Significance: Vinylselenide resin underwent cycloaddition with nitrile oxides to give isoxazolines. Resin cleavage was achieved either under oxidative or alkylative conditions to give the oxazoline and iodo-oxazoline respectively.

174/2006

Title: [3 + 2] Cycloaddition reactions in the solid-phase synthesis of 1,2,3-triazoles.

Authors: Gao, Y.; Lam, Y.*

National University of Singapore, Singapore

Source: *Org. Lett.* **2006**, 8, 3283–3285.

Significance: Sulfone resins were condensed with aldehydes to give an intermediate α,β -unsaturated sulfone. These underwent cycloaddition with sodium azide under microwave-assisted conditions to yield triazole heterocycles. More than ten examples are reported.

Solid-phase Synthesis (abstracts 172–183)

DOI: 10.1002/qsar.200660012

172/2006

Title: Solid-phase synthesis of phenols and pyridinones via arylboronation/oxidation protocol using aryl bromides.

Authors: Lee, Y.*; Kelly, M. J.

Locus Pharmaceuticals, USA

Source: *Tetrahedron Lett.* **2006**, 47, 4897–4901.

Significance: The sequence of arylboronation and oxidation was employed to access phenols and pyridones with substitution patterns not commonly accessible. The phenols were then loaded onto Wang resin, and further diversification of the scaffolds demonstrated.

173/2006

Title: Traceless solid-phase synthesis of 3-substituted isoxazoles and 3-substituted 5-iodoisoxazolines using polystyrene-supported vinyl selenide.

Authors: Sheng, S.-R.*; Xin, Q.; Liu, X.-L.; Sun, W.-K.; Guo, R.; Huang, X.

Jiangxi Normal University, China

Source: *Synthesis* **2006**, 2293–2296.

176/2006

Title: Aminolysis of resin-bound N-nosylaziridine-2-carboxylic acids.

Authors: Olsen, C. A.*; Christensen, C.; Nielsen, B.; Mohamed, F. M.; Witt, M.; Clausen, R. P.; Kristensen, J. L.; Franzyk, H.; Jaroszewski, J. W.

Danish University of Pharmaceutical Sciences, Denmark

Source: *Org. Lett.* **2006**, 8, 3371–3374.

175/2006

Title: A general solid phase synthesis of 4-substituted quinolinones via Pd-catalyzed cross coupling.

Authors: Xu, C.*; Yang, L.; Bhandari, A.; Holmes, C. P.

Affymax, USA

Source: *Tetrahedron Lett.* **2006**, 47, 4885–4888.

Significance: Methyl anthranilate was attached to an aldehyde resin by reductive amination. After acylation and Claisen condensation, the hydroxyquinolinone was tosylated. The tosylate was substituted by Suzuki and Negishi cross-coupling reactions, 12 examples are given.

Significance: Activated aziridines were immobilized on solid-phase as precursors to various heterocycles. In the example shown, the aziridine is ring-opened by phenylalaninol. Subsequent Mitsunobu cyclization provides the piperazine scaffold.

177/2006

Title: Screening of a combinatorial library of synthetic polyamines displaying selectivity in multiple ion-pairing interactions with model polyanionic compounds in aqueous organic solutions.

Authors: Manku, S.; Hall, D. G.*

University of Alberta, Canada

Source: *J. Comb. Chem.* **2006**, 8, 551–561.

Significance: A polyamine library was assembled on solid-phase using the trityl resin. On-bead screening was performed for binding to polysulfate dyes, and a series of active beads deconvoluted. Hits were resynthesized, and anion binding affinity determined by NMR.

178/2006

Title: Potent antibacterial lysine–peptoid hybrids identified from a positional scanning combinatorial library.

Authors: Ryge, T. S.; Hansen, P. R.*

KVL, Denmark

Source: *Bioorg. Med. Chem.* **2006**, 14, 4444–4451.

Significance: A positional scanning library of potentially 390,625 members was prepared on solid-phase from N-alkylglycines and lysines. The library had the format XXXXKKK, where K = lysine and X = one of 25 N-alkylglycines. From screening, a lead with 1 μ M activity against bacterial strains was identified.

179/2006

Title: Solid-phase combinatorial synthesis of aeruginosin derivatives and their biological evaluation.

Authors: Doi, T.; Hoshina, Y.; Mogi, H.; Yamada, Y.; Takahashi, T.*

Tokyo Institute of Technology, Japan

Source: *J. Comb. Chem.* **2006**, 8, 571–582.

Significance: The amino acid Choi was immobilized on a silyl linker and used in the solid-phase synthesis of the natural product aeruginosin 298-A and 23 additional analogues. Compounds were tested for trypsin inhibition, and the analogue lacking a hydroxymethyl group in the arginyl sidechain was 300 fold more potent than the natural product.

180/2006

Title: Rapid identification of potent nonpeptidic serine protease inhibitors.

Authors: Salisbury, C. M.; Ellman, J. A.*

University of California-Berkeley, USA

Source: *ChemBioChem* **2006**, 7, 1034–1037.

Significance: An optimization library of 24 isoxazolines linked to a fluorescent coumarin was prepared as chymotrypsin substrates. The best substrate was then converted to the inhibitor shown by replacing the coumarin by a phosphonate. The inhibitor showed selectivity between serine proteases.

181/2006

Title: An efficient method for the synthesis of peptide aldehyde libraries employed in the discovery of reversible SARS coronavirus main protease (SARS-CoV Mpro) inhibitors.

Authors: Al-Gharabli, S. I.; Shah, S. T. A.; Weik, S.; Schmidt, M. F.; Mesters, J. R.; Kuhn, D.; Klebe, G.; Hilgenfeld, R.; Rademann, J.*

Leibniz Institute, Germany

Source: *ChemBioChem* **2006**, 7, 1048–1055.

Significance: A library of peptide aldehydes was prepared on solid-phase. The latent aldehyde was masked as a carbinolamine and released at the end. From the library, four micromolar inhibitors were identified. Combination of their

features into a single peptide led to a decrease in potency, suggesting that multiple binding modes are involved.

182/2006

Title: Synthesis of tetramic and tetronic acids as β -secretase inhibitors.

Authors: Larbig, G.; Schmidt, B.*
Darmstadt Technical University, Germany

Source: *J. Comb. Chem.* **2006**, 8, 480–490.

Significance: The well-known cyclative cleavage promoted by base was the key step in the solid-phase synthesis of tetramic acids and tetronic acids. Compounds were assayed against β -secretase, and inhibitors in the high micromolar range identified.

183/2006

Title: Design, synthesis, and biological evaluation of the combinatorial library with a new spirodiketopiperazine scaffold.

fold. Discovery of novel potent and selective low-molecular-weight CCR5 antagonists.

Authors: Habashita, H.;* Kokubo, M.; Hamano, S.-i.; Hamanaka, N.; Toda, M.; Shibayama, S.; Tada, H.; Sagawa, K.; Fukushima, D.; Maeda, K.; Mitsuya, H.

Ono Pharmaceuticals, Japan

Source: *J. Med. Chem.* **2006**, 49, 4140–4152.

Significance: The sequence of Ugi condensation with a resin-bound isonitrile followed by acidic deprotection/cyclization was used to prepare a 576-member library of spirodiketopiperazines. Screening against CCR5 identified micromolar leads, which were optimized to give nanomolar compounds with anti-HIV activity.