

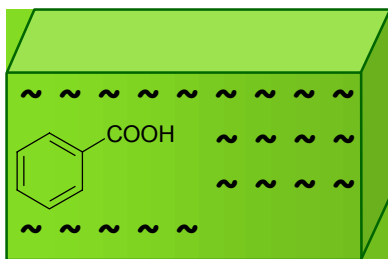
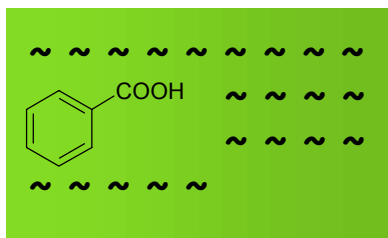
Databases and Documents: Breaking down the Barriers



Doug Hounshell
Skolnik Award Symposium
Chicago ACS Meeting
August 28, 2001

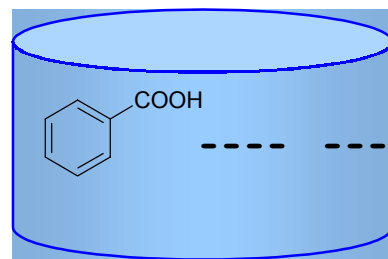
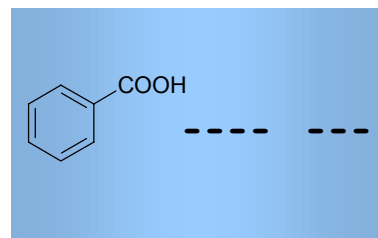
Documents to Databases

Documents

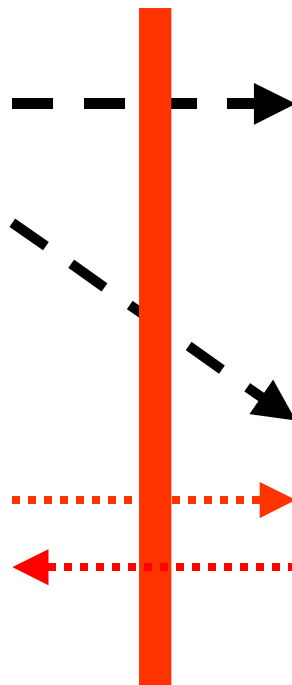


E-Journals

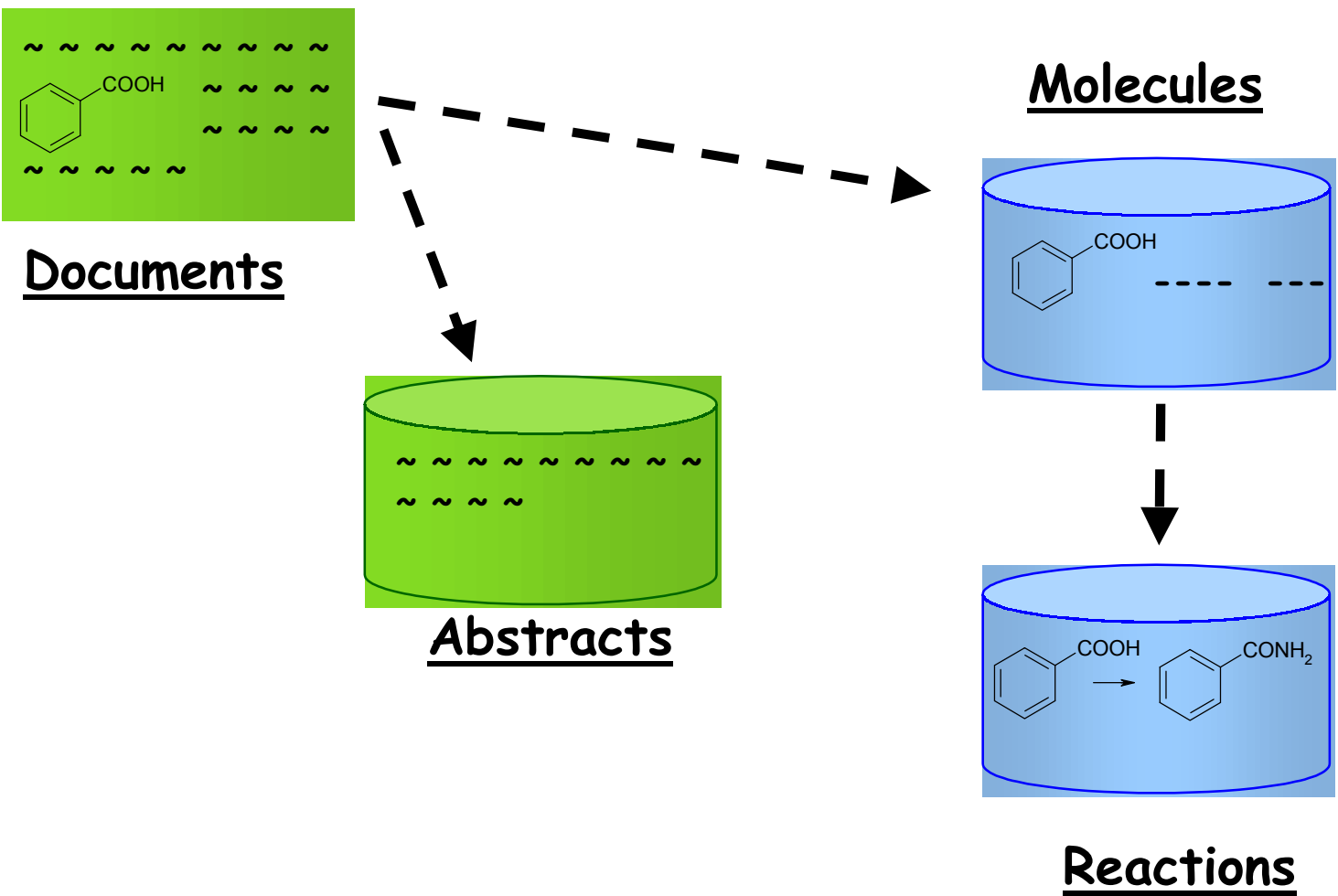
Handbooks

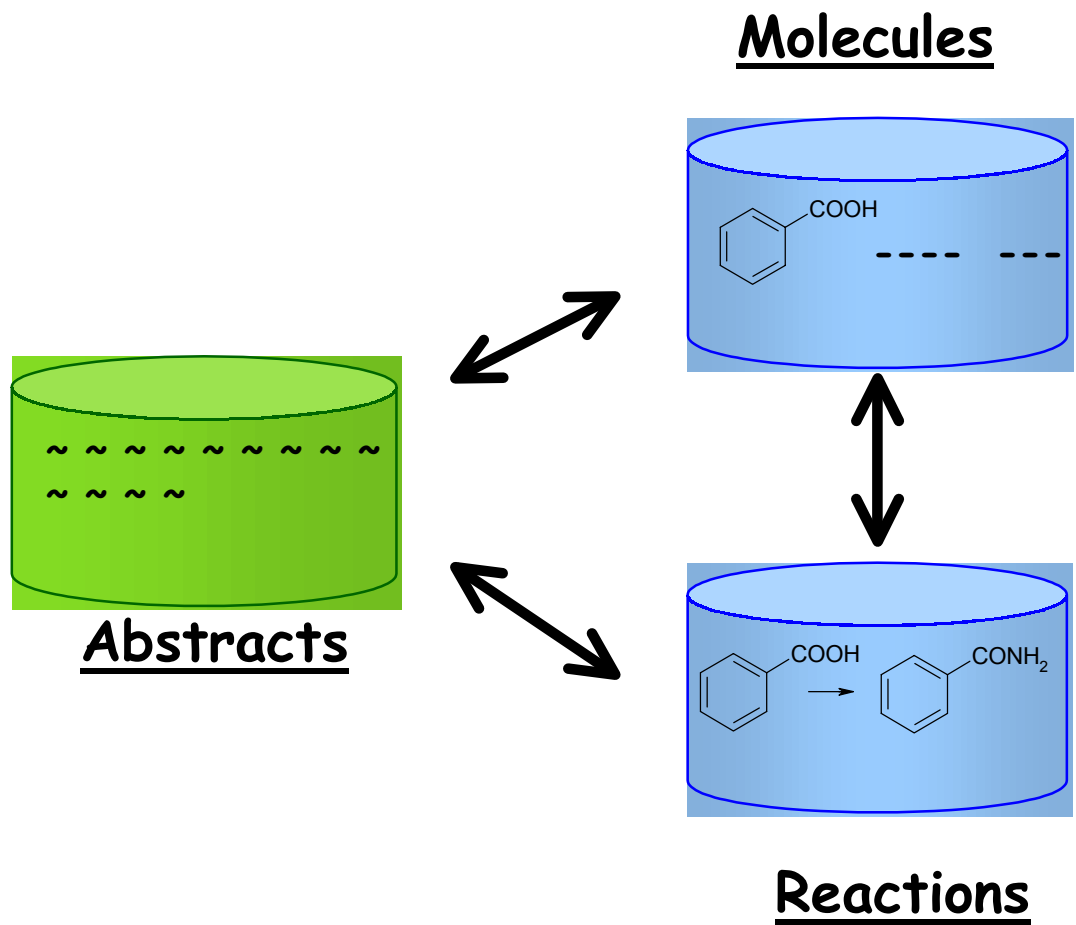


Databases



Beilstein CrossFire





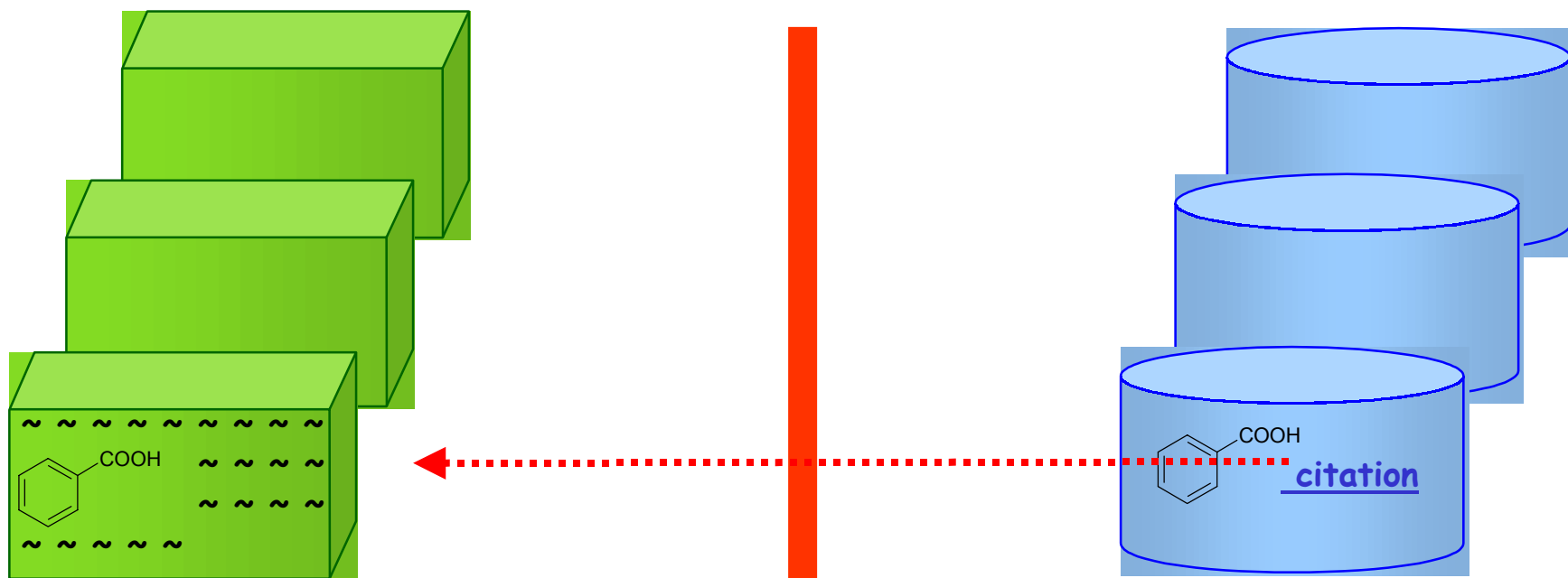
Reality = Multiple Systems

- ▶ But...
 - ◆ Beilstein Commander (mid 90's) was all one system
- ▶ In reality...
 - ◆ Multiple repositories (sources of information)
 - ◆ Multiple systems
- ▶ Intersystem context change
 - ◆ More difficult (e.g. no internal pointers)
 - ◆ Made easier by use of hyperlinking paradigms with the advent of internet technologies and access

- ▶ Problem: Given a citation to a document, retrieve the document
 - ◆ Citation from a database or elsewhere
 - ◆ Retrieve the document or information related to the document

- ▶ Solution: LitLink
 - ◆ Introduced at Boston ACS Fall 1998
 - ◆ Launched at London Online 1998
 - ◆ “One click access to the literature”
 - ◆ <http://www.litlink.com>

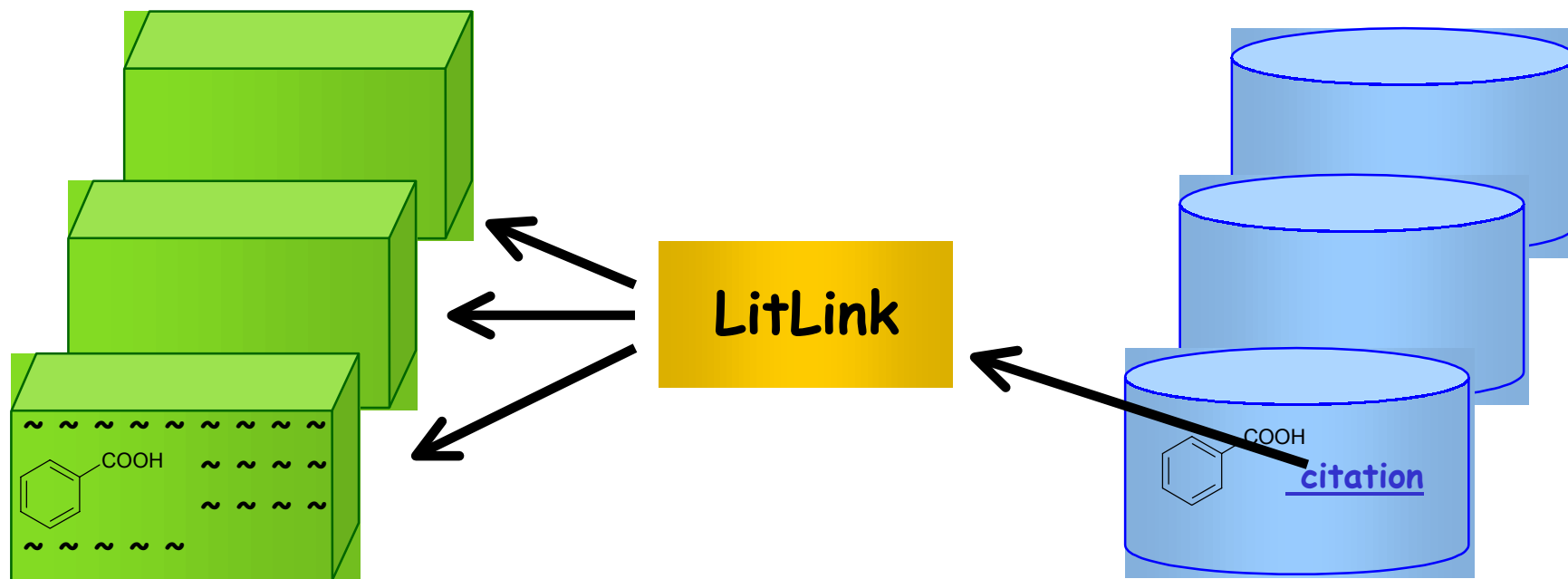
Multiple Systems



Multiple
Document
Repositories

Multiple
Databases

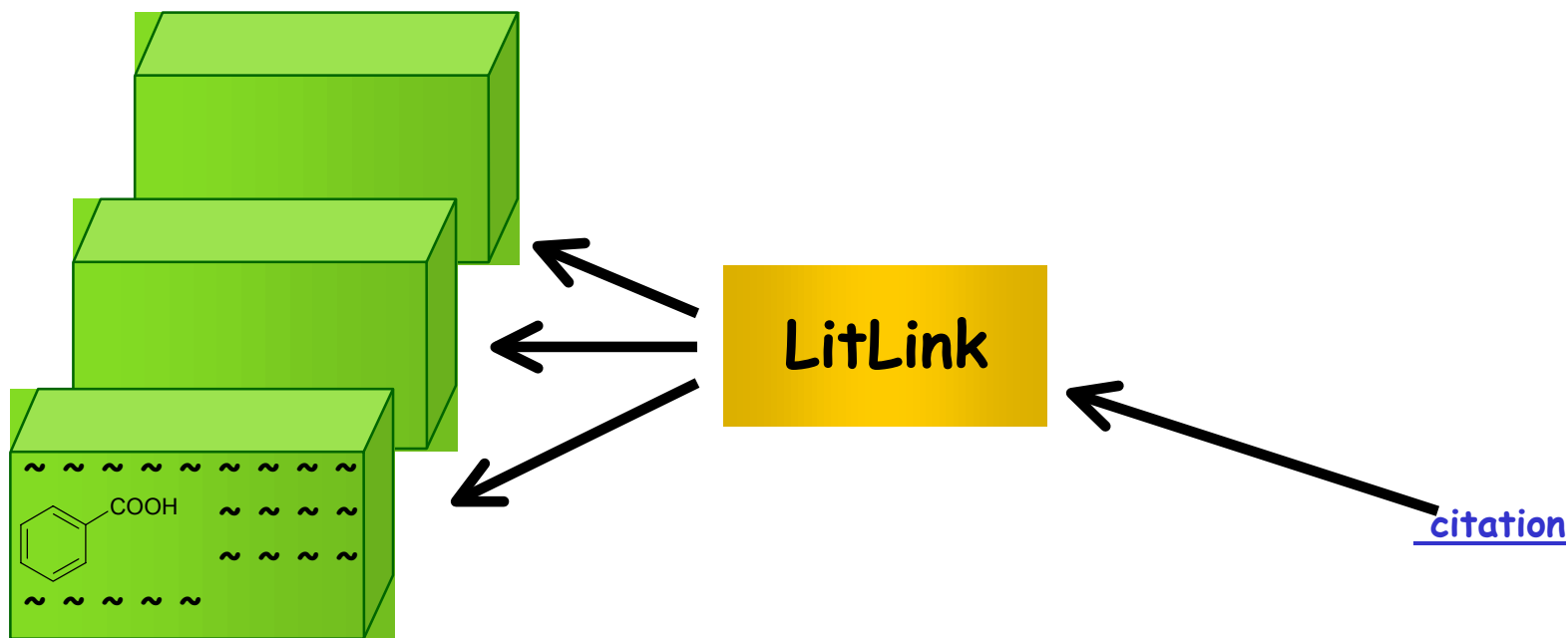
LitLink – Databases to Documents



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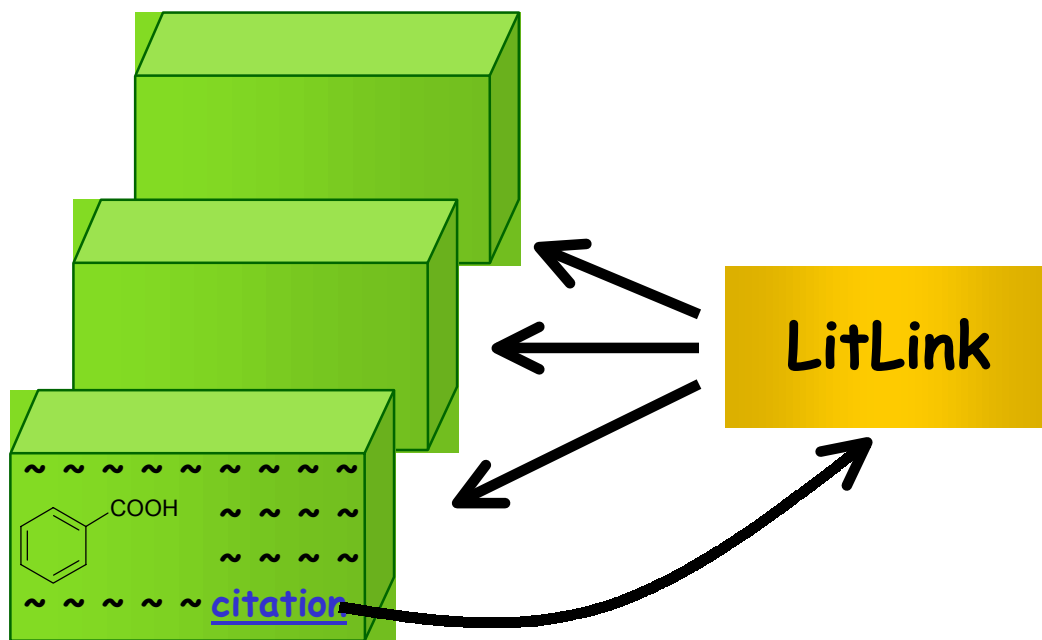
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LitLink "Intermediate Window"



Pergamon

Tetrahedron Letters, Vol. 38, No. 9, pp. 1501-1504, 1997
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0040-4039/97 \$17.00 + 0.00

PII: S0040-4039(97)00140-8

A Modified Sandmeyer Methodology and the Synthesis of (±)-Convolutamidine A.

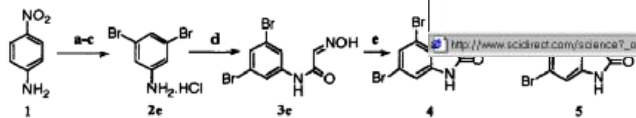
Simon J. Garden*, José C. Torres, Alexandre A. Ferreira, Rosângela B. Silva and Angelo C. Pinto.

Instituto de Química, Departamento de Química Orgânica, Universidade
Fla do Rio de Janeiro, Rio de Janeiro, CEP 21910-240, B

Abstract: (±)-Convolutamidine A (5) has been prepared by a concise synthe using a modified Sandmeyer methodology. The modified Sandmeyer metho to be beneficial for the synthesis of other α -isotonitroacetanilides. The 4 nucleus was further confirmed by comparison with the isomeric 5,7-dibromo © 1997 Elsevier Science Ltd. All rights reserved.

Convolutamidine A (5), a metabolite isolated from the marine Bryoz interesting 4,6-dibromohydroxyoxindole nucleus. This compound has been in the differentiation of HL-60 human promyelocytic leukemia cells. This of this compound, the 4,6-dibromo-2-oxindole nucleus was found to be a 4,6-dibromoaniline was a disappointing intermediate (3e, 10% yield) while the following cy (88%).

3,5-Dibromoaniline was prepared as its hydrochloride salt (2e, Sci nitroaniline (1) in glacial acetic acid⁴ followed by reductive deamination us to form the 3,5-dibromonitrobenzene.⁵ Raney nickel hydrogenation of 3, proceed with difficulty using some published methods of preparation o catalyst was prepared under more extreme conditions⁷ 3,5-dibromoaniline overall yield. The aniline was subsequently precipitated, and recrystallized



Scheme 1. a Acetic acid, Br₂, 98%; b ethanol, NaNO₂, H₂SO₄, 97%; c (i) ethanol, Raney Ni, H₂, (ii) aqueous ethanolic HCl, 86-96%; d Chloral, (H₂NOH)₂H₂SO₄, Na₂SO₄, H₂O/ethanol (3:1 v/v), 82-88%; e 86% H₂SO₄, 80-86%; f acetone, Et₂NH, 77%.

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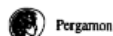
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Search Parameters
CODEN = TELEAY
YEAR = 1997
AUTHOR = GARDEN, S. J., TORRES, J. C., FERREIRA, A. A., SILVA, R. B., PINTO, A. C.
JOURNAL = Tetrahedron Lett
VOL = 38
NO = 9
PG = 1501-1504

Literature Reference
REIRA, A. A.; SILVA, R. B.; PINTO, A. C.; *Tetrahedron Lett* (TELEAY) 1997, 38

Product Yield	Product Grade
54	

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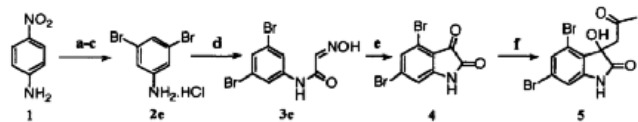
Simon J. Garden*, José C. Torres, Alexandre A. Ferreira, Rosângela B. Silva and Angelo C. Pinto.

Instituto de Química, Departamento de Química Orgânica, Universidade Federal do Rio de Janeiro,
Ilha do Fundão, Rio de Janeiro, CEP 21910-240, Brazil

Abstract: (±)-Convolutamidine A (5) has been prepared by a concise synthesis from 3,5-dibromoaniline using a modified Sandmeyer methodology. The modified Sandmeyer methodology has also been found to be beneficial for the synthesis of other α -isotonitrosoacetanilides. The 4,6-dibromohydroxyoxindole nucleus was further confirmed by comparison with the isomeric 5,7-dibromohydroxyoxindole.
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Convolutamidine A (5), a metabolite isolated from the marine Bryozoan *Amathia convoluta*, presents an interesting 4,6-dibromohydroxyoxindole nucleus. This compound has been described to exhibit a potent activity in the differentiation of HL-60 human promyelocytic leukemia cells.^{1,2} An obvious precursor to the synthesis of this compound, the 4,6-dibromoisatin (4), has been previously described although the global yield from 3,5-dibromoaniline was a disappointing 10%.³ The low yield can be ascribed to inefficient formation of the intermediate α -isotonitrosoacetanilide (3e, 11% yield) while the following cyclisation proceeds in excellent yield (88%).

3,5-Dibromoaniline was prepared as its hydrochloride salt (2e, Scheme 1) by initial bromination of *p*-nitroaniline (1) in glacial acetic acid⁴ followed by reductive deamination using sodium nitrite in acidified ethanol to form the 3,5-dibromonitrobenzene.⁵ Raney nickel hydrogenation of 3,5-dibromonitrobenzene was found to proceed with difficulty using some published methods of preparation of the catalyst,⁶ but when the nickel catalyst was prepared under more extreme conditions⁷ 3,5-dibromoaniline was smoothly produced in excellent overall yield. The aniline was subsequently precipitated, and recrystallised, as its hydrochloride salt (2e).



Scheme 1. a Acetic acid, Br₂, 98%; b ethanol, NaNO₂, H₂SO₄, 97%; c (i) ethanol, Raney Ni, H₂, (ii) aqueous ethanolic HCl, 86-96%; d Chloral, (H₂NOH)₂H₂SO₄, Na₂SO₄, H₂O/ethanol (3:1 v/v), 82-88%; e 86% H₂SO₄, 80-86%; f acetone, Et₃NH, 77%.

Results - Microsoft Internet Explorer

MDL Summary View: Records 50 - 50 of 118

50 [More details for this record](#) [View Scheme\(8720972\)](#)

Reference

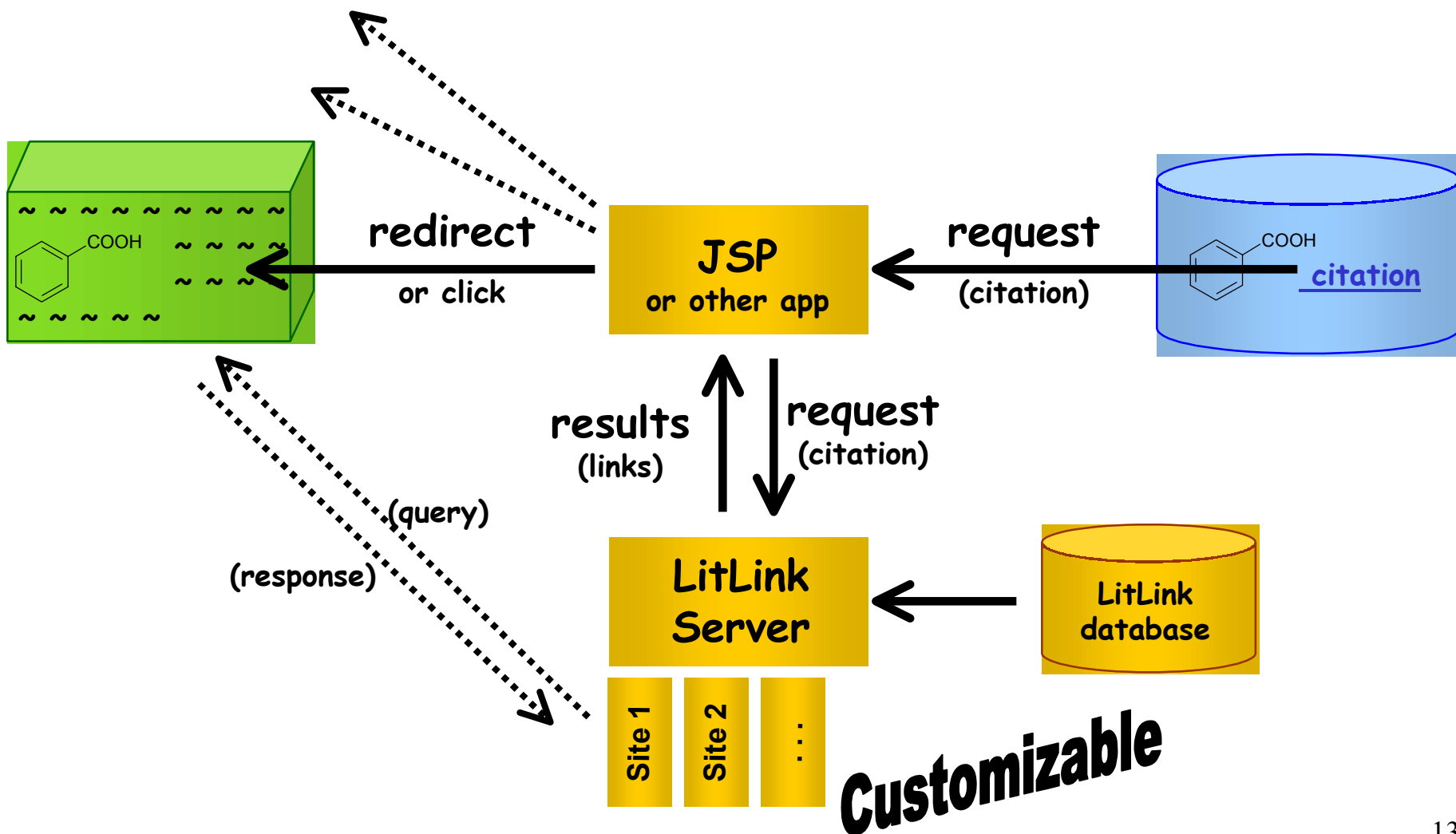
Literature Reference

S. J. GARDEN, J. C. TORRES, A. A. FERREIRA, R. B. SILVA, A. C. PINTO, A. C. PINTO, *Tetrahedron Lett.* 1997, 38, 1501-1504.

Reagents - no data			
Product Yield and Grade			
Vol.	Product No.	Product Yield	Product Grade
1	1	54	

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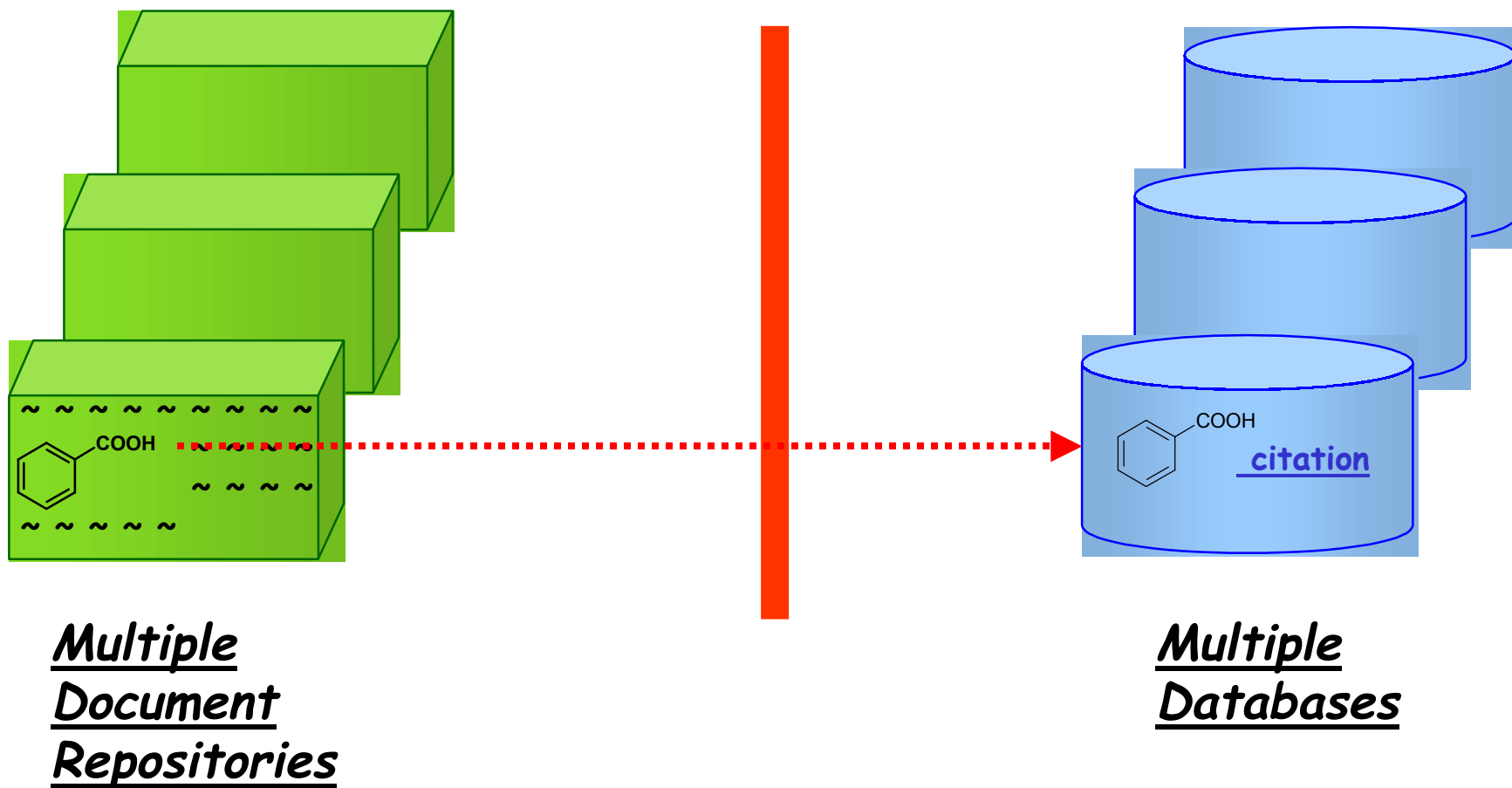
LitLink Architecture



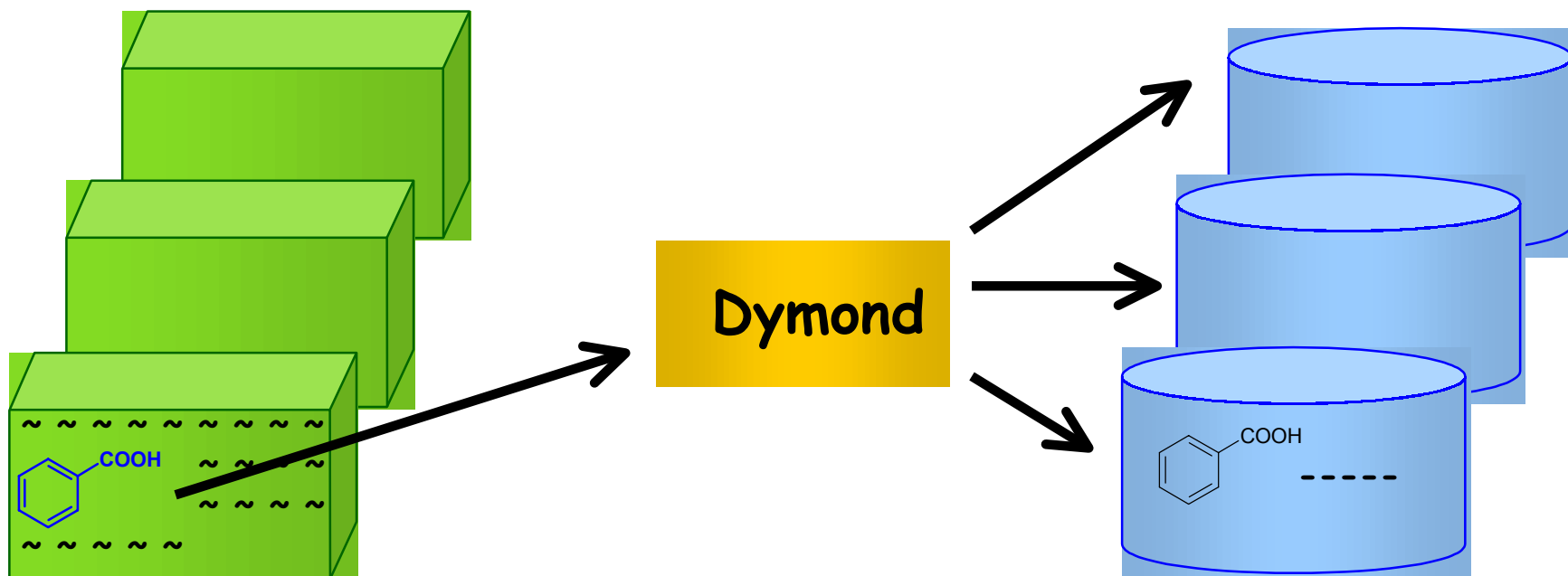
- ▶ Intranet (or internet) service, which
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 - ◆ provides urls (or instructions)
 - ◆ for accessing sites (internal or external systems)
 - ◆ that have the corresponding article (or related info)
- ▶ Results
 - ◆ display choices to the user and link to the selected choice, or ...
 - ◆ automatically redirect to the best choice
- ▶ Customizable – configuration and extension

- ▶ Problem:
 - ◆ Given a chemical structure (e.g. in a document), find information about that structure
- ▶ Solution: Dymond
 - ◆ Introduced at ACS San Diego, Spring 2001
 - ◆ <http://www.dymondlinking.com>

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The chemistry of vicinal tricarbonyls. Formation of oxomalondiamides

[Harry H. Wasserman](#)^a, [Kieseung Lee](#) & [Mingde Xia](#)

[Short Communication] *Tetrahedron Letters* 2000, **41**:15:2511-2514

Department of Chemistry, Yale University, P.O. Box 208107, New Haven, CT 06520-8107, USA

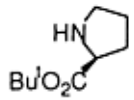
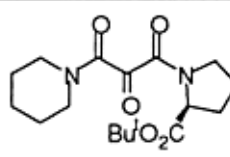
^a Corresponding author

Received 22 December 1999 Accepted 31 January 2000

We now report a further method for forming the tricarbonyl array starting from oxalic acid mono amides which are readily available by monoacylation of an amine such as piperidine with dimethyl oxalate or by treatment of the amine with the acid chloride of oxalic acid monomethyl ester. Hydrolysis of the ester with LiOH yields the corresponding carboxylic acid **1** (~98%).

To form the oxomalondiamides, the monoamide **1** was transformed to the acid chloride and then coupled with the cyano ylide in the presence of BSA to form the diacyl cyano ylide **2**.³ Oxidation of **2** yielded a labile triacyl nitrile **3** which was trapped by nucleophiles to give products **4**⁴ ([Table 1](#)).⁵

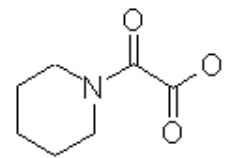
Table 1 Coupling of tricarbonyl intermediate **3** with various nucleophiles^a

Entry	NuH	Products (4)	Yield, %
a			89



The chemistry of vicinal tricarbonyls. Formation of oxomalondiamides

Harry H. Wasserman, Kieseung Lee, Mingde Xia
Tetrahedron Letters 2000, 41 : 15: 2511-2514



1

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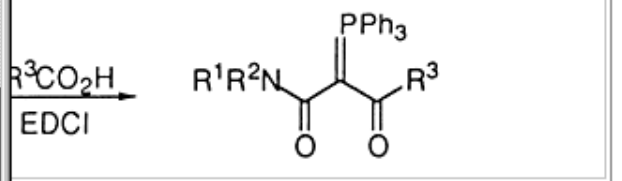
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coupling with a carboxylic acid to form the ylide precursor

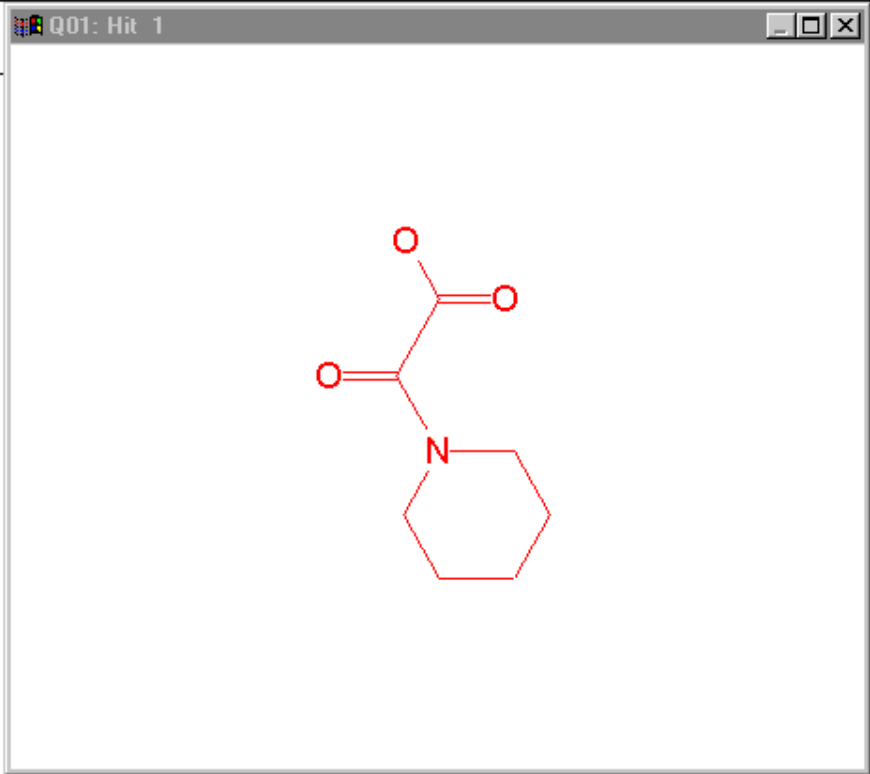
available by monoacylation of an amine such as piperidine with LiOH yields the corresponding carboxylic acid [1](#)

ylide in the presence of BSA to form the diacyl cyano ylide [1](#)

			Yield, %
			89
b			51
c			64

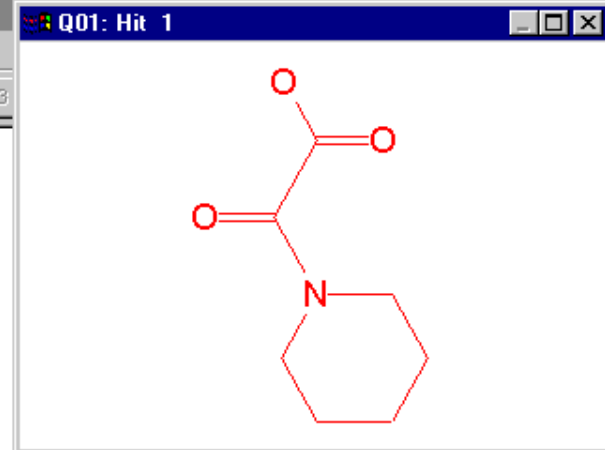
Substance

Beilstein Registry Number 130543
 Beilstein Preferred RN 4706-33-6
 CAS Registry Number 4706-33-6
 Chemical Name [oxo-piperidino-acetic acid](#)
 Autname oxo-piperidin-1-yl-acetic acid
 Molecular Formula $C_7H_{11}NO_3$
 Molecular Weight 157.17
 Lawson Number [24081](#), [1516](#)
 Compound Type heterocyclic
 Constitution ID 126811
 Tautomer ID 135802
 Beilstein Reference 0-20-00-00048, 6-20
 Entry Date 1988/06/27
 Update Date 2000/07/18

**Field Availability List 1-4 of 4** [Home](#)

Code	Field Name	Occ.
<u>RX</u>	Reaction	12
<u>RXB</u>	Non-Graphical Reaction	3
<u>CPD</u>	Crystal Property Description	1
<u>MP</u>	Melting Point	2

Reaction Classification	Preparation
Yield	53 percent (BRN=8058387)
Reagent	ammonium persulfate, silver nitrate
Solvent	acetonitrile
	H ₂ O
Time	2 hour(s)
Temperature	70 C



Ref. 1 [6118752](#), [LitLink](#) ; Journal; Kraus, George A.; Melekhov, Alex; TELEAY; Tetrahedron Lett.; EN; 39; 23; 1998; 3957-3960.

Reaction 12 of 12 [Home](#)

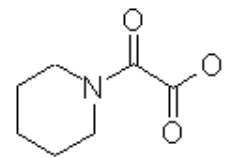
Reaction ID	5317651
Reactant BRN	130543 oxo-piperidino-acetic acid
Product BRN	8480511 oxo-piperidin-1-yl-acetyl chloride
No. of Reaction Details	1
Reaction Classification	Preparation
Reagent	oxalyl chloride
	DMF
Solvent	CH ₂ Cl ₂
Time	3 hour(s)
Temperature	0 - 20 C
Reaction Type	Chlorination

Ref. 1 [6220062](#), [LitLink](#) ; Journal; Wasserman, Harry H.; Lee, Kieseung; Xia, Mingde; TELEAY; Tetrahedron Lett.; EN; 41; 15; 2000; 2511 - 2514.



The chemistry of vicinal tricarbonyls. Formation of oxomalondiamides

Harry H. Wasserman, Kieseung Lee, Mingde Xia
Tetrahedron Letters 2000, 41 : 15: 2511-2514



1

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 Exact 60% similar Substructure

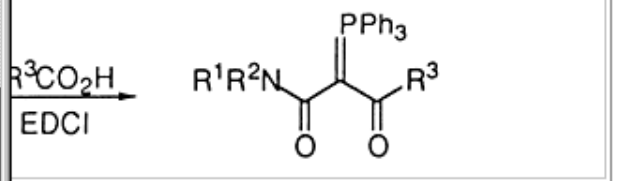
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Search for properties in the ACD/Labs databases [Go](#) [Help](#)
 Exact 60% similar Substructure
 logP pKa

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coupling with a carboxylic acid to form the ylide precursor

available by monoacylation of an amine such as piperidine with LiOH yields the corresponding carboxylic acid [1](#)

ylide in the presence of BSA to form the diacyl cyano ylide [1](#)

			Yield, %
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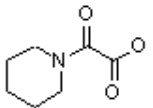
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AutoNom Standard Name

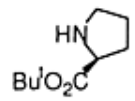
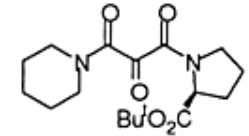

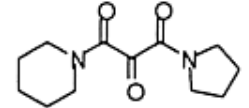
Name:	Oxo-piperidin-1-yl-acetic acid
Structure:	
Click here to expand structure	

[Back to AutoNom]

starting from oxalic acid mono such as piperidine with dimethyl acic acid monomethyl ester. kylic acid **1** (~98%).

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leophiles^a

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The chemistry of vicinal tricarbonyls. Formation of oxomalondiamides
Harry H. Wasserman, Kieseung Lee, Mingde Xia
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Display Hits - [Q01:BS0004PR hit 1 of 1]

1
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Substance

Beilstein Registry Number	130543
Beilstein Preferred RN	4706-33-6
CAS Registry Number	4706-33-6
Chemical Name	<u>oxo-piperidino-acetic acid</u>
Autoname	oxo-piperidin-1-yl-acetic acid
Molecular Formula	C ₇ H ₁₁ NO ₃
Molecular Weight	157.17
Lawson Number	<u>24081</u> , <u>1516</u>
Compound Type	heterocyclic
Constitution ID	126811
Tautomer ID	135802
Beilstein Reference	0-20-00-00048, 6-20
Entry Date	1988/06/27
Update Date	2000/07/18

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We now report a further method for the synthesis of oxomalondiamides from oxalic acid mono amides which are such as piperidine with diacyl chloride of oxalic acid and the corresponding secondary amine.

To form the oxomalondiamides, the diacyl chloride and then coupled with the diacyl cyano ylide 2. Oxidation of the intermediate was trapped by nucleophiles to give piperidine oxomalondiamide.

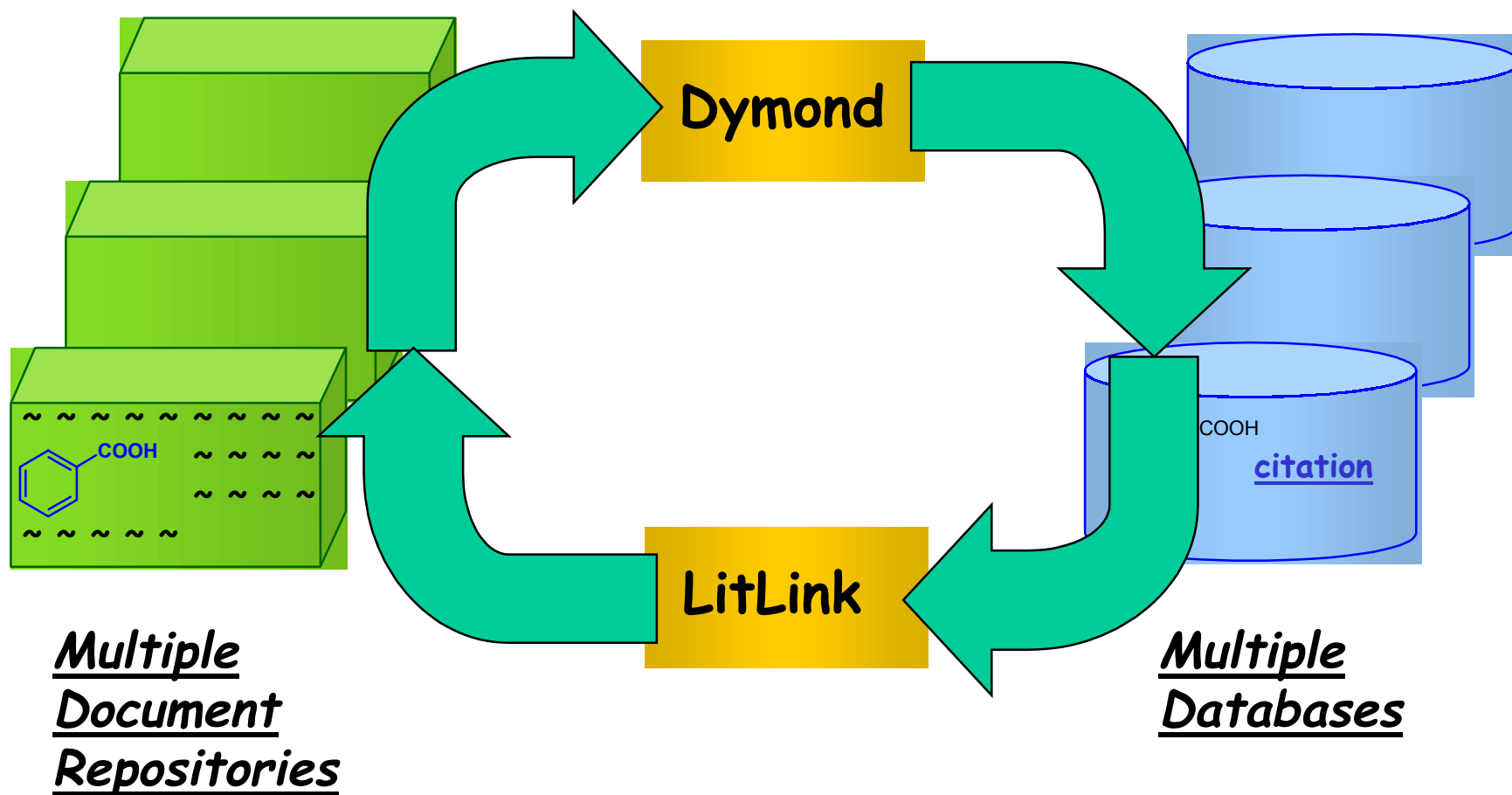
Table 1 Coupling of tricarbonyl intermediate 3 with various nucleophiles

Entry	NuH	Products (4)
a		

Field Availability List 1-4 of 4 [Home](#)

Code	Field Name	Occ.
<u>RX</u>	Reaction	12
<u>RXB</u>	Non-Graphical Reaction	3
<u>CPD</u>	Crystal Property Description	1
<u>MP</u>	Melting Point	2

Completed Circuit



LitLink and Dymond Philosophy

- ▶ The link is a query
- ▶ Multiple queries from one link
- ▶ Dynamic links

The Link is a Query

- ▶ Query Language => Query by Form => Query Links
 - ◆ Select _____ (determined by type of service linked to)
 - From _____ (determined by link location)
 - Where _____ (determined by link context)
- ▶ LitLink, e.g.
 - ◆ Select article
 - From ScienceDirect
 - Where citation = "Tet. Lett., 42, 3271 (2001)"
- ▶ Dymond, e.g.
 - ◆ Select molecule
 - From Beilstein
 - Where structure = <molfile>

Multiple Queries from One Link

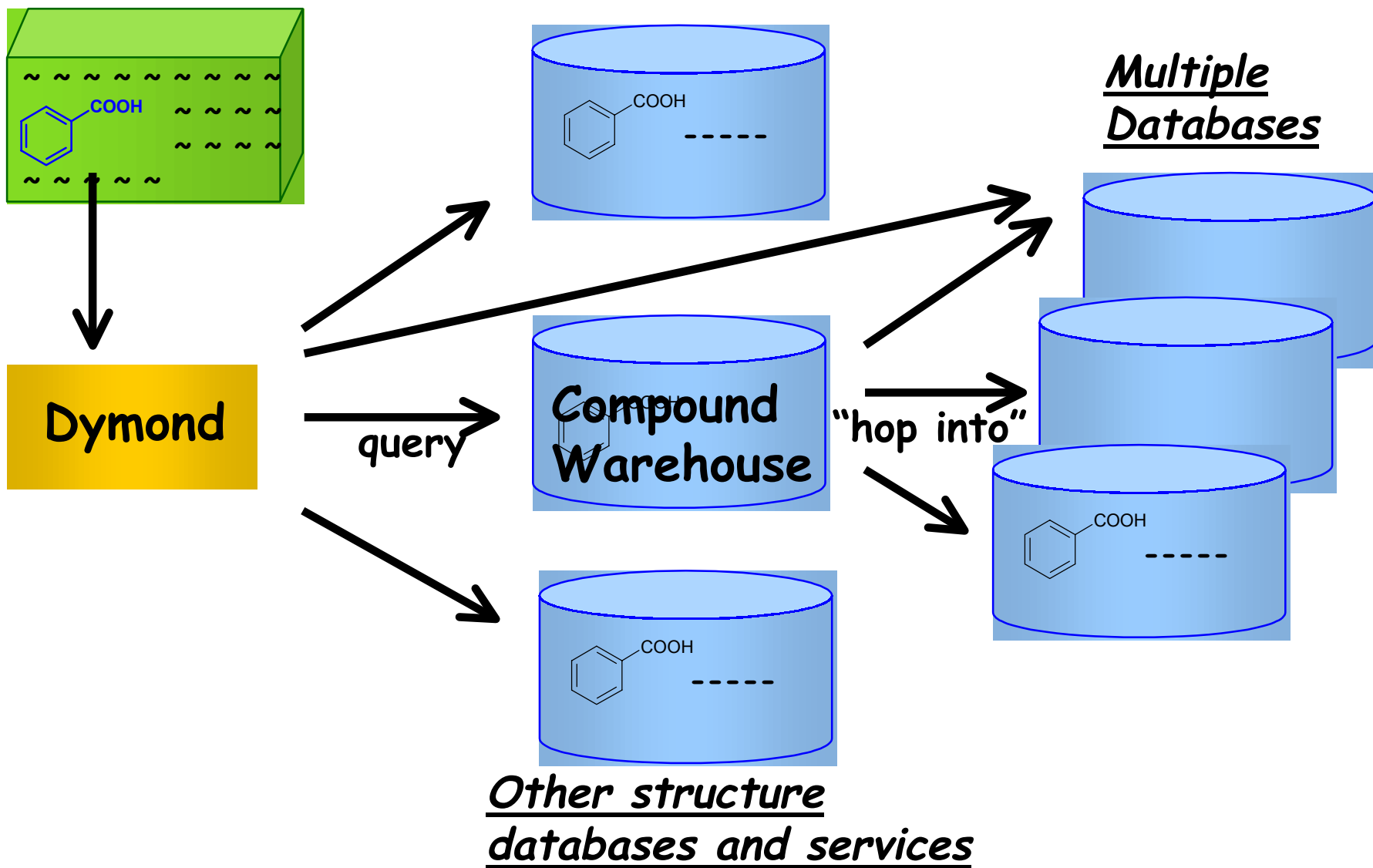
- ▶ The “Intermediate Window”
- ▶ Gives user choice of service without cluttering the initial rendering
- ▶ Gives user opportunity to refine query (e.g. specify operator)
- ▶ Can be configured for default behavior

- ▶ Links are Queries – not Answers
 - ◆ i.e. we store the **query** in the link, not the **answer**
 - ◆ or even that there **is** an answer
- ▶ + Immediate access
 - ◆ to new information
 - ◆ in (new) target sources
- ▶ - “Dead links”
 - ◆ But sometimes no information **is** information
- ▶ Three choices
 - ◆ Pay price by pre-computing (synchronization?)
 - ◆ Pay price at render time (link contains answers)
 - ◆ Pay price at request time (link contains query)

- ▶ Compound Warehouse
 - ◆ One query access to normalized structures from a variety of structure databases
 - ◆ In development

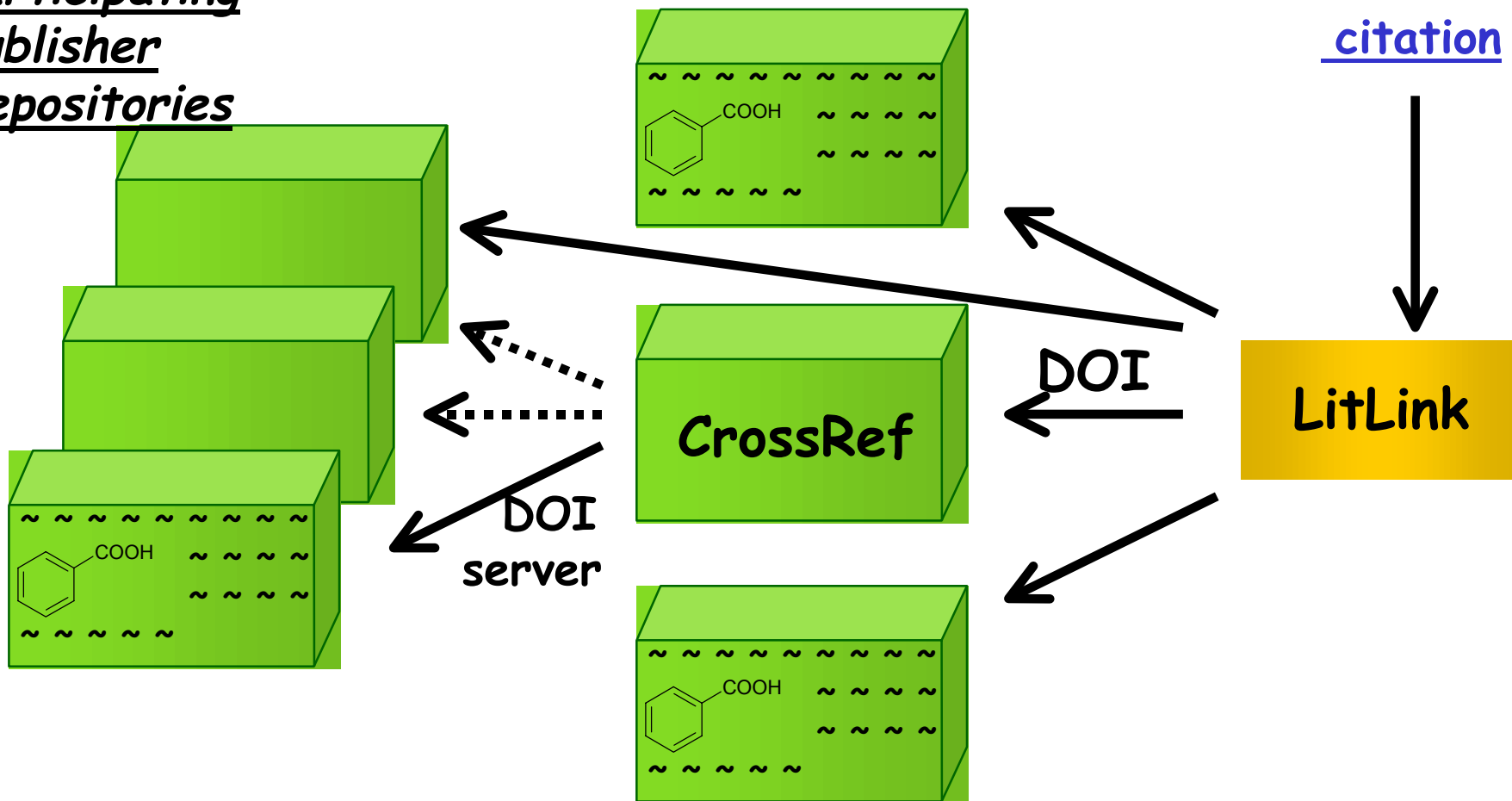
- ▶ CrossRef
 - ◆ Consortium of publishers
 - ◆ Access to electronic articles via DOI

Compound Warehouse



CrossRef

Participating
Publisher
Repositories



Other document
databases and services

- ▶ LitLink and Dymond provide
 - ◆ Integration of documents and databases
 - ◆ Linking to multiple sources
 - ◆ Dynamic (query-based) linking

- ▶ Compound Warehouse and CrossRef
 - ◆ Effectively reduce the number of sources
 - ◆ But not to 1

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