246/2005

**Title:** Heterogeneous hydrogenation reactions using a continuous flow high pressure device.

**Authors:** Desai, B.; Kappe, C. O.*

**Source:** J. Comb. Chem. 2005, 7, 641–643

**Significance:** A ‘H-cube’ apparatus was used in heterogeneous hydrogenation under continuous flow conditions. With dihydropyrimidines obtained from the Biginelli condensation, nitro reduction, benzyl ester deprotection and Raney nickel desulphurization were all demonstrated. Products were prepared in > 100 mg scale in 30 minutes.

247/2005

**Title:** A novel MCR of isocyanates, aldehydes, and dienophiles.

**Authors:** Strübing, D.; Neumann, H.; Hübner, S.; Klaus, S.; Beller, M.*

**Source:** Org. Lett. 2005, 7, 4321–4324

**Significance:** Reaction of isocyanates and conjugated aldehydes generates 1-amino-1,3-butadienes in situ with loss of carbon dioxide. These are intercepted by dienophiles in a Diels-Alder reaction to give the products.

248/2005

**Title:** Metathesis reactions of pyrazolotriazinones generate dynamic combinatorial libraries.

**Authors:** Wipf, P.; Mahler, S. G.; Okumura, K.

**Source:** Org. Lett. 2005, 7, 4483–4486

**Significance:** The pyrazolotriazinones are stable under buffered conditions, but undergo reversible aldehyde exchange at pH 4. Hence, the reaction has potential for the generation of dynamic libraries.

249/2005

**Title:** Solution-phase parallel synthesis of a 1,2,7-trialkyl-1H-imidazo[4,5-g]quinoxalin-6-ol library scaffold.

**Authors:** Zhang, J.; Zhang, L.; Zhang, S.; Wang, Y.; Liu, G.*

**Source:** J. Comb. Chem. 2005, 7, 644–647

**Significance:** The title heterocycle with three points of diversity was accessed in solution-phase starting from 1,5-difluoro-2,4-dinitrobenzene. A 2,500 member library was prepared.

250/2005

**Title:** Parallel synthesis of a library of acylsemicarbazides using a solution-phase one-pot method and their evaluation as crop-protection agents.

**Authors:** Grzyb, J. A.; Dekeysre, M. A.; Batey, R. A.*

**Source:** Synthesis 2005, 2384–2392

251/2005

**Title:** Hsp90 inhibitors identified from a library of novo-bioin analogues.

**Authors:** Yu, X. M.; Shen, G.; Neckers, L.; Blake, H.; Holzbeierlein, J.; Cronk, B.; Blagg, B. S. J.*

**Source:** J. Am. Chem. Soc. 2005, 127, 12778–12779

252/2005

**Title:** Library versus library recognition and inhibition of the HIV-1 Nef allelome.

**Authors:** Olszewski, A.; Weiss, G. A.*

**Source:** J. Am. Chem. Soc. 2005, 127, 12178–12179
Significance: An ‘allelome’ of Nef variants (~10^7) was generated by phage display. Functional variants were selected by binding to p53, and disruption of the binding then screened for by a guanidine library based on the bazzelladine alkaloids. One of the simpler library members was capable of effective binding to the allelome and less likely to be inactive upon protein mutation.

Phase Tags and Supported Reagents

253/2005
Title: Enantioselective synthesis of linear polypropionate arrays using anthracene-tagged organosilanes.
Authors: Kesavan, S.; Su, Q.; Shao, J.; Porco, J. A., Jr.;* Panek, J. S.*
Boston University, USA
Source: Org. Lett. 2005, 7, 4435–4438

Significance: The anthracene tagged reagent was used in enantioselective crotylations. Afterwards, the product was captured onto a supported maleimide resin, and oxidative cleavage released an aldehyde for further iterative crotylation.

254/2005
Title: Oligosaccharide synthesis by affinity separation based on molecular recognition between podand ether and ammonium ion.
Authors: Fukase, K.;* Takashina, M.; Hori, Y.; Tanaka, D.; Tanaka, K.; Kusumoto, S.
Osaka University, Japan
Source: Synlett 2005, 2342–2346

Significance: A phase tagging system based on a podand ether and its recognition by a polymer-supported ammonium group is described. The podand ether is simpler to prepare than the crown ether based system previously reported by the same group. Its application in oligosaccharide synthesis is demonstrated.

255/2005
Title: Polymer-micelle incarcerated scandium as a polymer-supported catalyst for high-throughput organic synthesis.
Authors: Takeuchi, M.; Akiyama, R.; Kobayashi, S.*
University of Tokyo, Japan
Source: J. Am. Chem. Soc. 2005, 127, 13096–13097
Significance: Solvent effects were found to be critical in the microencapsulation of scandium (III) triflate. In toluene, random aggregation was observed, while in THF-cyclohexane, spherical micelles were formed. The latter were used as catalysts in Mukaiyama aldol, Mannich and Michael reactions. The catalysts can be reused without significant leaching of scandium.

256/2005
Title: Solid/solution-phase annulation reagents: Single-step synthesis of cyclic amine derivatives.
Authors: Dolle, R. E.;* MacLeod, C.; Martinez-Teipel, B.; Barker, W.; Seida, P. R.; Herbertz, T.
Adolor, USA
Source: Angew. Chem. Int. Ed. 2005, 44, 5830–5833

Significance: A series of solution and solid-phase reagents are described that enable the single-step conversion of a primary amine into a cyclic derivative. For example, the immobilized bromobenzyl esters react with an amine via cyclative cleavage to release the nitrogen heterocycle.

Solid-phase Synthesis

257/2005
Title: The removal of the t-BOC group by electrochemically generated acid and use of an addressable electrode array for peptide synthesis.
Authors: Maurer, K.* McShea, A.; Strathmann, M.; Dill, K.
CombiMatrix, USA
Source: J. Comb. Chem. 2005, 7, 637–640

Significance: Peptide synthesis was carried out on a silicon chip with 1024 individually addressable platinum electrodes. The synthesis used Boc amine protecting groups, which were cleaved by acid electrochemically generated by the oxidation of hydrazines to azo compounds.

258/2005
Title: Facile preparation of carbohydrate microarrays by site-specific, covalent immobilization of unmodified carbohydrates on hydrazide-coated glass slides.
Authors: Lee, M.-R.; Shin, I.*
Yonsei University, Korea
Significance: Carbohydrate microarrays were prepared by linkage of glycans to hydrazides on a glass slide. Applications involving binding of lectin antibodies and pathogenic E. coli strains to the microarray were demonstrated.

259/2005

Title: Small molecule macroarray construction via Ugi four-component reactions.
Authors: Lin, Q.; O’Neill, J. C.; Blackwell, H. E.*
University of Wisconsin-Madison, USA
Source: Org. Lett. 2005, 7, 4455–4458

Significance: An array of Ugi products was prepared on planar cellulose support, under aqueous microwave assisted reaction conditions.

260/2005

Title: A facile solid-phase synthesis of 1,2,4,5-tetrasubstituted imidazoles using sodium benzenesulfinate as a traceless linker.
Authors: Li, Wei.; Lam, Y.*
National University of Singapore, Singapore
Source: J. Comb. Chem. 2005, 7, 644–647

Significance: Condensation between an immobilized sulfinic acid with an aldehyde and amide gave a sulfonamide intermediate. Subsequent benzoin-type reaction released an $\alpha$-ketoamide. Under inert atmosphere, this was cyclized to an imidazole with ammonium acetate, while reactions with triphenylphosphine or Lawesson’s reagent respectively yielded oxazoles and thiazoles.

261/2005

Title: Solid-phase synthesis of 3,4-dihydro-1H-pyrimidine-2-ones using sodium benzenesulfinate as a traceless linker.
Authors: Li, W.; Lam, Y.*
National University of Singapore, Singapore
Source: J. Comb. Chem. 2005, 7, 721–725

Significance: A selenide resin was propargylated, followed by 1,3-dipolar cycloaddition with an organic azide generated.
in situ. The selenide was then alkylated with an allylic bromide and a second dipolar cycloaddition with a nitrile oxide. Oxidative cleavage from the resin then releases the bis-heterocycle.

264/2005

**Title:** An efficient synthesis of carlosic acid and other 5-carboxymethyltetronates from malates.

**Authors:** Schobert, R.;* Jagusch, C. Bayreuth University, Germany

**Source:** *Synthesis* 2005, 2421–2425

**Significance:** A domino addition-Wittig alkenation reaction with Ph₃PCCO was the pivotal step in the synthesis of the title compounds. The solid-phase variant featured an immobilized malate.

265/2005

**Title:** Amino acid bromides: their utilization for difficult couplings in solid-phase peptide synthesis.

**Authors:** Ni, M.; Esposito, E.; Kaptein, B.; Broxterman, Q. B.; Dal Pozzo, A.* Ronzoni Institute, Italy

**Source:** *Tetrahedron Lett.* 2005, 46, 6369–6371

**Significance:** Amino acid bromides are among the most reactive acylating agents known, but their instability precludes routine use. Here, peptides containing multiple Aib units were synthesized by generating the acid bromide in situ. Amines could be protected as the Fukuyama sulfonamide, or present in latent form as an azide.

266/2005

**Title:** Efficient synthesis of a β-peptide combinatorial library with microwave irradiation.

**Authors:** Murray, J. K.; Farooqi, B.; Sadowsky, J. D.; Scalf, M.; Freund, W. A.; Smith, L. M.; Chen, J.; Gellman, S. H.* University of Wisconsin, USA

**Source:** *J. Am. Chem. Soc.* 2005, 127, 13271–13280

**Significance:** Optimized conditions were developed for solid-phase β-peptide synthesis using Fmoc-β-amino acid monomers. To ensure functionalization of the bead interior, couplings and deprotections were carried out with cycles of 2 minute microwave irradiation (6 cycles for coupling, 3 for deprotection) and LiCl added to break down aggregation. A 100 member library was prepared.

267/2005

**Title:** A positional scanning approach to the discovery of dipeptide-based catalysts for the enantioselective addition of vinylzinc reagents to aldehydes.

**Authors:** Sprout, C. M.; Richmond, M. L.; Seto, C. T.* Brown University, USA

**Source:** *J. Org. Chem.* 2005, 70, 7408–7417

**Significance:** A series of oxytocin analogues was prepared in which the disulfide bridge was replaced by an all-carbon linker. The synthesis was carried out on solid-phase, using ring-closing metathesis for macrocyclization. Both the alkene and alkane linkers (obtained by hydrogenation) were evaluated. The analogue shown is an oxytocin antagonist with improved half-life over atosiban.

268/2005

**Title:** Efficient solid-phase-based total synthesis of the bisintercalator TANDEM.

**Authors:** Malkinson, J. P.; Anim, M. K.; Zloh, M.; Searcey, M. *; Hampshire, A. J.; Fox, K. R. University of London, UK

**Source:** *J. Org. Chem.* 2005, 70, 7654–7661

**Significance:** An N-demethylated analogue of the natural product triostin A was synthesized and its DNA binding properties evaluated. The route involved solid-phase synthesis of a linear depsipeptide, formation of a disulfide bridge, followed by cleavage and macro lactamization in solution-phase.

269/2005

**Title:** Synthesis of oxytocin analogues with replacement of sulfur by carbon gives potent antagonists with increased stability.

**Authors:** Stymiest, J. L.; Mitchell, B. F.; Wong, S.; Vederas, J. C.* University of Alberta, Canada

**Source:** *J. Org. Chem.* 2005, 70, 7799–7809

**Significance:** A set of dipeptides were prepared by solid-phase synthesis and evaluated as catalysts for vinylzinc addition to aldehydes. Positional scanning enabled the identification of the optimised catalyst shown, which gave products with high enantioselectivity.
Significance: A genetic algorithm approach was taken to identify peptide inhibitors of GG transferase. In the first round, 30 amphiphilic tetrapeptides were prepared and screened for activity. The 16 most potent compounds were selected, and in the second round an arbitrarily chosen building block is substituted. After five generations, low micromolar inhibitors such as the peptide shown were identified.

271/2005

Title: Screening and identification of linear B-cell epitopes and entry-blocking peptide of severe acute respiratory syndrome (SARS)-associated coronavirus using synthetic overlapping peptide library.

Authors: Hu, H.; Li, L.; Kao, R. Y.; Kou, B.; Wang, Z.; Zhang, L.; Zhang, H.; Hao, Z.; Tsui, W. H.; Ni, A.; Cui, L.; Fan, B.; Guo, F.; Rao, S.; Jiang, C.; Li, Q.; Sun, M.; He, W.; Liu, G.*

Peking Union Medical College, China

Source: J. Comb. Chem. 2005, 7, 648–656

Significance: A 10-mer overlapping peptide library, prepared by IRORI tagging, was employed in the identification of epitopes from the structural proteins of the SARS-associated coronavirus. The peptide S471–503 derived from the S protein had high immunogenicity and inhibited viral entry into host cells in vitro.

272/2005

Title: Discovery of a potent and selective 5-HT{sub 5A} receptor antagonist by high-throughput chemistry.

Authors: Corbett, D. F.*; Heightman, T. D.; Moss, S. F.; Bromidge, S. M.; Coggon, S. A.; Longley, M. J.; Roa, A. M.; Williams, J. A.; Thomas, D. R.

GlaxoSmithKline, UK

Source: Bioorg. Med. Chem. Lett. 2005, 15, 4014–4018

Significance: Lead optimisation of biphenylmethylamines was accomplished by a solid-phase route involving reductive alkylation, Suzuki cross-coupling, and acylation reactions.

273/2005

Title: Solid-phase synthesis and anti-infective activity of a combinatorial library based on the natural product anisomycin.

Authors: Shi, S.;* Zhu, S.; Gerritz, S. W.; Esposito, K.; Padmanabha, R.; Li, W.; Herbst, J. J.; Wong, H.; Shu, Y. Z.; Lam, K. S.; Sofia, M. J.

Bristol-Myers Squibb, USA

Source: Bioorg. Med. Chem. Lett. 2005, 15, 4014–4018

Significance: A library of over 8,000 anisomycin analogues was prepared by solid-phase synthesis. Compounds with antimicrobial activity and reduced cytotoxicity relative to the natural product were identified.