar ratios: methanol/toluene 1320:1, toluene/Rh 14:1; reaction conditions: **6** (0.02 mmol), **5** (1.0 mmol), 1 bar total pressure, methanol (15.0 mL), 25.0 °C.

the rate constants for the pseudo-first-order reaction that despite the clear excess of methanol (molar ratio methanol/toluene 1320:1), already 25% of the catalyst for the asymmetric hydrogenation is blocked by the arene derivative. This finding from the quantitative analysis of the hydrogenation curve can be confirmed by NMR spectroscopy. A batch that contained the quantities specified in the legend of Figure 2 in only 1 mL of [D_4]methanol (methanol/toluene 88:1) gave a methanol/toluene complex ratio of 3.5 (^{31}P NMR at 298 K), which agrees well with the value obtained from the kinetic investigation (2.93).

Hydrogenations of prochiral olefins, which form more stable rhodium complexes, can also be slowed down substantially by adding small amounts of aromatic compounds. The hydrogenation of methyl (*Z*)-β-(*N*-acetyl)-aminocrotonate (**7**), a model compound for the asymmetric hydrogenation of β-dehydroamino acids[15] with [Rh(dipamp)(MeOH)$_2$]BF$_4$ (DIPAMP = 1,2-ethylenebis[(2-methoxyphenyl)phenylphosphane]) occurs in the saturation region of the underlying Michaelis–Menten kinetics (Figure 3a). The maximum rate (pseudo-zero-order reaction) does not depend on the concentration of the substrate (in the investigated substrate/catalyst range from 100:1 to 700:1). In such cases, the equilibrium (solvent complex/prochiral olefin ⇄ diastereomeric substrate complexes) is shifted far toward the substrate complexes, as a result of the large stability constants. In this case, only the prochiral olefin and an arene derivative compete for the rhodium center, in contrast to hydrogenations with substrate complexes of low stability (see above). The addition of only 0.28 or 0.57 mmol *p*-xylene to a solution of **8** (0.01 mmol) and **7** (1.0 mmol) in methanol (15.0 mL) leads to a clearly diminished activity (Figure 3b, c). The enantioselectivity does not change within experimental errors. Interestingly, the hydrogenation is no longer a pseudo-zero-order reaction. However, if one considers that the concentration of the prochiral olefin decreases with increasing conversion and that the concentration of the aromatic compound remains constant, it is clear that the proportion of blocking arene complex increases with increasing substrate conversion, and thus the activity decreases continuously. The amount of blocking *p*-xylene complex at the beginning of the hydrogenation (23% or 53%) can be determined from the ratio of the initial rates, or by means of ^{31}P NMR spectroscopy, which gave values of 25% or 50%. This is substantiated by the ^{103}Rh NMR shift for the species present beside the substrate complex (Figure 4).

Importantly, asymmetric hydrogenations can also be carried out in aromatic solvents. Eventually, the concentrations and stability constants of all compounds present in solution determine the extent of the decrease in activity.

The practical relevance of these results is finally demonstrated in an example. The hydrogenation of **7** with the Me-DuPHOS system in toluene as solvent (ambient temperature, 20 bar H_2) for 24 hours gives rise to the product with an *ee* value of 64%.[15] When methanol as solvent and **4** are used,

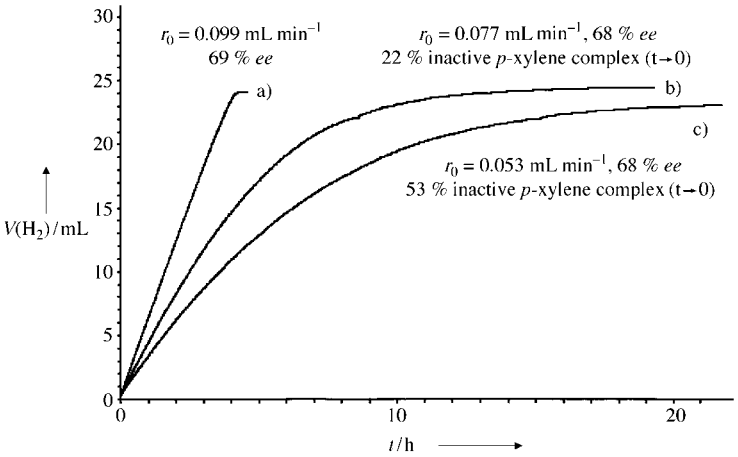

Figure 3. Hydrogenation of **7** in a) pure methanol and after the addition of b) *p*-xylene (0.28) or c) *p*-xylene (0.57 mmol); molar ratios: methanol/*p*-xylene 1323:1 (b), 650:1 (c); reaction conditions: **8** (0.01 mmol), prochiral olefin (1.0 mmol), methanol (15.0 mL), 1 bar total pressure, 25.0 °C; r_o = initial rate.

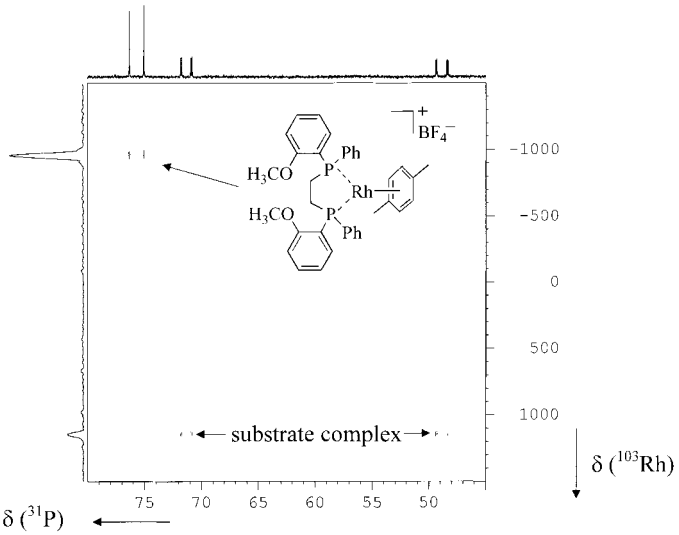

Figure 4. ^{31}P,^{103}Rh{^{1}H}-HMQC spectrum of a solution of **8** (0.01 mmol) in methanol, which was treated with **7** (1 mmol) and *p*-xylene (0.57 mmol); molar ratio of xylene complex/substrate complex = 1.0); the chemical shifts of the Rh signals for the xylene complex and for the substrate complex are −956 and 1148 ppm, respectively.

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the product is obtained with 87.8% after only 4 min of hydrogenation at normal pressure at 25 °C.[16] The lower activity in toluene is a result of the "induction periods"[7] as well as the formation of stable, blocking arene complexes, as we have now shown quantitatively.[17]

In summary, we have shown that arene complexes of Rh^I can have an unexpectedly large influence on the activity of asymmetric hydrogenation reactions. A different interpretation is now possible for past investigations in which catalyst activities were determined in alcohol/aromatic solvent mixtures or in aromatic solvents.[18] At the moment, we are examining whether the inhibiting effect can also be induced by P-ligands and by substrates with aromatic substituents, and whether it is also relevant for other Rh^I-catalyzed reactions, for example, hydroformylations.

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[1] "Hydrogenation of Functionalized Carbon–Carbon double bonds": J. M. Brown in *Comprehensive Asymmetric Catalysis* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, Chap. 5.1, pp. 121 – 182.

[2] M. J. Burk, C. S. Kalberg, A. Pizzano, *J. Am. Chem. Soc.* **1998**, *120*, 4345 – 4353.

[3] a) J. Halpern, D. P. Riley, A. S. C. Chan, J. S. Pluth, *J. Am. Chem. Soc.* **1977**, *99*, 8055 – 8057; b) C. R. Landis, J. Halpern, *Organometallics* **1983**, *2*, 840 – 842.

[4] J. M. Townsend, J. F. Blount, *Inorg. Chem.* **1981**, *20*, 269 – 271.

[5] P. Hübler, J. Bargon, *Angew. Chem.* **2000**, *112*, 3849 – 3852; *Angew. Chem. Int. Ed.* **2000**, *39*, 3701 – 3703, and references therein.

[6] a) I. D. Gridnev, N. Higashi, K. Asakura, T. Imamoto, *J. Am. Chem. Soc.* **2000**, *122*, 7183 – 7194; b) I. D. Gridnev, M. Yasutake, N. Higashi, T. Imamoto, *J. Am. Chem. Soc.* **2001**, *123*, 5268 – 5276.

[7] By hydrogenation of the diolefin, the cyclooctadiene precatalyst is easily transferred into the solvent complex. a) H.-J. Drexler, W. Baumann, A. Spannenberg, C. Fischer, D. Heller, *J. Organomet. Chem.* **2001**, *621*, 89 – 102; b) A. Börner, D. Heller, *Tetrahedron Lett.* **2001**, *42*, 223 – 225; similar results for seven-membered chelates can be found in: c) D. Heller, S. Borns, W. Baumann, R. Selke, *Chem. Ber.* **1996**, *129*, 85 – 89.

[8] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-163839 (**1**) and -163840 (**2**). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk). Further information can be found in the Supporting Information.

[9] a) R. Benn, A. Rufińska, *Angew. Chem.* **1986**, *98*, 851 – 871; *Angew. Chem. Int. Ed.* **1986**, *25*, 861 – 881; b) W. von Philipsborn, *Chem. Soc. Rev.* **1999**, *28*, 95 – 105.

[10] a) J. M. Ernsting, C. J. Elsevier, W. G. J. de Lange, K. Timmer, *Magn. Reson. Chem.* **1991**, *29*, S118 – S124; b) W. Leitner, M. Bühl, R. Fornika, C. Six, W. Baumann, E. Dinjus, M. Kessler, C. Krüger, A. Rufińska, *Organometallics* **1999**, *18*, 1196 – 1206, and references therein.

[11] a) B. E. Mann, *Adv. Organomet. Chem.* **1974**, *12*, 135 – 213; b) G. M. Bodner, L. J. Todd, *Inorg. Chem.* **1974**, *13*, 360 – 363.

[12] The possible hydrogenation of aromatic compounds with similar catalysts[3b] does not occur under these conditions. For example, treatment of benzene (2.8 mmol) in methanol (7 mL) with [Rh(Et-DuPHOS)(cod)]BF_4 (0.02 mmol) at 25 °C for 66 h and normal pressure did not give rise to any products of benzene hydrogenation (NMR spectroscopy).

[13] C. R. Landis, J. Halpern, *J. Am. Chem. Soc.* **1987**, *109*, 1746 – 1754.

[14] D. Heller, R. Thede, D. Haberland, *J. Mol. Catal. A* **1997**, *115*, 273 – 281.

[15] G. Zhu, Z. Chen, X. Zhang, *J. Org. Chem.* **1999**, *64*, 6907 – 6910.

[16] D. Heller, J. Holz, H.-J. Drexler, J. Lang, K. Drauz, H.-P. Krimmer, A. Börner, *J. Org. Chem.* **2001**, *66*, 6816 – 6817.

[17] The simultaneous increase in the selectivity can be explained easily with the well-known pressure dependence of the enantioselectivity of asymmetric hydrogenations.[13]

[18] E. I. Klabunowski, Y. T. Struchkov, A. A. Voloboev, A. I. Yanovsky V. A. Pavlov, *J. Mol. Catal.* **1988**, *44*, 217 – 243.

The Core Structure of TMC-95A Is a Promising Lead for Reversible Proteasome Inhibition**

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The proteasome is an intracellular multicatalytic protease complex which in combination with the ubiquitin pathway plays a central role in major cellular processes, such as antigen presentation, cell proliferation and differentiation, and apoptosis.[1] Proteolysis occurs in a barrel-shaped core structure known as 20S proteasome, which consists of four stacked rings arrayed in an $\alpha_7\beta_7\beta_7\alpha_7$ mode.[2a] In eukaryotic proteasome three β-subunits of each β-ring are enzymatically active with an N-terminal threonine residue as the active nucleophile involved in proteolysis[2b] with three more or less distinct substrate specificities, that is chymotrypsin-like (CL), trypsin-like (TL), and peptidyl-glutamyl-peptide hydrolase (PGPH) activities.[3]

Because of the physiological role of proteasome in critical intracellular processes, this enzyme represents a promising target for drug development in inflammatory and autoimmune diseases as well as in tumor therapy.[4] Correspondingly, great attention has recently been paid to the discovery of potent and selective proteasome inhibitors by structure-based design or natural product screening approaches. Most of the synthetic inhibitors consisting of peptide aldehydes, boronates, and vinylsulfones, as well as the natural products lactacystin and epoxymicins inhibit in a more or less selective manner the proteasome by reaction with the N-terminal threonine residue (for a recent review see ref. [5]). A notable exception is the highly selective and competitive proteasome inhibitor TMC-95A, which was isolated from the fermentation broth of *Apiospora montagnei* Sacc. TC 1093.[6]

This cyclic peptide metabolite consists of L-tyrosine, L-asparagine, a highly oxidized L-tryptophane, and the (*Z*)-1-

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