Open Medicine

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An epic drama of adventure and exploration.

2001: a space odyssey
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CINERAMA Super Panavision® and Metrocolor

Men's galaxy on the Moon... a whole new generation has been born and is living here... a quarter-million miles from Earth.
Open Medicine Roadmap

• Where we came from
• What we are
• Our impact
• Our future
Acknowledgement

- Claire Kendall, Deputy Editor, OM
- Dean Giustini, UBC Health Librarian and OM Blogger
- MJ Suohonos, Sage Advisor, Public Knowledge Project
Where did we come from?

http://www.flickr.com/photos/apophysis_rocks/280238861/
What is Open Medicine?

- Peer-reviewed, independent, open-access general medical journal
- Examines issues relevant to health and clinical medicine both in Canada and internationally
What is Open Medicine?

• Collaborative team
• Unique venture
• A new model of scholarly publishing
What is Open Medicine?
What is Open Medicine?

- Collaborative team
- **Unique venture**
- A *new model* of scholarly publishing
Unique venture: Two key drivers

1. Editorial independence

2. The internet changes everything
Unique venture

The internet changes everything

• Cheap
• Fast
• Global
• Search and retrieval
What is Open Medicine?

• Collaborative team
• Unique venture
• A new model of scholarly publishing
A new model - 4 principles

- Freedom
- Transparency
- Creativity
- Community
Our goal is to make Open Medicine itself a publicly available resource.
Freedom

Open Journal Systems

• Open source Journal management and publishing system
• Goal to expand and improve access to research
• Active participant in the development of ideas and code
Freedom

Lemon8-XML

XML never tasted so good!
Freedom
You are free:

- to Share — to copy, distribute and transmit the work
- to Remix — to adapt the work

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Freedom in Usage

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Display
Derivative works
Attribute
Free, **unrestricted** access

“If you have an apple and I have an apple and we exchange these apples then you and I will have each one apple. But if you have an idea and I have an idea and we exchange these ideas, then each of us have two ideas.”

*George Bernard Shaw*
Quinone-Annulated N-Heterocyclic Carbenes: Transition-Metal Complexes. Observation of σ-Backbonding Using FT-IR Spectroscopy and Cyclic Voltammetry

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Since Arndtsen’s seminal isolation of 1,3-diaminomethylimidazolium (DAMI) in 1963, N-heterocyclic carbenes (NHCs) have found enormous utility in the development of new transition metal complexes and as catalytic precursors for promoting organic reactions. We have recently initiated a program that uses NHCs as bridging ligands for the organometallic polymers, with an emphasis on tuning the electronic interactions between NHCs and their ligated transition metals.1

The complexation of NHCs to transition metals is strongly governed by coordination from the carbene to the metal center. σ-Backbonding from the metal into the π-system of the carbene has traditionally been considered to be negligible owing to competing overlap of the electron-rich nitrogen atoms adjacent to the carbene. In fact, recent theoretical analyses and synthetic advances have challenged this view. By constructing computational models with long bond distances and angles observed in similar ranges of metal-NHC X-ray crystal structures, Light, Meyer, Funk, and Jacobson demonstrated that σ-backbonding can be significant for some of the observed NHC-metal interactions.8 However, Bickelhaupt demonstrated that metal complexes formed with carbon- and nitrogen-donor ligands did not exhibit these models. As a result, the nature of the NHC-metal interaction, including the existence of σ-backbonding, remains controversial.1,9

The differences between the calculated structures can be traced to challenges associated with computing σ- and π-contributions in NHC-metal complexes. For NHC featuring a functional group in conjugation with the nitrogen atom sensitive to π-donation would be ideal for identifying σ-backbonding in its respective metal complexes. We envisioned this could be accomplished by coupling a pyramidal nitrogen to the 4.5 positions of a pyrazolepyridine. With two naphthyl groups formally conjugated to the pyrazole nitrogen, a quinone-annulated NHC was anticipated to offer three distinct advantages for studying metal-NHC interactions: (1) Cyclic vibrations frequently are sensitive to weak electronic changes in σ-systems and can be continuously monitored using IR spectroscopy; (2) The electronic-withdrawing nature of the quinone should result in increased propensity for σ-backbonding upon ligandation to a transition metal; and (3) Quinone exhibit reduction potentials that are sensitive to subtle electronic changes on their substituents. Collectively, this enables the use of IR spectroscopy and cyclic voltammetry to observe structural and electronic changes, including the existence of various C=N-types, on the NHC ligand upon complexation. Hence, we report the syntheses of the first NHCs with a quinone and present evidence for σ-backbonding in its respective quinone-metal complexes. Quinazolin-2(1H)-one 1 was synthesized in 74% yield by refluxing commercially available 2,4-dinitrophenyl diethylamine under basic conditions (Scheme 1). A signal assigned to the minimum proton was found at 12.3 ppm in the 1H NMR spectrum (CDCl3). To the best of our knowledge, this is the largest downfield shift reported for any known intramolecular compound and reflects a highly electron-donating nature of the quinone moiety. Free base 1 was obtained in 70% yield by deprotonating 1 with sodium hydride (dissolved in a catalytic amount of potassium tert-butoxide). NHC 2 exhibited a signal at 352 ppm in the 13C NMR spectrum (CDCl3), which was similar to those heterobidentate ligands and other annulated carbenes.8 Combined with the 1H NMR data for 1, this result highlights the advantage of using NMR spectroscopy in isolating and characterizing a complex 3,2,2-crystal obtained by slowly cooling a hot saturated toluene solution and analyzed using X-ray diffraction analysis. The molecular structure of 2 reveals a planar ring system, with a long C=O bond distance (1.392 Å) and a narrow N–C–N bond angle (128.1°) which suggested that the π-system of the quinone moiety was effectively conjugated to the carbenes.

Table 1. Summary of Selected Physical Data for Compounds 1–5

<table>
<thead>
<tr>
<th>Compound</th>
<th>% yield</th>
<th>H-1 (ppm)</th>
<th>C-4 (ppm)</th>
<th>C=O (ppm)</th>
<th>Mass (m/z)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74</td>
<td>-12.3</td>
<td>148.5</td>
<td>164.5</td>
<td>250.2</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>-12.5</td>
<td>149.5</td>
<td>162.5</td>
<td>244.2</td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>-12.6</td>
<td>148.6</td>
<td>162.0</td>
<td>234.2</td>
</tr>
</tbody>
</table>

1 Chemical shift of the carbene atom found in its respective 13C NMR spectrum (CDCl3). Difference between the carbene atom and adjacent aromatic ring (1,2-dichlorobenzene; δ (CDCl3)) observed for the free ligands indicates the larger N–C–N bond; the smaller N–C–N bond expected for coordinated NHCs (1,2-dichlorobenzene; δ (CDCl3)) was assigned on the basis of the downfield shift. Values are δ (ppm); 1H NMR: (360 MHz, CDCl3) δ (ppm) H NHC-1: 12.3. 

2 Yield reported as determined using GC-MS analysis. For compounds 1 and 4, NHC-1 (δ (CDCl3) 12.3 ppm) was hydrolyzed to 2-aminothiazole (δ (CDCl3) 4.1 ppm). Values are m/z (amu); 241 Mp (calc: 241.12, exp: 241.14) for NHC-1.

3 After isolation and characterization of 2, the utility of 1 to synthesize organometallic complexes was investigated. With the goal of evaluating a backbonding characteristics in mind, a metal complex was secured with sodium 2-ido-4-iodobenzene and without disturbing other structural characteristics of the complex (oxidation state, geometry, coordination number). Consequently, we desired a system where C=N was ligated with relatively little π-backbonding overlap; e.g., an imidazolyl could be substituted with a ligand that is highly capable (e.g., carbone) to exchange
Open Medicine is a peer-reviewed, independent, open-access journal.
Drug Development Pipeline

- **Discovery**
  - Basic research is published but preclinical research is not considered worthwhile.

- **Predevelopment**
  - Gap 1
  - Gap 2
    - Validated candidate drugs don’t enter clinical development because of profit-based company choices.

- **Development**
  - Gap 3
    - Drugs never reach the patient (registration problems, lack of production, high prices or drugs poorly adapted to local conditions).

- **Availability to patients**
  - Gap 4

Open Medicine
Re-mix

DNDi project pipeline 2005

Design: Cleveron Musk
Source: JAMA Internal Medicine 2005 Volume 1 Issue 1 DO: 10.1001/jama.293.1.100

**Gap 3**
Drugs never reach the patient (registration problems, lack of production, high prices or drugs poorly adapted to local conditions).

Availability to patients

High throughput screening (HAT)
Trypanothione reductase inhibitors (leish & trypan)
Cysteine protease inhibitors (tryps)
Protein farnesyltransferase inhibitors (HAT)
Cysteine protease inhibitors (tryps)
Novel nitroheterocycles (HAT)
Benzofuran (Chagas)
Ascorbamine for HAT
Nitrimidazoles (tryps) - exploratory
Natural products (leish & tryps) - exploratory

**Combination therapy for VL**
Protease inhibitor for Chagas
Ravuconazole (Chagas) - exploratory

**Clinical development**
Nilurtimex - Eternithine for HAT
Artesunate-Amodiaquine FDC (malaria)
Artesunate-Mefloquine FDC (malaria)
Peromyscrits (VL in Africa)
Imiquimed adjunct immunotherapy (CL)

HAT: Human African trypanosomiasis
VL: Visceral leishmaniasis
CL: Cutaneous leishmaniasis
TR: Trypanosomiasis

Projects ongoing 2004
New projects 2005

Open Medicine
Transparency

Political

• Governance with Board of Directors

Financial

• Advertising policy - no pharma
• Sponsorship policy
• Means thinking about new economic models
Transparency

• Content
  • No embargo policy
  • Data sharing
  • Competing interest policy
    • Editors
    • Reviewer
    • Authors
Creativity

- Rolling TOC
- Audio podcast
- Editorial workflow (Lemon8, XML-based layout)
- Reader involvement
  - Post a comment, linking to Pubmed, Google, Open Medicine blog
- Low cost
A conversation with Richard Smith

Richard Smith discusses haggis, Tim Berners-Lee, the future of medical publishing and much, much more...

Listen to “Can the Public Trust Medical Journals?”—a fun, provocative and thoroughly entertaining conversation with Richard Smith, former editor-in-chief of the British Medical Journal and author of The Trouble With Medical Journals. This Open Medicine event was recorded live at the University of Toronto on November 21, 2007.
Open Medicine has a desire to contribute back to the communities we are involved with and supported by:

- Open Source Community
- Scholarly Community
- Library Community
Open Medicine, Vol 1, No 2 (2007)

ANALYSIS AND COMMENT

Science and ideology

STEPHEN W. HWANG

Stephen W. Hwang is a research scientist at the Centre for Research on Inner City Health, the Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, Ont., and is an associate professor of medicine in the Division of General Internal Medicine, Department of Medicine, University of Toronto.

More than 130 prominent Canadian physicians, scientists and public health professionals have endorsed this commentary. They are listed at:
http://www.gim.utoronto.ca/Research/Research/inner_city_health/Hwang_SW.htm

Competing interests: None declared.
August 21, 2007

“Science and Ideology” written by Dr. Stephen Hwang, Associate Professor of Medicine, University of Toronto has been published in the peer-reviewed, independent, open-access scientific journal Open Medicine. More than 130 prominent Canadian physicians, scientists, and public health professionals have endorsed Dr. Hwang’s commentary, and their names are listed below. Institutional affiliations are provided for identification purposes only; no endorsement by any of these institutions is intended or should be inferred.

1. Barry Adam, PhD, University of Windsor
2. Alix Adrien, MD, CM, MSc, Direction de santé publique de Montréal
3. Michel Alary, MD, PhD, Université Laval
5. Jonathan Angel, MD, University of Ottawa
6. Nelson Arruda, MSc, Direction de santé publique de Montréal
7. Mark Asbridge, PhD, Dalhousie University
8. Greta Bauer, PhD, MPH, University of Western Ontario
9. Ahmed Bayoumi, MD, MSc, University of Toronto
10. Hallgrimur Benediktsson, MD, University of Calgary
11. Cecilia Benoit, PhD, University of Victoria
12. Philip Berger, MD, University of Toronto
Reader Comments

The Pot Calling the Kettle Black

DR Colin Richard Mangham (2007-08-28)

EMAIL REPLY  POST REPLY  DELETE THIS COMMENT

Dr. Hwang seems to assert that those disagreeing with the philosophy and approach of harm reduction in the form it has taken in Canada ignore science in favour of ideology. I strongly challenge this line of... Read more

Time for Reasoned Academic Debate on Safer Injection Facilities

Evan Wood (2007-09-07)

EMAIL REPLY  POST REPLY  DELETE THIS COMMENT

As the external evaluators of the Vancouver medically supervised safer injection facility (SIF), we read the commentary by Dr. Stephen Hwang (REF Open Medicine Commentary) and... Read more
Homelessness and Addictions

by Sandra Klune
September 4, 2007

Bums by Peter Bagge is a great comic e-book (it’s short, just four pages) with some of the most all-around rational views on homelessness I’ve ever read. Includes a description of the Housing First approach, which is to get people sleeping indoors and *then* work on treatment.

In Vancouver, BC the InSite safe injection site illustrates a major roadblock in dealing with homelessness: moral judgments and ideology obstructions science and clinical mental health care. A letter published in Open Medicine signed by 134 doctors, scientists, politicians, police members and community workers protests the federal government’s
Policy-makers may legitimately decide on ethical, moral, political, or economic grounds to severely restrict or even prohibit the use of an intervention, such as Vancouver’s supervised injection site, that careful scientific inquiry has shown to have significant health benefits. In these situations, however, policy-makers must provide cogent reasons for their decision and make the basis for their actions explicit and transparent. Such decisions must not be justified by resorting to deceptive claims that cast doubt on the effectiveness of the intervention, or that raise unsupported fears of harmful side effects.

At the same time, physicians, scientists, and public health professionals must be willing to speak out in the public arena when the accumulated body of research evidence clearly supports a health intervention that faces resistance because of entrenched beliefs. As stated in a declaration by Scientists and Engineers for America, a grassroots organization that counts 15 Nobel laureates among its board of advisors, “[t]he principal role of the science and technology community is to advance human understanding. But there are times when this is not enough. Scientists and engineers have a right, indeed an obligation, to enter the political debate when the nation’s leaders systematically ignore scientific evidence and analysis, [or] put ideological interests ahead of scientific truths.”

Vancouver isn’t even close to adopting a Housing First
Bums and Conservatives

Category: Culture Wars - Drugs - Medicine - Mental Health - Policy & Politics - Religion - Stupid People - Truth - Vice - Webcomics

Posted on: September 5, 2007 8:00 AM, by Sandra Klune

Bums by Peter Bagge is a great comic book (it's short, just four pages) with some of the most accurate and insightful commentary on people, politics and the human condition. It's also quite entertaining. The author combines his wit and the ability to sketch the character of humans in a way that is both funny and spot on. It's a great way to ponder the world around you and laugh at the same time.

Comments

And with the current crop of conservatives in power at the municipal, provincial, and federal level, there will be no further progress in dealing with homelessness and addiction in Vancouver (or other Canadian cities).

Posted by: Richard | September 5, 2007 12:03 PM

Yeah, it's a shame to see Canada, who has done some stuff at least better than we in the states, have crap like this happen.

Honestly, it's almost like some people have a kind of cultural suicide wish - they wish to deny anything that'd actually help people for some sick reason.

Posted by: DragonScholar | September 5, 2007 1:25 PM

Sad but true, both comments.

Posted by: Sandra | September 5, 2007 3:41 PM
Harper Continues To Ignore Evidence Around Safe Injection Site

August 22, 2007

OTTAWA - Prime Minister Stephen Harper must put his personal ideologies aside and heed the scientific evidence that supports Canada's only safe injection site, Liberal Health Critic Bonnie Brown and Senator Larry Campbell said today.

"Today we had a group of 130 prominent doctors, scientists and public health professionals condemning the Harper government for putting political ideology ahead of scientific evidence when considering the future of Vancouver's Insite," said Ms. Brown.
Open Medicine submissions - 2007-08

- Launch April 2007
- 232 submissions
- 139 submissions peer-reviewed
- Days to peer review ~36 d
- Published 54 articles
  - Acceptance rate ~23%
  - Registered website users: 3123
How we do it?

Blood, sweat, mutual support
Collaboration
Passionate volunteers
other journals especially PLoS
Belief that we are making a difference to the way we share scientific knowledge