The cover picture shows the alignment of the two geometric isomers (E isomer in blue, Z in turquoise) of 2-(3-benzylidene)-3-oxo-2,3-dihydrobenzo[b]thiophene-7-carboxylic acid methyl ester at the active site of rabbit 12/15-lipoxygenase. In the Z configuration, the benzoyl moiety conflicts with the side chain of the C-terminal I663, which normally ligates the catalytic non-heme iron. Light irradiation induces Z-to-E isomerization, which flips the benzoyl ring over towards I593, the side chain of which limits the depth of the substrate binding pocket. There are no steric constraints for binding of the E isomer. Further details can be found in the article by H. Kuhn et al. on p. 1089 ff.

**MINIREVIEWS**

**Bioluminescence in BIA.** Bioluminescence resonance energy transfer (BRET) can be utilised for biomolecular interaction analysis (BIA) to quantify protein–protein interactions in living cells. This was demonstrated with the cAMP-dependent protein kinase regulatory and catalytic subunits fused to Renilla luciferase (Rluc) and GFP\(^2\), respectively.

A. Prinz, M. Diskar, F. W. Herberg*  
1007 – 1012  
Application of Bioluminescence Resonance Energy Transfer (BRET) for Biomolecular Interaction Studies
A. Fernández-Gacio, A. Codina, J. Fastrez, O. Riant, P. Soumillion*

1013 – 1016

Transforming Carbonic Anhydrase into Epoxide Synthase by Metal Exchange

Enantioselective epoxidation of styrene was observed in the presence of manganese-containing carbonic anhydrase as catalyst. The probable oxygen-transfer reagent is peroxymonocarbonate, which has a structural similarity with the hydrogenocarbonate substrate of the natural reaction. Styrene was chosen as the enzyme possesses a small hydrophobic cavity close to the active site.

G. Chen, M. Chien, M. Tsuji, R. W. Franck*

1017 – 1022

E and Z α-C-Galactosylceramides by Julia–Lythgoe–Kocienski Chemistry: A Test of the Receptor-Binding Model for Glycolipid Immunostimulants

Does aglycone linker conformation matter? Both E- and Z-linked α-C-galactosylceramides have been prepared by application of the Julia–Lythgoe–Kocienski synthesis to a C-formylgalactose and sulfones derived from phytosphingosine. Assays of cytokine levels induced by GalCers in mice suggest that the E geometry better resembles the preferred conformations of the flexible, saturated C-glycoside and the O-glycoside when bound to the CD1d molecule of antigen-presenting cells.

A. Valade, D. Urban, J.-M. Beau*

1023 – 1027

Target-Assisted Selection of Galactosyltransferase Binders from Dynamic Combinatorial Libraries. An Unexpected Solution with Restricted Amounts of the Enzyme

Fix and look: Dynamic combinatorial chemistry coupled to an irreversible transformation has been used to identify enzyme binders in a library directed towards an α-1,3-galactosyltransferase. Small amounts of the protein induce an accumulation of the nonbinding amine products such as A resulting from the reduction of the corresponding imine binders. The binding properties of the imines are best mimicked by amides such as B.

J. Müllegger, H.-M. Chen, W. Y. Chan, S. P. Reid, M. John, R. A. J. Warren, H. M. Salleh, S. G. Withers*

1028 – 1030

Thermostable Glycosynthases and Thioglycoligases Derived from Thermotoga maritima β-Glucuronidase

By using active-site mutants of the Thermotoga maritima β-glucuronidase, glucuronic acid-containing glycosides and thioglycosides have been made in high yields. These enzymes have potential use in the chemoenzymatic synthesis of a range of glycoconjugates, such as glycosaminoglycans (X = OH, NAc, H), that contain β-linked glucuronic and galacturonic acids.
**No substituent required**: In contrast to previous assumptions, unsubstituted dicationic penta- and hexacycles show preferential binding to triplex DNA with high affinity, as demonstrated by DNA melting studies and competition dialysis experiments.

**Substrate activity screening** was used to rapidly identify a novel and potent ($K_{\text{act}}/K_i = 59000 \text{ M}^{-1} \text{s}^{-1}$) nonpeptidic chymotrypsin inhibitor with $M_W < 500$. The inhibitor is more potent than the best reported tetrapeptidyl phosphonate chymotrypsin inhibitor and demonstrated selectivity over a panel of other serine proteases, including the closely related enzyme cathepsin G.

**A gripping tail.** The formation of stable triplexes of parallel tail-clamps with mRNA molecules is shown under acidic and also under neutral and slightly basic pH conditions (see schematic representation). As an example of the foreseen applications of this process, efficient and specific purification of *Listeria innocua* iap mRNA molecules was achieved from an *L. innocua* total RNA solution by triplex affinity capture.

**A new starting point for an anti-SARS drug?** We have developed an efficient method for the synthesis of peptide aldehyde inhibitors and studied their binding to the SARS coronavirus main protease (SARS-CoV Mpro). The results reveal a new and unexpected binding mode for the most active inhibitors that should be helpful for developing nonpeptide inhibitors.
**M. A. Kubasik,* E. Daly, A. Blom**

**1056 – 1061**

19F NMR Chemical Shifts Induced by a Helical Peptide

Electric fields perturb 19F chemical shifts. The electric field of the helical peptide (shown) induces solvent dielectric-dependent perturbations of the 19F chemical shift of the polarizable fluoroaryl N-protecting group (shown), but virtually no influence on the 19F chemical shifts of a less polarizable 4-trifluoromethylbenzoyl N-terminal group.

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**S. Maiya, A. Grundmann, S.-M. Li, G. Turner**

**1062 – 1069**

The Fumitremorgin Gene Cluster of *Aspergillus fumigatus*: Identification of a Gene Encoding Brevianamide F Synthetase

Tremorgenic mycotoxins. A gene encoding a putative dimodular nonribosomal peptide synthetase (NRPS) found in the genome sequence of *Aspergillus fumigatus* has been overexpressed in both *Aspergillus fumigatus* and *Aspergillus nidulans*. It was shown by HPLC, MS and NMR that the resulting product is cyclo-L-Trp-L-Pro (brevianamide F), the first intermediate in fumitremorgin biosynthesis.

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**T. Liu, M. K. Kharel, C. Fischer, A. McCormick, J. Rohr**

**1070 – 1077**

Inactivation of *gilGT*, Encoding a C-Glycosyltransferase, and *gilOIII*, Encoding a P450 Enzyme, Allows the Details of the Late Biosynthetic Pathway to Gilvocarcin V to be Delineated

Road map to gilvocarcin V. Two structural features that are crucial for the biological activity of antitumor antibiotic gilvocarin V—its C8 vinyl group and C-glycosidically bound α-fucose residue—are shaped in late biosynthetic steps by the enzymes GilOIII and GilGT, respectively (see scheme). We demonstrate this by a series of experiments that include the analysis of mutant strains in which the *gilOIII* and *gilGT* genes were deleted.

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**J. R. Faulkner, S. R. Hussaini, J. D. Blankenship, S. Pal, B. M. Branan, R. B. Grossman, C. L. Schardl**

**1078 – 1088**

On the Sequence of Bond Formation in Loline Alkaloid Biosynthesis

Who’s next? The order of bond-forming steps in the biosynthetic pathway to loline alkaloids was determined by feeding deuterated compounds to *Neotyphodium uncinatum*. Proline and homoserine combine to form N-(3-amino-3-carboxypropyl)proline, which is decarboxylated and cyclized to form 1-amino-pyrrolizidine. The addition of an oxygen atom to 1-amino-pyrrolizidine completes the biosynthesis.
Switched-on inhibition. (2Z)-2-(3-Benzylidene)-3-oxo-2,3-dihydrobenzo[b]thiophene-7-carboxylic acid methyl ester (see left-hand structure) is only a poor inhibitor of 12/15-lipoxygenases (IC\textsubscript{50} = 0.7 mm). However, photoactivation that induces a Z-to-E isomerization strongly augmented the inhibitory potency (IC\textsubscript{50} = 0.021 mm). Since light-induced isomerization may proceed in the skin, such photoreactive compounds might be developed as potential drugs for inflammatory skin diseases.

Fibril discrimination. Under suitable conditions, conjugated polyelectrolytes bind specifically to amyloid deposits, and this is then seen as an orange-red emission from the polyelectrolyte. Furthermore, the probes emit light of different colors when bound to different amyloid deposits or other intracellular structures. This phenomenon arises from differences in the protein conformations in these structures, these different protein conformations generating geometrical alterations of the polyelectrolyte backbone, affording different emission from the bound probe. Conformation-sensitive probes thus provide a direct link between spectral signal and protein conformation.

Molecular recognition in water. An arginine-rich peptide that is able to interact with a hydrophilic patch (shown) at the surface of the antitumor transcription factor p53 tetramerization domain has been designed, synthesized, and evaluated by several techniques. A library of peptides has also been prepared and evaluated in order to examine the different factors that contribute to the recognition event.
Supporting information on the WWW (see article for access details).

* Author to whom correspondence should be addressed.

### BOOKS

**Protein Degradation Vol. 2: The Ubiquitin-Proteasome System**

- R. J. Mayer, A. J. Ciechanover, M. Rechsteiner (Eds.)

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### ADDENDUM

Shortly before the submission of our manuscript on microarrays of lipolytic enzymes to *ChemBioChem* in 2005, Dr. Funeriu and his colleagues published a study that described "Enzyme family-specific and activity-based screening of chemical libraries using enzyme microarrays". The authors named this type of application "Thematic Enzyme Microarrays" (TEMA). In ref. [8] on p. 532 of our publication, we wanted to emphasize that the same authors had already successfully applied hydrogel NHS slides in enzyme microarray technology before our laboratory used them for the preparation of lipase and esterase chips.

[1] D. P. Funeriu, J. Eppinger, L. Denizot, M. Miyake, J. Miyake, *Nat. Biotech.* **2005**, 23, 622 – 627.

**H. Schmidinger, H. Susani-Etzerodt, R. Birner-Gruenberger, A. Hermetter**

**Inhibitor and Protein Microarrays for Activity-Based Recognition of Lipolytic Enzymes**

*ChemBioChem* **2006**, 7, 527–534

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