Building an integrated system for chemistry markup and online publishing integrated to online chemistry resources
The Future of Publishing?

- Publishers know that embracing electronic publication is a must.

“Cell Press and Elsevier have launched a project called Article of the Future … to redefine how the scientific article is presented online. ” Prototype: http://beta.cell.com/
Publishers are experimenting

...invited researchers to prototype tools dealing with the ever-increasing amount of online life sciences information

The winners built:
Reflect: Automated Annotation of Scientific Terms: http://reflect.ws
Reflect highlights protein and small molecule names, such as p53 and Lipitor.

To find out more about a highlighted term, just click on it.
Atorvastatin

From Wikipedia, the free encyclopedia
(Redirected from Lipitor)

Atorvastatin (INN) (pronounced /ə tɔrˈvæstətən/) (Lipitor, Pfizer), is a member of the drug class known as statins, used for lowering blood cholesterol. It also stabilizes plaque and prevents strokes through anti-inflammatory and other mechanisms.

Atorvastatin inhibits HMG-CoA reductase, the rate-determining enzyme located in hepatic tissue that produces mevalonate, a small molecule used in the synthesis of cholesterol and other mevalonate derivatives. This lowers the amount of cholesterol produced which in turn lowers the total amount of LDL cholesterol. Atorvastatin was first synthesized in 1985 by Bruce Roth while working at Parke-Davis Warner-Lambert Company (now Pfizer). With 2008 sales of US$12.4 billion, Lipitor is likely the top-selling drug in the world. US patent protection is scheduled to expire in June 2011. However, Pfizer made an agreement with Ranbaxy Laboratories to delay the generic launch in the US until November 2011.

Lipitor is not the only statin; there are several other statins on the market.
Entity-Extraction, Mark-up, Annotate
And linked to STITCH...
Success Depends on Dictionaries

and Food Interactions

Combinations with clofibrate, fenofibrate, gemfibrozil, which are fibrates used in accessory therapy in many forms of hypercholesterolemia, usually in combination with statins. The statins, including atorvastatin, can cause myositis. Administration of Atorvastatin with one of CYP3A4 inhibitors like itraconazole, telithromycin, and voriconazole, may increase serum concentrations of atorvastatin, which is also true for other CYP3A4 inhibitors like diltiazem, erythromycin, fluconazole, ketoconazole, clarithromycin, cyclosporine, protease inhibitors, verapamil, amiodarone, and aprepitant. Often, bosentan, fosphenytoin, and phenytoin which are CYP3A4 inducers can decrease the plasma concentrations of atorvastatin. Oral contraceptives like norethindrone and ethinyl estradiol, these increases should be considered when selecting an oral contraceptive for a woman taking atorvastatin. Small increases can rarely decrease the plasma concentrations of atorvastatin but do not affect the LDL-C lowering efficacy.
Tomatoes Don't Prevent Prostate Cancer
Study Shows That Lycopene Doesn't Cut Risk of Prostate Cancer

By Sallynn Boyles
WebMD Health News

May 17, 2007

Lycopene, found in tomatoes, has been touted as good to be the cure for the prostate. The latest research, however, is not so positive.

Lycopene is a pigment that gives tomatoes their red color. It has been linked to lower incidence of prostate cancer in some studies. However, a new study suggests that lycopene does not play a significant role in preventing prostate cancer.

The study, published in the journal Cancer, involved over 40,000 men who were followed for an average of 12 years. The researchers found that lycopene intake was not significantly associated with a reduced risk of prostate cancer.

The study also found that dietary factors such as vitamin E, vitamin C, and selenium were more strongly associated with a reduced risk of prostate cancer.

So, while lycopene is certainly a beneficial pigment, it appears that it does not play a significant role in preventing prostate cancer. Other dietary factors may be more important in reducing the risk of this disease.
Finding disease-specific coordinated functions by multi-function genes: Insight into the coordination mechanisms in diseases

Wencai Ma, Da Yang, Yunyan Gu, Xinwu Guo, Wenyuan Zhao and Zheng Guo

*College of Bioinformatics Science and Technology, Harbin Medical University, Harbin 150086, China

Received 19 February 2009; accepted 4 May 2009. Available online 8 May 2009.

Abstract

We developed an approach using multi-function disease genes to find function pairs whose co-deregulation might induce a disease. Analyzing cancer genes, we found many cancer-specific coordinated function pairs co-deregulated by dysfunction of multi-function genes and other molecular changes in cancer. Studying two subtypes of cardiomyopathy, we found they show certain consistency at the functional coordination level. Our approach can also provide important information for finding novel disease genes as well as their mechanisms in diseases.

Keywords: Disease gene; Gene functions; Gene ontology; Cancer; Gene mutation; Protein–protein interaction

Article Outline
Semantic Mark-up for Chemistry

- Semantic mark-up for chemistry is here
  - RSC project prospect (structure linking, IUPAC Gold Book ontology and other ontologies)
  - Nature publishing group compound linking
  - ChemSpider Journal of Chemistry
pecolic acid. Significant experimental evidence has been found that azaoctane core common to all of these natural products is formed via an intramolecular hetero-Diels–Alder (IMDA) reaction [1H]-one. Indeed, we have applied such intramolecular synthetic strategies to the total synthesis of several of these prenylated indolizines [refs 11,12], D,L-brevianamide B (ref. 16), D,L-neroamide B (ref. 12), D,L- and (-)-19-nor prenylated bromofolic acid, B. Precedent studies have shown that the number of stereocenters in these natural products is relatively large. For example, natural products possessing an anti relative configuration at C19 stereocenter, like paraherquamide and nofoamide family members, have relatively large numbers of non-CH2 groups in the molecule, that is, no double bonds or ions. Owing in part to this lack of flexibility, versicolamide B (8) attracted our interest. Nature Chemistry Compound Pages
6,7-Dimethylumazine as a potential ligand for selective recognition of adenine onosite an abasic site in DNA duplexes

Zuqiang Ye†∥, Burk Rajendran‡∥, Dai Qing†∥, Seiichi Nishizawa∥ and Naoto Teranaka∥∥

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Received (in Cambridge, UK) 31st September 2008; Accepted 20th October 2008

First published on the web 20th October 2008

Single nucleotide polymorphism (SNP) analysis is an important tool for understanding genetic diversity and for linkage analysis in the human genome. Several methods have recently been developed to detect SNPs, and they succeed in most instances. On the other hand, we have developed a new fluorescence-labeled probes for allele-specific hybridization to microarrays containing DNA fragments containing SNP nucleotides. We are developing an assay based on the principle that the stability of DNA duplexes can be directly related to the binding constants for the corresponding nucleosides. Several recent studies have also shown that mismatches in the DNA duplex favor the formation of 1.21 × 10^6 M−1. This is the highest binding constant ever reported for DNA. In conclusion, the high stability of DNA duplexes containing SNP nucleotides can be directly related to the binding affinities and to the detection of generic mutations. Consistently, considerable efforts have focused on the development of genetic tests that can be used to detect missense mutations. We have recently reported a novel method for detecting base-pairing mutations by using a novel fluorescent dideoxyribonucleotide analog. The method relies on the fact that the binding constants of DNA duplexes containing mismatched base pairs are significantly lower than those of the corresponding DNA duplexes containing base-pairing sites. In conclusion, the high stability of DNA duplexes containing SNP nucleotides can be directly related to the binding affinities and to the detection of generic mutations.
ChemSpider and Publishing

- The curation efforts on ChemSpider led to a set of validated dictionaries

- Integrate best-in-class **entity extraction** (SureChem) with validated name dictionaries

- Additional dictionaries gave reactions, groups, families, hardware and software vendors etc
ChemMantis and CJOC

MoIback 2004, M371

Synthesis of 2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde. A new aldehyde for the preparation of biologically active molecules.

A. A. Jarrahpour*, A. R. Esmailbeig and M. Zarei

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Received: 8 October 2003 / Accepted: 20 February 2004 / Published: 24 February 2004

Keywords: azoaldehyde, p-anisidine, o-vanillin, Schiff bases, biological activity

Diazot compounds have interesting biological activities [1-4]. It was shown that the presence of an azo functionality in many compounds is essential for the exhibition of pesticidal activity [5]. In addition, the existence of the methoxy groups on some molecules enhanced the biological activities [6]. As such, we synthesized a new aldehyde 4 possessing an azo as well as the methoxy groups. Reaction of this novel azoaldehyde with various aromatic amines afforded the corresponding Schiff bases. Their antibacterial and antifungal activities are under study to be presented in the near future.

\[
\begin{align*}
\text{MeO} & \quad \text{NH}_2 \\
& \xrightarrow{\text{HCl}, \text{NaNO}_2} \\
\text{MeO} & \quad \text{N} = \text{N}^+ \text{Cl}^-
\end{align*}
\]

\[
\begin{align*}
\text{CHO} & \quad \text{OH} \\
\text{O} & \quad \text{MeO}
\end{align*}
\]

Experimental: A solution of aqueous HCl (1.61 mL, 17.92 mmol) in 30 mL water was added to the p-anisidine 1 (1.00 g, 8.12 mmol). It was stirred and cooled to 0 °C and then an aqueous solution of NaNO₂ (0.62 g, 9.00 mmol; 8 mL H₂O) was added dropwise. The so-formed diazonium chloride 2 was consecutively coupled with o-vanillin 3 (1.24 g, 8.12 mmol), dissolved in 10.00 mL of aqueous 2N NaOH (0.80 g, 20.00 mmol). The reaction mixture was stirred for 1 hour at 0 °C, and then allowed to warm-up slowly to room temperature. The brown precipitate thus obtained was filtered and washed with H₂O (3 x 20 mL). Then it was dissolved in CH₂Cl₂ and dried (NaSO₄), filtered, and the solvent was evaporated under reduced pressure [7]. The crude product was purified by column chromatography (silica gel, CH₂Cl₂/hexane, 1:1, VM as eluant) to give 2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde 4 (1.77 g, 6.18 mmol) in 76.20% yield.
Name-Structure Pairs

Accepted: 20 February 2004 / Published: 24 February 2004

nisidine, \textit{o-vanillin}, Schiff bases, biological activity.

Interesting biological activity of \textit{o-vanillin} may be due to the presence of an \textit{azo} functionality in its methoxy groups, which make it susceptible to the formation of Schiff bases. Thus, we synthesized the corresponding Schiff bases. Their synthesis involves the reaction of \textit{o-vanillin} with a primary amine, followed by the addition of a methyl group to the resulting Schiff base.
Converting Detected Names…

- Names are searched against a validated dictionary (this expands as ChemSpider is curated)

- If not found then they are passed through a Name to Structure algorithm

- If they cannot convert then ChemSpider is searched for non-validated names
Manual Curation is Necessary
Deposit Structures

Synthesis of 2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde


Department of Chemistry, Shiraz University, Shiraz 71454, Iran
jarrah@chem.susc.ac.ir

Received: 8 October 2005; Accepted: 24 February 2006

Abstract: The title compound was synthesized by diazotization of an aromatic amine in the presence of a strong base. The compound was characterized by elemental analysis, IR, MS, and NMR spectroscopic methods and it was shown that the preparation of the azo compound was successful.

Keywords: azoaldehydes; diazotization; aromatic amine; biological activity.

Diazocompounds [5]. In addition, the substituent groups, such as methoxy groups, in the aromatic ring have a strong influence on the biological activity. These molecules enhanced the biological activity of the aromatic amines. Afforded a new structure into ChemSpider.
Custom Dictionaries

- Entity Extraction built around modified algorithms from SureChem
- Optimized for “publications”
- Dictionaries for chemical entities, groups, reactions, elements, families, species…
- Dictionaries can be expanded
Dictionaries are Easily Enhanced

- Copy-Paste into appropriate Entity Dictionary
- Impacts all future markups
- Expanding knowledgebases of information
- Linked out to rich sources of information
Build Dictionaries
Species – linked to Wikipedia

Bacillus subtilis, known as the hay bacillus or grass bacillus, is a Gram-positive, catalase-positive bacterium commonly found in soil. A member of the genus Bacillus, B. subtilis is rod-shaped, and has the ability to form a tough, protective endospore, allowing the organism to tolerate extreme environmental conditions. Unlike several other well-known species, B. subtilis has historically been classified as an obligate aerobe, though recent research has demonstrated that this is not strictly correct. Read more or Edit at Wikipedia.

Species: B. subtilis

B. subtilis

B. subtilis

S. aureus, B. subtilis, K. pneumonia, P. aeruginosa

2

\begin{equation}
\text{NO}_2 
\end{equation}

\begin{equation}
\text{N} \ \ \ \ \text{N}
\end{equation}

\begin{equation}
\text{Cl}
\end{equation}

\begin{equation}
\text{NO}_2
\end{equation}
Semantic Linking of Structures

- What would you want to link off a structure?
  - Chemical suppliers
  - Other publications
  - Analytical Data
  - Related Reactions
  - Wikipedia
  - Patents
  - “Everything”
ChemSpider and its content

- ChemSpider is:
  - An online database of chemical entities
  - A link farm for > 21 million compounds and 200 data sources
  - A curation platform to improve the quality of data online
  - A deposition platform for chemicals and content
Link off a structure in ChemSpider

- Chemical suppliers
- Other publications
- Analytical Data
- Related Reactions
- Wikipedia
- Patents
- “Everything”
SureChem Services

- The SureChem Portal is a gateway for patent searching – can be searched by structure/substructure
- ChemSpider previously integrated by depositing structures and linking out

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<td>Alprazolam</td>
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Previously integration lacked any sense of numbers of patents, titles etc

**New integration:**

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<th>Patent</th>
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<tr>
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<td>Delivery of alprazolam, estazolam, midazolam or triazolam through an inhalation route</td>
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<td>Delivery of alprazolam, estazolam, midazolam or triazolam through an inhalation route</td>
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<td>6599532</td>
<td>Osmotic device containing alprazolam and an antipsychotic agent</td>
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<tr>
<td>4683231</td>
<td>Method of preventing withdrawal symptoms associated with the cessation or reduction of tobacco smoking</td>
</tr>
<tr>
<td>3980789</td>
<td>8-Chloro-1-methyl-6-phenyl-4H-s-triazolo[4,3-a][1,4]-benzodiazepine compositions and method of treatment</td>
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<tr>
<td>4508726</td>
<td>Treatment of panic disorders with alprazolam</td>
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<tr>
<td>5370473</td>
<td>Transdermal administration of short or intermediate half-life benzodiazepines</td>
</tr>
</tbody>
</table>

6260 patents found. First 10 are shown. Click here to see all.
Title: Delivery of alprazolam, estazolam, midazolam or triazolam through an inhalation route
Patent Number: 7060255

Abstract:
The present invention relates to the delivery of alprazolam, estazolam, midazolam or triazolam through an inhalation route. Specifically, it relates to aerosols containing alprazolam, estazolam, midazolam or triazolam that are used in inhalation therapy. In a method aspect of the present invention, alprazolam, estazolam, midazolam or triazolam is administered to a patient through an inhalation route. The method comprises: a) heating a thin layer of alprazolam, estazolam, midazolam or triazolam, on a solid support to form a vapor; and, b) passing air through the heated vapor to produce aerosol particles having less than 5% drug degradation products. In a kit aspect of the present invention, a kit for delivering alprazolam, estazolam, midazolam or triazolam through an inhalation route is provided which comprises: a) a thin coating of an alprazolam, estazolam, midazolam, or triazolam composition and b) a device for dispensing said thin coating as a condensation aerosol.

Issue Date: 20060613
Application Date: 20040129

Inventor Name          Inventor Country Inventor State Inventor City
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Zaffaroni, Alejandro C. US  CA  Atherton

Assignee Name          Assignee Country Assignee State Assignee City
Alezza Pharmaceuticals, Inc. US  CA  Palo Alto

Current US Classification: 424 45, 424 46, 424489, 424499, 424514, 424568, 424728, 42420014, 42420024, 42420315, 424 45, 424 46, 424489, 424499, 424 43, 42434, 424789, 424165, 42420014, 42420024, 514220, 514988, 12820021, 12820024, 12820035

Application Serial: 10769167
Pubmed Articles Linked

CJOC to ChemSpider Synthesis

- ChemSpider will support synthesis procedures moving forward

- The ChemSpider Journal of Chemistry is an ideal platform for text-based procedures
A 500mL three-necked round flask equipped with a reflux condenser, internal thermometer, pressure-equalised addition funnel and a large egg-shaped magnetic stir bar was charged with 25% sodium methoxide in methanol 31.55g (Aldrich; 146mmol) and methanol 100mL. The flask was placed on an ice slush bath and after 15 min a solution of 1,3-acetonedicarboxylic acid dimethyl ester 25.00g (Acrros; 143.55 mmol) in methanol 10mL was added within 15 min, the addition funnel was washed with methanol (2×20mL) and the washings were also added into the mix. The cooling bath was then removed and the flask was placed on a 65°C oil bath and stirred for approximately 30 min. (The mixture gradually became homogeneous as the precipitated Na-enolate salt of the 1,3-acetonedicarboxylic acid dimethyl ester.) When the internal temperature in the flask has stabilized, a mixture of 40% aqueous glyoxal 12.00g (Alfa; 82.7 mmol, 115% of the theoretic amount) with methanol 30mL was introduced dropwise from the addition funnel — very slowly — over a period of 1h45min, with a vigorous stirring on the 65°C oil bath. After the complete addition the funnel was washed with methanol (10mL) and the washings were also added to the mix. The resulting cloudy reaction mixture was stirred for extra 15 min at 65°C, then diluted with THF 200mL and the flask was removed from the heating bath. The mixture was stirred at RT overnight (12 hours). The precipitated intermediate (as a disodium salt hydrate) was collected by filtration using a large sintered-glass Buchner funnel. The collected solids were washed thoroughly with THF and then dried by suction for about 2 hours.
3-Methyl-3-(6,6a-trimethyl-hexahydro-cyclopenta[\(b\)]furan-2-yl)-butan-2-one

Juan M. Castro, Ramón Porras, Pablo J. Linares-Palomino, Sofia Salido, Joaquin Alcarejos,* Manuel Nogueras and Adolfo Sánchez

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Received: 16 February 2004 / Accepted: 30 March 2004 / Published: 1 July 2005

Keywords: Acid-catalyzed rearrangement, intramolecular cyclisation, hexahydrocyclpent[a][b]furan derivative.

A 40% aqueous solution of sulfuric acid (0.5 mL) was added to a stirred solution of 3,3-dimethyl-4-hydroxy-5-(2,2,3-trimethyl cyclopentenyl) penta-2-one (1) (630 mg, 2.65 mmol) in methanol (5 mL) and the mixture refluxed for 1.5 h. The resulting solution was partially evaporated under reduced pressure, resolved in EtOAc and washed with saturated NaHCO\(_3\) (3 x 25 mL) and brine (3 x 25 mL). The organic layer was dried over anhydrous Na\(_2\)SO\(_4\) and evaporated under reduced pressure to give a crude which was filtered through a silica gel pad to yield the cyclized and rearranged title compound 2 (504 mg, 2.11 mmol, 80%) as a yellow liquid.

IR (neat, cm\(^{-1}\)): 1705 (CO), 1077, 906 (C-O-C).

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 0.82 (\text{H}, \text{Me}-6'); 0.96 (\text{H}, \text{Me}-6); 1.03 (\text{H}, \text{Me}-5); 1.09 (\text{H}, \text{Me}-3); 1.16-1.28 (1\text{H}, \text{Me}-4); 1.35 (1\text{H}, \text{Me}-3); 1.50-1.63 (2\text{H}, \text{Me}-3', \text{H}-5'); 1.78-1.88 (1\text{H}, \text{Me}-4'); 2.00 (2\text{H}, \text{Me}-4); 2.31-2.42 (1\text{H}, \text{Me}-3a); 3.97 (1\text{H}, \text{Me}-3); 12.2 Hz, 8.1 Hz, 8.5 Hz). Some signals were assigned by means of 2D NMR experiments.

\(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 26.87 (\text{C}-1); 213.73 (\text{C}-2); 50.09 (\text{C}-3); 18.53 (\text{C}-4); 21.82 (\text{Me}-3); 84.68 (\text{C}-2'); 34.81 (\text{C}-3'); 46.84 (\text{C}-3a); 29.33 (\text{C}-4'); 40.54 (\text{C}-5'); 46.43 (\text{C}-5); 94.96 (\text{Me}-6'); 22.08 (\text{Me}-6); 25.23 (\text{Me}-6); 19.60 (\text{Me}-6).

Some signals were assigned by means of 2D NMR experiments.

EI-MS (70 eV, m/z): 238 (M\(^+\), 0.2%); 223 (M\(^+\)–Me, 0.4); 195 (M\(^+\)–COMe, 0.1); 153 (M\(^+\)–CH\(_3\)O, 15); 109 (10); 96 (22); 87 (47); 71 (13); 55 (13); 43 (CH\(_3\)CO\(^+\)), 100.
One-pot synthesis of terpyridine derivatives; 4'-{(2-thienyl)-2,2':6',2''-terpyridine

Jérôme Husson (jerome.husson@univ-franche.fr),
A contribution from the Knorr Group, Besançon

Chemicals Used
2-Acetylpyridine (Avocado), thiophene-2-carboxaldehyde (Acrex), 25 % aqueous ammonia solution (Merck), Potassium hydroxide pellets (Prolabo), absolute ethanol (Carlo-Erba).

Procedure
To a solution of 2-acetylpyridine (4.84 g, 40 mmol, 2 equiv.) in ethanol (100 ml), are added thiophene-2-carboxaldehyde (2.74 g, 20 mmol, 1 equiv.), potassium hydroxide (3.08 g, 55 mmol, 2.75 equiv.) and ammonia solution (38 ml). The resulting mixture is stirred at room temperature for 15 hours. The resulting pale yellow precipitate is filtered off and successively washed with water (4 x 25 ml) and cold 50% ethanol (25 ml). The yellow product is first air dried for 48 hours and then in a desiccator over phosphorus pentoxide. The yield is 2.40 g (38%).

Author's Comments
This method for the synthesis of 4'-{(hetaryl) terpyridine is a very simple one pot procedure which allows preparation of variously substituted terpyridine derivatives. The products so obtained are generally sufficiently pure to be used as ligands in coordination chemistry. The first step is an aldol reaction between 2-acetylpyridine and the aldehyde, followed by a Michael addition of a second equivalent of 2-acetylpyridine yielding a 1,5-diketo derivative. The latter undergoes ring closure upon reaction with ammonia to form the central pyridine ring.
High-yielding synthesis of Nefopam analogues (functionalized benzoxazocines) by sequential one-pot cascade operations

Dheenapanthi B. Ramachary, Vidadala V. Narayana, M. Shiva Prasad and Kithada Ramakumar

An efficient amine-ruthenium-catalyzed three-step process for the synthesis of Nefopam analogues was achieved through combinations of cascade enamineamination/π-sigmatropic cyclization and diene or diyne metathesis as key steps starting from functionalized Hugmann’s salts. In this communication, we discovered the application of ruthenium-catalysis on olefins containing free amines without in situ formation of salts.
Organic & Biomolecular Chemistry

The international home of synthetic, physical and biomolecular organic chemistry.

Materials: All solvents and commercially available chemicals were used as received. Hagemann's esters 1a-n was prepared from alkyl acetates and aldehydes with high yields in one-step according to our recent modified method. Hagemann's ester 1n was prepared from benzylidene acetone with high yield in two-steps according to literature procedures (see Scheme S1). Hagemann's ester 1o was prepared from trimethyl-(1-methylene-allyloxy)-silane and propynoic acid ethyl ester with high yield in two-steps according to literature procedure (see Scheme S2).

Scheme S1. Synthesis of Hagemann's ester 1n

Scheme S2. Synthesis of Hagemann's ester 1o
ChemSpider Synthesis

- ChemSpider Synthesis will be a home for all things “synthetic”
- An online resource for synthetic procedures from blogs, other online resources, RSC supplementary info, other publishers etc.
- We will mine the RSC supplementary info backfile for reactions
- Public peer-review and feedback for synthetic procedures
Online Journals and Live Data

Thus, 3.4 g (30 mmol) of hydrogen peroxide (30%) were added dropwise between -10 and 0 °C to 5.2 g (45 mmol) of ethyl pyruvate with stirring. The viscous liquid was kept at the same temperature for 15 min, then it was added dropwise to a vigorously stirred mixture of chloropyrazine (1.14 g, 10 mmol), water (7 ml), concentrated sulfuric acid (3.0 g, 50 mmol), ferrous sulfate heptahydrate (8.3 g, 30 mmol), and toluene (30 ml) at -5 to 0 °C. Stirring was continued for another 15 min, then the mixture was poured into ice-water and it was extracted several times with dichloromethane. The combined extracts were washed with water, dried and evaporated. Excess ethyl pyruvate was removed by Kugelrohr distillation (30 °C, 1 mbar). The liquid residue [4] was purified by column chromatography on silica gel, eluting with ethyl acetate/light petroleum (1+3), followed by Kugelrohr distillation (110 °C, 1 mbar) to afford the title compound as a colorless lipid (1.04 g, 56%). Storage in a refrigerator is recommended.

$^1$H NMR (300 MHz, CDCl$_3$): 8.54-8.46 (AB system, J$_{5,6}$ = 2.5 Hz, 2 H, H-5, H-6), 4.45 (q, J = 7.1 Hz, 2 H, CH$_2$), 1.39 (t, J = 7.1 Hz, 3 H, CH$_3$).

$^{13}$C NMR (75 MHz, CDCl$_3$): 163.2 (C=O), 147.2 (C-3), 145.3 (C-5), 144.7 (C-2), 141.7 (C-6), 62.6 (CH$_2$), 13.9 (CH$_3$).
Moving forward

- Integrate ChemMantis and Project Prospect as appropriate – best of both worlds
- Expand ChemSpider validated dictionaries with RSC content
- Expand information in “Compound Boxes” after markup – take advantage of all ChemSpider resources
- Invite the community to help build ChemSpider Synthesis
Acknowledgments

- SureChem (Nicko Goncharoff and Richard Koks)
- RSC – Richard Kidd and Colin Batchelor
- CJOC – multiple authors and reviewers
- ChemSpider curation – a cast of many