Alfred Bader fonds

Correspondence

Toronto, Univ. of
1993-2005

The Chemical Institute of Canada
L'Institut de chimie du Canada

130 Slater Street, Suite 550
Ottawa, Ontario, Canada K1P 6E2
Tel.: (613) 232-6252
Fax: (613) 232-5862

130, rue Slater, bureau 550
Ottawa (Ontario) Canada K1P 6E2
Tél. : (613) 232-6252
Téléc. : (613) 232-5862

info@cheminst.ca
www.cheminst.ca

September 9, 2005

Dr. Mark Lautens
University of Toronto
Department of Chemistry
80 St. George Street
Toronto, ON M5S 3H6

Dear Dr. Lautens:

On behalf of Dr. Yves Deslandes, FCIC, President of The Canadian Society for Chemistry, I am very pleased to inform you that you are the winner of the **2006 Alfred Bader Award in Organic Chemistry**.

This award consists of a $3,000 cash prize, a framed scroll and travel expenses to attend the conference up to a maximum of $500. This award will be presented to you during the *89th Canadian Chemical Conference*, which is taking place in Halifax, Nova Scotia from May 27 – 31, 2006.

A member of the Halifax Conference Organizing Committee will be in touch with you directly regarding your award lecture at the conference. Please note that the *title and abstract of your presentation* should be submitted, to Myra Gordon, Technical Program Administrator, as well as Gale Thirlwall-Wilbee, Awards Coordinator by November 30, 2005. Their e-mails are program@csc2006.ca and gwilbee@cheminst.ca respectively.

You will need to register for the conference as a regular invited speaker. You do not, however, need to register for the awards dinner as the CIC will take care of those details and costs for you and one accompanying person.

Please forward a photograph (a head and shoulders photo is preferred) and a brief biography of yourself (100-200 words). This information will be included in an upcoming issue of *Canadian Chemical News* and posted on the Web site. Please send both your biography and photo via email to Gale Thirlwall-Wilbee at: gwilbee@cheminst.ca. Digital photos must be a minimum of 300 dpi as sized in order to be used for hard copy printing.

... /2

Canadian Society for Chemistry
Société canadienne de chimie

Canadian Society for Chemical Engineering
Société canadienne de génie chimique

Canadian Society for Chemical Technology
Société canadienne de technologie chimique

Once again, we would like to extend our sincere congratulations on winning this prestigious award.

Sincerely,

Roland Andersson, MCIC
Executive Director
The Chemical Institute of Canada

c,c, Yves Deslandes, FCIC, President, The Canadian Society for Chemistry
Scott Mabury, Nominator
Alfred Bader, FCIC
Jan Kwak, FCIC, Halifax Conference Chair
Russell Boyd, FCIC, Halifax Technical Program Chair
Myra Gordon, MCIC, Halifax Technical Program Administrator
Gale Thirlwall-Wilbee, Awards Coordinator, The Chemical Institute of Canada

Department of Chemistry
UNIVERSITY OF TORONTO

phone (416) 978-3564
http://www.chem.utoronto.ca/

Lash Miller Chemical Laboratories 80 St. George Street Toronto, Ontario M5S 3H6

Trip file

Dr. Alfred Bader and Dr. Isabel Bader,
924 East Juneau, Suite 622,
Milwaukee,
Wisconsin 53202,
U.S.A.

April 24th, 1997

Dear Alfred and Isabel,

I simply wanted to say how delighted I am that you will be in the Department once again to give a talk on May 28th. I am also delighted that our Department is in the unique position of having three members of our Faculty as winners of the CSC Alfred Bader Award, Bryan Jones, Ron Kluger and Bob McClelland. This is indeed a great honour for the Department.

I am looking forward to seeing you on May 28th. With best personal regards,

Yours sincerely,

Martin Moskovits
Professor and Chair

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

(414) 962-5169

May 19, 2005

Dr. Robert C. Brandeis, Chief Librarian
Victoria University
Toronto ON M5S 1K7
CANADA

Dear Dr. Brandeis,

Thank you for your e-mail of May 16th.

Enclosed please find my cheque for C $179 for the ten books and the shipment of the letters.

I have been invited to speak to the local section of the Queen's alumni in Toronto at the Royal York Hotel at their breakfast meeting on Thursday, September 10th, after which we will travel to Queen's for my 60th reunion.

Would it be possible for you to get those ten books to me and for me to return Isabel's original letters which you sent me then?

Of course we very much hope to meet you shortly at Herstmonceux Castle.

With best wishes I remain

Yours sincerely,

Alfred Bader
AB/az
Enc. – ck.

Subject: Re: books etc
From: "Robert C. Brandeis" <robert.brandeis@utoronto.ca>
Date: Mon, 16 May 2005 11:49:38 -0400
To: Alfred Bader Fine Arts <baderfa@execpc.com>

Hello Dr. Bader, I am now back at the Library having been to Montreal to visit my Mother..she is in her 100th year and still living more or less independently !

The books are $15 CDN each so $150 for the 10 (no GST tax!)

The package of letters was $29 but I don't expect you to pay for this as I was pleased to be able to send them and we expect to have some costs to service our various special collections.

Have a good flight and I hope to be able to meet with you in the UK. Best wishes, Robert

On 11 May 2005 at 11:52, Alfred Bader Fine Arts wrote:

> Robert C. Brandeis wrote:
> Hello Dr. Bader, I now have ten (10) copies of the book for you and they are here in my office at the Vic Library.
>
> I am going to Montreal tomorrow for a few days but will be back in the office on Monday.. I am still scheduled to go to London on the 19th and if I don't speak to you before that I will try to contact you from there. Best wishes, Robert
>
> Robert C. Brandeis
> Chief Librarian
> Victoria University
> Toronto On M5S 1K7
>
> _____
> This message scanned for viruses by CoreComm

Dear Dr. Brandeis,

Thank you so much for your e-mail of today.

Of course we very much hope to be able to meet you at Herstmonceux Castle at the end of the month.

Could you please e-mail me how much I owe you in Canadian dollars for the ten books and for the package of letters which you sent me so very promptly.

With many thanks,
Alfred Bader

TAX OVERPAID

FAX COVER PAGE

Date: May 1, 2000

Fax to 905 829 9292

To: Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin

To Mr. Ward
EA Canada

Fax No.: 414-277-0709

From: Professor A. G. Brook
Tel. (416) 978-3573
Fax (416) 978-8775
E-mail abrook@alchemy.chem.utoronto.ca

Could we meet at 3 pm next Monday - Prof. Brook is on the 6th floor. Best wishes Anna Bader

Number of Pages to Follow Cover Page: 0

MESSAGE

Dear Dr. Bader:

Thanks for your letter of April 24th which I received only this morning indicating that you will be in Toronto next weekend and that we could arrange for the sale of my samples. While I will be out of town for the weekend, I will be back on May 8th, and I will arrange to be in the Department by mid afternoon (say 3.00 pm). I trust that time will be suitable to you, and a representative from Sigma-Aldrich, and I will try to arrange that the Chairman of the Department, David Farrar, also be present. I look forward to seeing you then.

Yours sincerely

Adrian Brook

A. G. Brook
Professor of Chemistry

[illegible]

[illegible]

[illegible]

[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

Post-it® Fax Note 7671	Date 25/4	# of pages ▶ 1
To MR. WARD	From AB	
Co./Dept. ES Canada	Co.	
Phone #	Phone #	
Fax # 416 [illegible]	Fax #	

April 24, 2000

Professor Adrian Brook
Department of Chemistry
University of Toronto
Lash Miller Chemical Laboratories
80 St. George Street
Toronto, Ontario M5S 3H6
CANADA

Dear Professor Brook,

I am happy to have your letter of April 18th, regarding your most interesting collection of research samples.

Isabel and I plan to be in Toronto from Sunday afternoon, May 7th, until late Tuesday afternoon, May 9th. We will be staying very close to the Chemistry Department and of course also to the Isabel Bader Theatre being built. Please let me know when would be a good time to visit you.

Perhaps it would also be possible to have someone from Sigma-Aldrich Canada join us and then – if we agree on a fair price – take the samples for shipment to Milwaukee.

The last time we helped acquire a Canadian collection was that of Professor Ian Spenser at McMaster and the shipment through Sigma-Aldrich Canada to Milwaukee went flawlessly.

With all good wishes and best regards, also to your son, I remain

Yours sincerely,

Alfred Bader
AB/az

Department of Chemistry
UNIVERSITY OF TORONTO

phone (416) 978-3564
http://www.chem.utoronto.ca/

Lash Miller Chemical Laboratories 80 St. George Street Toronto, Ontario M5S 3H6

direct
416 978 3573

April 18, 2000

To Bob Buckley
Please call me to discuss
Alfred

Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin 53202
USA

Dear Dr. Bader:

I haven't had the pleasure of seeing you or Mrs. Bader for some time but I can tell you that the theatre under construction at Victoria College (my alma mater) toward which Mrs. Bader so generously contributed, appears to be coming along well.

Several times in the past, including your letter of October 30, 1995, you indicated that Aldrich would be interested in acquiring my collection of samples when I finally give up active laboratory research. That time now seems to have arrived since I am no longer active in the laboratory myself and no longer have post-doctoral fellows working with me.

When you saw my samples in 1995, there were eleven cardboard sample boxes, each 3" x 12" x 5", nominally containing 100 samples, although not all the boxes were full. What I didn't remember to show you were four much larger aluminum boxes (approx. 9" x 12" x 3") mostly containing larger samples, some as large as 10 grams, particularly of compounds we have been working with in the last few years. There are probably another 200 samples in these boxes, although some will be duplicates of compounds in the cardboard boxes. These sample boxes are available for collection at any time at your convenience.

I hope that you are keeping well, and look forward to hearing from you in the near future.

Yours sincerely

Adrian Brook

A. G. Brook
Professor of Chemistry

cc: Prof. David Farrar, Chairman

Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin 53202
Phone: 414/277-0730
Fax: 414/277-0709
E-mail: baderfa@execpc.com

A Chemist Helping Chemists

April 25, 2000

Professor William F. Reynolds
Department of Chemistry
University of Toronto
80 Saint George Street
Toronto, Ontario M5S 1A1
CANADA

Dear William,

Isabel and I plan to be in Toronto from Sunday, May 7th, to late afternoon of Tuesday, May 9th.

May we stop by and perhaps look at your final draft of the Loschmidt paper? Has that been submitted and perhaps even accepted?

With best wishes I remain

Yours sincerely,

Alfred Bader
AB/az

Sent JRD catalogue
on 5-11-2000

AB/AZ

September 17, 2003

UNIVERSITY OF TORONTO *at* MISSISSAUGA
A GREAT UNIVERSITY FOR A GREAT COMMUNITY

Dr. Alfred Bader
2961 Shepard Avenue
Milwaukee, Wisconsin
U.S.A.
53211 - 3435

Dear Dr. Bader,

Enclosed is a cheque for $412.42 to cover the portion of your expenses incurred while speaking at the Canadian Perspectives Series here at the University of Toronto at Mississauga (UTM) last May.

The Associates of Erindale College (UTM), who organize the perspectives series, appreciate the time and obvious care you took in preparation for your talk which also included wonderful slides of paintings in your personal collection. Thank you for such an insightful and entertaining presentation.

We wish you well in your future endeavours and all the best to both you and Isabel.

Sincerely yours,

Maryann Wells

Maryann Wells
for The Associates of Erindale College (UTM)

3359 Mississauga Road North, Mississauga, Ontario L5L 1C6
www.utm.utoronto.ca

Subject: Message for Drs. Alfred and Isabel Bader
From: Vic Alumni Office <alumni.vic@utoronto.ca>
Date: Tue, 08 Jun 2004 14:35:55 -0400
To: baderfa@execpc.com

Hello,
A classmate of Dr. Isabel Bader, a Mr. Cyril Hammond, has requested your contact information. He mentioned that Dr. Bader had given him his card at a recent Victoria College Spring Reunion event but unfortunately Mr. Hammond has since lost the card. Since we do not give out the personal information of our alumni/ae I am writing to ask permission to give it out to Mr. Hammond.

Patricia Glover
Victoria Alumni Office

--
Victoria Alumni Office
150 Charles St. W.
Toronto ON M5S 1K9
TEL: (416) 585-4500
FAX: (416) 585-4594
http://vic1.utoronto.ca

A very nice man — Please give info.

This message scanned for viruses by CoreComm

Please tell John Long that I want to give talk #3 on my menu: Auspitz, Canyon & Lapchinski.

OK w/Isabel. 2 yrs

Returning Dec. 21 is fine
You need Isabel's "pin #"
What is that?
For BA Executive Club
is 47839260

Yes Herbert
A

1997 DIRECTORY OF CHEMISTS RESEARCH

File - Reynolds Toronto

Tong Jiang, Alan J. Lough, Geoffrey A. Ozin, David Young and Robert L. Bedard, Synthesis and Structure of the Novel Nanoporous Tin(IV) Sulfide Material TPA-SnS-3, Chem. Mater., 7, 245-8(1995).

Oemer Dag, Alex Kuperman and Geoffrey A. Ozin, $Si_{1-x}Ge_xY$ alloy nanocluster materials. Chemical vapor deposition of Si_2H_6/Ge_2H_6 mixtures of zeolite Y, Mater. Res. Soc. Symp. Proc., 358, 87-92(1995).

Geoffrey A. Ozin, Nanomaterials: endosemiconductors and exosemiconductors, Adv. Chem. Ser., 245, 335-71(1995).

Raz Jelinek, Andrzej Malek and Geoffrey A. Ozin, ^{23}Na Synchronized Double-Rotation NMR Study of Cs^+, Ca^{2+}, and La^{3+} Cation-Exchanged Sodium Zeolite Y, J. Phys. Chem., 99, 9236-40(1995).

Oemer Dag, Alex Kuperman and Geoffrey A. Ozin, Nanostructures. New forms of luminescent silicon, Adv. Mater. (Weinheim, Ger.), 7, 72-8(1995).

Patricia Enzel, Grant S. Henderson, Geoffrey A. Ozin and Robert L. Bedard, Imaging the surfaces of nanoporous semiconductors by atomic force microscopy, Adv. Mater. (Weinheim, Ger.), 7, 64-8(1995).

Homayoun Ahari, Carol L. Bowes, Tong Jiang, Alan Lough, Geoffrey A. Ozin, Robert L. Bedard, Srebri Petrov and David Young, Nanoporous tin(IV) chalcogenides. Flexible open-framework nanomaterials for chemical sensing, Adv. Mater. (Weinheim, Ger.), 7, 375-8(1995).

Homayoun Ahari, Geoffrey A. Ozin, Robert L. Bedard, Srebri Petrov and David Young, Synthesis and compositional tuning of the band properties of isostructural tetramethylammonium (TMA)-SnS_xSe_{1-x} nanoporous materials, Adv. Mater. (Weinheim, Ger.), 7, 370-4(1995).

Andrzej Malek and Geoffrey Ozin, On the nature of methyltrioxorhenium(VII) encapsulated in zeolite Y, Adv. Mater. (Weinheim, Ger.), 7, 160-3(1995).

Tong Jiang, Geoffrey A. Ozin and Robert L. Bedard, Nanoporous tin(IV) sulfides. Thermochemical properties, Adv. Mater. (Weinheim, Ger.), 7, 166-70(1995).

Scott Oliver, Alex Kuperman, Neil Coombs, Alan Lough and Geoffrey A. Ozin, Lamellar aluminophosphates with surface patterns that mimic diatom and radiolarian microskeletons, Nature (London), 378, 47-50(1995).

S. J. Kirkby, A. J. Lough and G. A. Ozin, Crystal structure of potassium aluminum fluoride phosphate, $KAlFPO_4$, Z. Kristallogr., 210, 956(1995).

Scott Oliver, Geoffrey A. Ozin and Linda A. Ozin, Skeletons in the cupboard. Rediscovery in science, Adv. Mater. (Weinheim, Ger.), 7, 948-51(1995).

Geoffrey A. Ozin and Scott Oliver, Skeletons in the beaker. Synthetic hierarchical inorganic materials, Adv. Mater. (Weinheim, Ger.), 7, 943-7(1995).

Scott Oliver, Neil Coombs and Geoffrey Ozin, A., Synthetic hollow aluminophosphate microspheres, Adv. Mater. (Weinheim, Ger.), 7, 931-5(1995).

A. Malek, Synthesis and characterization of $n(WO_{3-x})$-$M_{56}Y$, redox-tunable tungsten oxides in zeolite Y. (D)

C. L. Bowes, Low dimensional tin sulfide materials. (D)

S. J. Kirkby, Spectroscopy and crystallography of metal germanium chalcogenide framework materials and precursors. (D)

POË, ANTHONY JOHN (b. 1929), Professor Emeritus. B.Sc., 1951, Oxford University; M.A., 1954, Oxford University; Ph.D., 1961, London University; D.I.C., 1961, Imperial Coll. (London); D. Sc., 1971, London University; Sc.D., 1990, Cambridge University. *Inorganic Chemistry*. Kinetic and mechanistic studies of reactions of organometallic transition metal carbonyl complexes with a special focus on metal-metal bonds and metal carbonyl clusters. TEL: (416)978-3924 FAX: (416)978-3924 APOE@ALCHEMY.CHEM.UTORONTO.CA

Anthony J. Poë and Ying Zheng, Kinetics of associative reactions of $Fe_2C(CO)_{12}$ with P-donor nucleophiles, Inorg. Chim. Acta, 252, 311-3189(1996).

Robert H. E. Hudson and Anthony J. Poë, Systematic kinetic studies of nucleophile addition to $(\mu_2\text{-}H)_2Os_3(CO)_{10}$, Organometallics, 14, 3238-48(1995).

Anton Neubrand, Anthony J. Poe, and Rudi van Eldik, Activation parameter correlations for nucleophile addition to $(\mu_2\text{-}H)_2Os_3(CO)_{10}$, Organometallics, 14, 3249-58(1995).

Lezhan Chen and Anthony J. Poe, Substitution kinetics of tetracarbonyl(η^2-alkene)ruthenium complexes: alkene = ethene and methyl acrylate, Inorg. Chim. Acta, 240, 399-404(1995).

Nancy M. J. Brodie and Anthony J. Poe, Systematic substitution kinetics of the clusters $Ru_3(CO)_{11}L$ and $Ru_3(CO)_{10}L_2$ (L = P-donor ligands): the unimolecular path, Can. J. Chem., 73, 1187-95(1995).

Lezhan Chen and Anthony J. Poe, Associative reactions of metal carbonyl clusters: systematic kinetic studies of some ruthenium and other clusters, Coord. Chem. Rev., 143, 265-95(1995).

David H. Farrar, Alan J. Lough, Anthony J. Poe and Tatiana A. Stromnova, Bis[tricarbonyl(triisopropyl phosphite) cobalt](Co-Co) dichloromethane solvate, Acta Crystallogr., Sect. C: Cryst. Struct. Commun., c51, 2008-10(1995).

POLANYI, JOHN CHARLES (b. 1929), Professor. B.Sc., 1949, University of Manchester; M.Sc., 1950, University of Manchester; Ph.D., 1952, University of Manchester; D.Sc., 1964, University of Manchester. Postdoctoral Fellow, 1952-54, National Res. Council; 1954-56, Princeton Univ. *Physical Chemistry*. Experimental and theoretical stud. of the ener. distri. among. reagents and prod. of atomic reac. in gases and, esp., at surfaces; applin. of lasers to reac. dynam. and study of photo- induced proc. at surfaces; FTIR, XPS, UPS and STM in ultrahigh vacuum. TEL: (416) 978-3580 FAX: (416)978-7580 JPOLANYI@ALCHEMY.CHEM.UTORONTO.CA JPOLANYI@CHEM.UTORONTO.CA

V. J. Barclay, W.-H. Hung, W. J. Keogh, R. Kuhnemuth, J. C. Polanyi, G. Zhang, Y. Yelri, D. R. Jennison and Y. S. Li, Photochemistry of adsorbed molecules. XV. Localized atomic scattering in the photolysis of HI/LiF(001) and HI/NaF(001), J. Chem. Phys., 105, 5005-5019(1996).

John C. Polanyi and Ahmed H. Zewail, Direct Observation of the Transition State, Acc. Chem. Res., 28, 119-32 (1995).

R. C. Jackson, J. C. Polanyi and P. Sjoevall, Photodissociation dynamics of $(NO)_2$ on LiF(001): Characterization of vibrationally excited NO fragments, J. Chem. Phys., 102, 6308-26(1995).

D. V. Heyd, E. T. Jensen and J. C. Polanyi, Photochemistry of adsorbed molecules. XIV. Photoejection of CH_3X (X = Cl, Br) from $CH_3Br/LiF(001)$, J. Chem. Phys., 103, 461-4 (1995).

John C. Polanyi and Ji-Xing Wang, Photoinduced charge-transfer dissociation in van der Waals complexes. 4. $Na\cdots(FCH_3)_n$ (n = 1-4), J. Phys. Chem., 99, 13691-700(1995).

X. H. Chen, Q. Kong, J. C. Polanyi, D. Rogers and S. So, The adsorption of C_6H_5Cl on Si(111)7×7 studied by STM, Surf. Sci., 340, 224-30(1995).

J. C. Polanyi and Y. Zeiri, Dynamics of adsorbate photochemistry, Adv. Ser. Phys. Chem., 5, 1241-91(1995).

R. C. Jackson, The photodissociation dynamics of nitric oxide dimer in the adsorbed state. (D)

POWELL, JOHN (b. 1943), Professor. B.Sc., 1964, University of Leeds; Ph.D., 1967, University of Leeds. *Inorganic Chemistry*. Structure, bonding and reactivity of coordination and organotransition metal compounds; homogeneous catalysis. New synthetic routes to radio - pharmaceuticals. TEL: (416)978-3581 JPOWELL@ALCHEMY.CHEM.UTORONTO.CA

John Powell, Michael J. Horvath and Alan Lough, Silver-iodocarbon complexes: crystal structures of eight compounds obtained from the reactions of $AgPF_6$ or $AgNO_3$ with CH_2I_2, $I(CH_2)_2I$ and simple aryl iodides, J. Chem. Soc., Dalton Trans., 1669-77(1996).

John Powell, Michael J. Horvath and Alan Lough, Synthesis and structural characterization of $[PtCl_2\{meso\text{-}Ph(HO)PCH_2CH_2P(OH)Ph\}]$ and structurally related derivatives, J. Chem. Soc., Dalton Trans., 1679-85(1996).

John Powell, Michael Horvath and Alan Lough, Synthesis and structural characterization of platinum(II) bis(chelate) complexes derived from the ligand system meso/rac-Ph(O)$HPCH_2CH_2PH(O)Ph$, J. Chem. Soc., Dalton Trans., 2975-89 (1995).

REED, JUTA KUTTIS (b. 1942), Associate Professor. B.A., 1966, Queen's University; M.Sc., 1967, University of Western Ontario; Ph.D., 1972, University of Wisconsin. Post-doctoral Research Fellow, 1973-75, California Institute of Technology. *Biochemistry*. Regulation of neurotransmitter release in neurosecretory cells; purinergic receptors and signal transduction mechanisms. TEL: (905)828-3806 FAX: (905)828-5425 JREED@CREDIT.ERIN.UTORONTO.CA

Frank Merante, Sandeep Raha, Juta K. Reed and Gerald Proteau, The simultaneous isolation of RNA and DNA from tissues and cultured cells, Methods Mol. Biol. (Totowa, N. J.), 58, 3-9(1996).

L. R. de Souza, H. Moore, S. Raha and J. K. Reed, Purine and pyrimidine nucleotides activate distinct signalling pathways in PC12 cells, J. Neurosci. Res., 41, 753-63(1995).

S. Raha, Characterization of a P_{2U} purinoceptor in pheochromocytoma (PC12) cells. (D)

L. de Souza, Nucleotide-evoked cellular responses in pheochromocytoma (PC12) cells. (D)

H. Moore, Regulation of pH homeostasis by extracellular ATP in pheochromocytoma cells. (M)

REYNOLDS, WILLIAM FRANCIS (b. 1937), Professor. B.Sc., 1959, University of Manitoba; M. Sc., 1961, University of Manitoba; Ph.D., 1964, University of Manitoba. Postdoctoral Fellow, 1963-65, Univ. Coll., London. *Physical Chemistry; Organic Chemistry*. Magnetic resonance spectroscopy; development of new 2D NMR techniques, determination of structures of natural products and microstructures of polymers by 2D NMR, medicinal chemistry, investigations of polymer mobility by pulsed gradient NMR. TEL: (416)978-3563 FAX: (416) 978-3563 BGRANOZI@ALCHEMY.CHEM.UTORONTO.CA

R. G. Enriquez, B. Ortiz, I. Leon, G. Magos, S. Capella, A. Pena, W. F. Reynolds and D. Gnecco, The presence of kaurenic derivatives in aqueous infusions of Montanoa Tomentosa by GC-MS and 2D NMR, Planta Med., 62, 569-571 (1996).

G. Henry, H. Jacobs, C. M. S. Carrington, S. McLean and W. F. Reynolds, Plukenetrione A, an unusual adamantyl ketone from Clusia Plakenetii (Guttiferae), Tetrahedron Lett., 37, 8633-8666(1996).

W. F. Reynolds and R. G. Enriquez, Concerning the recently reassigned spectrum of Taraxasteryl acetate, Plant Med., 62, 484(1996).

E. P. Mazzola, S. A. Turujman, S. J. Bell, J. N. Barrows, E. G. Mouchachoir, S. Prescott, M. D. Archer, M. Oliver, W. F. Reynolds and K. W. Nielsen, NMR investigation of azohydrazone, acid-base equilibria of FD and C Yellow No. 6, Tetrahedron, 52, 5691-5698(1996).

Anderson Maxwell, Mohindra Seepersaud, Ramish Pingal, David R. Mootoo, William F. Reynolds and Stewart McLean, Two 3α-aminospirosolane steroidal alkaloids from Solanum triste, J. Nat. Prod., 59, 200-1(1996).

Navindra P. Seeram, Patrick A. Lewis, Helen Jacobs, Stewart McLean, William F. Reynolds, Li-Lin Tay and Margaret Yu, 3,4-Epoxy-8,9-dihydropiplartine. A new imide from Piper verrucosum, J. Nat. Prod., 59, 436-7(1996).

Baldwin S. Mootoo, Russel Ramsewak, Ayub Khan, Winston F. Tinto, William F. Reynolds, Stewart McLean and Margaret Yu, Tetranortriterpenoids from Ruagea glabra, J. Nat. Prod., 59, 544-7(1996).

Anderson Maxwell, Ramish Pingal, William F. Reynolds and Stewart McLean, Two steroidal glycoalkaloids from Solanum arboreum, Phytochemistry, 42, 543-545(1996).

B. S. Mootoo, R. Ramsewak, R. Sharma, W. F. Tinto, A. J. Lough, S. McLean, W. F. Reynolds, J.-P. Yang and M. Yu, Further briareolate esters and briareolides from the Caribbean gorgonian octocoral Briareum asbestinum, Tetrahedron, 52, 9953-9962(1996).

Stewart McLean, William F. Reynolds, Winston F. Tinto, Wilfred R. Chan and Veronica Shepherd, Complete ^{13}C and ^1H spectral assignments of prenylated flavonoids and a hydroxy fatty acid from the leaves of Caribbean Artocarpus communis, Magn. Reson. Chem., 34, 719-722(1996).

Dino Gnecco, J. L. Teran, Raul G. Enriquez, William F. Reynolds and C. Marazano, An improved preparation of 1-methyl-4-cyano-4-phenylpiperidine, Org. Prep. Proced. Int., 28, 478-480(1996).

Anderson Maxwell, Ramish Pingal, William F. Reynolds and Stewart McLean, 3-Aminospirosolane alkaloids from Solanum arboreum, Phytochemistry, 43, 913-915(1996).

Navindra P. Seeram, Helen Jacobs, Steward McLean and William F. Reynolds, Prenylated hydroxybenzoic acid derivatives from Piper murrayanum, Phytochemistry, 43, 863-865 (1996).

Samuel L. Miller, Winston F. Tinto, Ji-Ping Yang, Stewart McLean and William F. Reynolds, 9,11-Seco-24-hydroxydinosterol from Pseudopterogorigia americana, Tetrahedron Lett., 36, 1227-8(1995).

William F. Reynolds, Margaret Yu, Benuamin Ortiz, Angel Rodriguez, Francisco Yuste, Fernando Walls, Raul G. Enriquez and Dino Gnecco, Detailed characterization by two-dimensional NMR of two unusual bicyclo[2.2.2]octenedione derivatives produced by the reaction of perezone with thiourea, Magn. Reson. Chem., 33, 3-7(1995).

Raul G. Enriquez, Juan M. Fernandez-G., Ismael Leon, William F. Reynolds, Ji-Ping Yang and Margaret Yu, Investigation of the effect of ring size on the product distribution for the Schiff base reaction of 2-acetylcycloalkanones with diaminoalkanes, Can. J. Chem., 73, 16-21(1995).

Anderson Maxwell, Mohindra Seepersaud, Ramish Pingal, David R. Mootoo and William F. Reynolds, 3β-Aminospirosolane steroidal alkaloids from Solanum triste, J. Nat. Prod., 58, 625-8(1995).

Geneive E. Henry, Helen Jacobs, Stewart McLean, William F. Reynolds and Ji-Ping Yang, Xerophenones A and B. New isoprenylated derivatives of 11-oxatricyclo[4.3.1.1^{4,10}]undecane-7,9-dione from Clusia portlandiana (Guttiferae), Tetrahedron Lett., 36, 4575-8(1995).

Alex D. Bain, Ian W. Burton, Katherine A. Carpenter, Ji-Ping Yang and William F. Reynolds, Complete spin dynamics of the AX, AX_2 and AX_3 spin systems. Application to BIRD pulses, Magn. Reson. Chem., 33, 201-11(1995).

William F. Reynolds, Anderson Maxwell, Balchandur Telang, Kishore Bedaisie and Gangadeen Ramcharan, Total assignment of the ^1H and ^{13}C NMR chemical shifts of four bufadienolides by 2D NMR spectroscopy, Magn. Reson. Chem., 33, 312-14(1995).

Samuel L. Miller, Winston F. Tinto, Ji-Ping Yang, Stewart McLean and William F. Reynolds, Axinellamide, a new alkaloid from the marine sponge Axinella sp., Tetrahedron Lett., 36, 585102(1995).

Samuel L. Miller, Winston F. Tinto, Stewart McLean, William F. Reynolds and Margaret Yu, Bisabolane sesquiterpenes from Barbadian Pseudopterogorgia sp., J. Nat. Prod., 58, 1116-19(1995).

William F. Reynolds, Ji-Ping Yang and Raul G. Enriquez, Distinguishing two-bond and three-bond ^{13}C-^1H connectivities by 2D BIRD-decoupled difference spectra: the DODO pulse, Magn. Reson. Chem., 33, 705-9(1995).

Samuel L. Miller, Winston F. Tinto, Stewart McLean, William F. Reynolds, Margaret Yu and Charles A. G. Carter, Quassiols B-D, new Squalene triterpenes from Quassia multiflora, Tetrahedron, 51, 11959-66(1995).

Samuel L. Miller, Winston F. Tinto, Stewart McLean, William F. Reynolds, Margaret Yu and Charles A. G. Carter, Isolation and characterization of a new glabretal triterpene from Quassia multiflora., J. Nat. Prod., 58, 1640-2(1995).

Wayne W. Harding, Patrick A. Lewis, Helen Jacobs, Stewart McLean, William F. Reynolds, Li-Lin Tay and Ji-Ping Yang, Glabrescol. A unique squalene-derived penta-THF diol from Spathelia glabrescens (Rutaceae), Tetrahedron Lett., 36, 9137-40(1995).

William F. Reynolds, Margaret Yu, Raul G. Enriquez, Hilda Gonzalez, Ismael Leon, Gil Magos and Maria L. Villareal, Isolation and characterization of cytotoxic and antibacterial tetrasaccharide glycosides from Ipomoea stans, J. Nat. Prod., 58, 1730-4(1995).

Winston F. Tinto, Richard S. Laydoo, Samuel L. Miller, William F. Reynolds and Stewart McLean, 11-Gorgiacerol, a new pseudopteranoid from Pseudopterogorgia acerosa, J. Nat. Prod., 58, 1975-7(1995).

Raul G. Enriquez, Benjamin Ortiz, Enrique Alducin, Fernando Walls, Dino Gnecco, Margaret Yu and William F. Reynolds, The reaction of perezone and isoperezone with hydroxylamine: a surprisingly facile method for introducing an NH_2 group into the quinone functionality, Nat. Prod. Lett., 6, 103-109(1995).

J. -P. Yang, The development of improved and more user friendly pulse sequences and software for 2D NMR. (D)

SHOICHET, MOLLY SANDRA (b. 1965), Assistant Professor. B.S.., 1987, Massachusetts Institute of Technology; M.Sc., 1989, University of Massachusetts, Amherst; Ph.D., 1992, University of Massachusetts, Amherst. *Polymer Science; Tissue Engineering*. Polymer synthesis and surface modification for the development of biohybrid artificial organs. Specific applications include nerve regeneration, bone regeneration and glaucoma. Drug delivery and 3-dimensional scaffolds are also being pursued. TEL: (416)978-1460 FAX: (416)978-8605
MOLLY@ECF.UTORONTO.CA

M. S. Shoichet, R. H. Li, M.L. White and S. R. Winn, Stability of hydrogels used in cell encapsulation: An in vitro comparison of alginate and agarose, Biotechn. Bioeng., 50, 374-381(1996).

M. S. Shoichet and D. H. Rein, In vivo biostability of a polymeric hollow fiber membrane for cell encapsulation, Biolmaterials, 17, 285-290(1996).

Y. Ren, M. S. Shoichet, T. McCarthy, H. Stidham and S. Hsu, Spectroscopic characterization of polymer adsorption at the air-solution interface, Macromolecules, 28, 358-365 (1995)

M. S. Shoichet, F. T. Gentile and S. R. Winn, The use of polymers in the treatment of neurological disorders, Trends in Polymer Science, 3, 374-380(1995).

F. T. Gentile, E. J. Doherty, D. H. Rein, M. S. Shoichet and S. R. Winn, Polymer science for cell encapsulation, J. Reactive Polym., 25, 207-227(1995).

T. J. McCarthy, T. Bee, J. Brennan, E. Cross, N. L. Franchina, A. J. Dias, K.-W. Lee and M. S. Shoichet, Polymer surface modification, in Organic Thin Films and Surfaces: Directions for the Nineties, Vol. 1, A. Ulman, Ed., Academic Press, San Diego, 1995.

M. S. Shoichet, S. R. Winn, S. Athavale, J. M. Harris and F. T. Gentile, Poly(ethylene-oxide)-grafted thermoplastic membranes for use as cellular hybrid bio-artificial organs in the central nervous system, Biotechn. Bioeng., 43, 563-72 (1994).

T. A. Zawodzinski, Jr., S. Gottesfeld, M. S. Shoichet and T. J. McCarthy, The contact angle between water and the surface of perfluorosulfonic acid membranes, J. Appl. Electrochem., 23, 86-8(1993).

T. G. Bee, A. J. Dias, N. L. Franchina, B. U. Kolb, K.-L. Lee, P. A. Patton, M. S. Shoichet and T. J. McCarthy, Surface chemistry of chemically resistant polymers, in Polymer Surfaces and Interfaces II, John Wiley and Sons, New York, 1993.

STILL, IAN WILLIAM JAMES (b. 1937), Professor. B.Sc., 1958, University of Glasgow; Ph. D., 1962, University of Glasgow; D.Sc., 1992, University of Glasgow. Research Assoc., 1962, Univ. of Toronto. *Organic Chemistry*. Synthetic organic chemistry; synthetic methods; synthesis of natural products of biological or pharmacological interest; novel types of functional group, especially among organic compounds of sulfur. TEL: (416)978-0873 TEL: (905) 828-5354 FAX: (905)828-5425
ISTILL@CREDIT.ERIN.UTORONTO.CA

Ian W. J. Still and F. Dean Toste, Reduction of Aryl Thiocyanates with SmI_2 and Pd-Catalyzed Coupling with Aryl Halides as a Route to Mixed Aryl Sulfides, J. Org. Chem., 61, 7677-7680(1996).

F. Dean Toste, Vittorio De Stefano and Ian W. J. Still, A versatile procedure for the preparation of aryl thiocyanates using N-thiocyanatosuccinimide (NTS), Synth. Commun., 25, 1277-86(1995).

F. Dean Toste and Ian W. J. Still, A New Route to the Synthesis of the Naturally Occurring Benzopentathiepin Varacin, J. Am. Chem. Soc., 117, 7261-2(1995).

F. Dean Toste, Frank LaRonde and Ian W. J. Still, Thiocyanate as a versatile synthetic unit: efficient conversion of ArSCN to aryl alkyl sulfides and aryl thioesters, Tetrahedron Lett., 36, 2949-52(1995).

F. Dean Toste and Ian W. J. Still, A simple method for the selective MOM protection of thiols, Synlett, 159-60(1995).

F. Dean Toste and Ian W. J. Still, Preparation of t-butyl sulfides by a novel ligand-transfer reaction of aryl thiocyanates, Tetrahedron Lett., 36, 4361-64(1995).

James McNulty and Ian W. J. Still, Selective methylation and stereoselective reduction of a β-carboline to a N(2)-methyl-1,2,3,4-tetrahydro-β-carboline, Tetrahedron Lett., 36, 7965-6(1995).

F. Dean Toste, Alan J. Lough and Ian W. J. Still, Preparation of 6,12-imino-6H,12H-dibenzo[b,f]-1,5-dithiocins, Tetrahedron Lett., 36, 6619-22(1995).

F. Dean Toste and I. W. J. Still, Sonication and aluminum amalgam in the Leimgruber-Batcho reaction. An improved preparation of 6-aminoindole, Org. Prep. Proced. Int., 27, 576-9(1995).

F. D. Toste, The total synthesis of varacin: novel applications of thiocyanate in organic synthesis. (M)

TAYLOR, SCOTT DOUGLAS (b. 1961), Assistant Professor. B.Sc., 1986, McGill University; M. Sc., 1988, University of Toronto; Ph.D., 1991, University of Toronto. NSERC Postdoctoral Fellow, 1992-94, Pennsylvania State University. *Organic Chemistry; Biochemistry*. Catalytic antibodies; enzyme structure and function; peptide chemistry; transition state analog syntheses; signal transduction enzymes. TEL: (905)828-5355 FAX: (905)828-5425
STAYLOR@CREDIT.ERIN.UTORONTO.CA

S. D. Taylor, A. N. Dinaut, A. N. Thadani and Z. Huang, Synthesis of benzylic mono(α, α- difluoromethylphosphonates) and benzylic bis(α, α-difluoromethylphosphonates) via electrophilic fluorination, Tetrahedron Lett., 37, 8089-8092 (1996).

Glen T. Anderson, Michael D. Alexander, Scott D. Taylor, David B. Smithrud, Stephen J. Benkovic and Steven M. Weinreb, Catalytic Antibodies in Synthesis: Design and Synthesis of a Hapten for Application to the Preparation of a Scalemic Pyrrolidine Ring Synthon for Pilomycalin A, J. Org. Chem., 61, 125-32(1996).

Louis J. Liotta, Richard A. Gibbs, Scott D. Taylor, Patricia A. Benkovic and Stephen J. Benkovic, Antibody-Catalyzed Rearrangement of a Peptide Bond: Mechanistic and Kinetic Investigations, J. Am. Chem. Soc., 117, 4729-41 (1995).

A. C. McClure, Towards the synthesis of a transition state analogue for intramolecular peptide bond cleavage. (M)

C. C. Kotoris, Studies on intramolecular peptide bond cleavage and design and synthesis of protein tyrosine phosphatase inhibitors. (M)

THOMPSON, JAMES CHARLTON (b. 1941), Professor. B.A., 1962, Cambridge University; Ph.D., 1965, Cambridge University. Postdoctoral Fellow, 1965-67, Rice Univ. *Inorganic Chemistry; Chemical Education*. High temperature chemistry; nmr spectroscopy; small ring systems. TEL: (416)287-7232 TEL: (416)978-3576 FAX: (416)287-7204
JTHOMPSO@ALCHEMY.CHEM.
UTORONTO.CA
JTHOMPSO@SCAR.UTORONTO.CA

Aki Hirai, Richard J. Bold, Jin Ishizuka, Masahi Hirai, Courtney M. Jr. Townsend and James C. Thompson, Hyperphosphorylation f retinoblastoma protein and stimulation of growth by okadaic acid in human pancreatic cancer, Dig. Dis. Sci., 41, 1975-1980(1996).

Graham P. Leese, James Thompson, Charles M. Scrimgeour and Michael J. Rennie, Exercise and the oxidation and storage of glucose, maize-syrup solids and sucrose determined from breath $^{13}CO_2$, Eur. J. Appl. Physiol. Occup. Physiol., 72, 349-356(1996).

M. G. Guttridge, J. Thompson, C. Burr and C. Darke, The differentiation of HLA-B* 1401 (B64) and B*1402(B65) by the polymerasw chain reaction using sequence-specific primers (PCR-SSP, Tissue Antigens, 45, 213-15(1995).

THOMPSON, MICHAEL (b. 1942), Professor. B. Sc., 1966, University Coll. of Swansea; Ph.D., 1970, McMaster University; F.R.I.C., 1975, Royal Inst. Chem. (U.K.); D.Sc., 1986, University of Wales; F. C.I.C., 1986, Canadian Institute of Chemicals. S. R.C. Postdoctoral Fellow, 1971, Univ. Coll. of Swansea. *Analytical Chemistry*. Analytical chemistry, analytical aspects of x-ray and vacuum ultraviolet photoelectron spectroscopy and Auger electron spectrometry, development of electrochemical sensors for organic compounds based on chemoreception, Langmuir-Blodgett film technology, a TEL: (416)978-3575
BGRANOZI@ALCHEMY.CHEM.
UTORONTO.CA

Hongbo Su, Sandra Chong and Michael Thompson, Interfaciai hybridization of RNA homopolymers studied by liquid phase acoustic network analysis, Langmuir, 12, 2247-55 (1996).

Hongbo Su and Michael Thompson, Rheological and interfacial properties of nucleic acid films studied by thickness - shear mode sensor and network analysis, Can. J. Chem., 74, 344-58(1996).

Biljana A. Cavic-Vlasak, Michael Thompson and Dennis C. Smith, Silicones and their determination in biological matrixes. A review, Analyst (Cambridge, U. K.), 121, 53R-63R(1996).

Paul C. H. Li and Michael Thompson, Mass Sensitivity of the Thin-Rod Acoustic Wave Sensor Operated in Flexural and Extensional Modes, Anal. Chem., 68, 2590-2597(1996).

Zhiping Deng, David C. Stone and Michael Thompson, Selective detection of aroma components by acoustic wave sensors coated with conducting polymer films, Analyst (Cambridge, U. K.), 121, 671-679(1996).

Hongbo Su, Patrick Williams and Michael Thompson, Platinum Anticancer Drug Binding to DNA Detected by Thickness-Shear-Mode Acoustic Wave Sensor, Anal. Chem., 67, 1010-13(1995).

Hongbo Su and Michael Thompson, Kinetics of interfacial nucleic acid hybridization studied by acoustic network analysis, Biosens. Bioelectron., 10, 329-40(1995).

A. Walter Dorn and Michael Thompson, Intrinsic conductance of inorganic ions through bilayer lipid membranes, Ion-Transfer Kinet., 55-69(1995).

Zhiping Deng, David C. Stone and Michael Thompson, Poly N-(2-cyanoethyl)pyrrole as a selective film for the thickness-shear-mode acoustic wave sensor, Can. J. Chem., 73, 1427-35(1995).

P. C. H. Li and M. Thompson, Carbon dioxide recognition by rhodium(I) complexes studied by infrared and nuclear magnetic resonance spectroscopies and acoustic wave sensor, Analyst (Cambridge, U. K.), 120, 2529-35(1995).

TIDWELL, THOMAS TINSLEY (b. 1939), Professor. B.S., 1960, Georgia Institute of Technology; A.M., 1963, Harvard University; Ph.D., 1964, Harvard University. NIH Fellowship, 1964-65, University of California, San Diego; NIH Fellowhip, 1966-167, University of East Anglia, UK. *Organic Chemistry; Materials Science*. Synthetic and mechanistic organic chemistry, ketenes, carbocations, fluorocarbons, molecular orbital calculations, polymers and materials science, substituent effects, chemistry in outer space. TEL: (416)287-7217 FAX: (416)287-7204
TIDWELL@SCAR.UTORONTO.CA
TTIDWELL@ALCHEMY.CHEM.
UTORONTO.CA

A. D. Allen, I. Egle, R. Janoschek, H. W. Liu, J. Ma, R. M. Marra and T. T. Tidwell, ^{13}C, ^{17}O and ^{29}Si NMR spectra and stabilization of silylated ketenes and bisketenes, Chem. Lett., 45-46(1996).

A. D. Allen, J. D. Colomvakos, I. Egle, R. Liu, J. Ma, M. A. McAllister and T. T. Tidwell, Ketenes and bisketenes: Organic chemistry in microcosm, Can. J. Chem., 74, 457-464 (1996).

K. Sung and T. T. Tidwell, The first stable and persistent 1,3-bisketene and the first trisketene, J. Am. Chem. Soc., 118, 2768-2769(1996).

A. D. Allen, A. J. Lough and T. T. Tidwell, Preparation and crystal structure of a stable and persistent twisted tetraketene, J. Chem. Soc., Chem. Commun., 2171-2172(1996).

G. Cerioni, R. Janoschek, Z. Rappoport and T. T. Tidwell, Cyclobutene-1,2-diones: A Theoretical and Spectroscopic Study, J. Org. Chem., 61, 6212-6217(1996).

R. Liu and T. T. Tidwell, Aryl substituent effects on the thermal interconversion of cyclobutenediones and 1,2-bisketenes, J. Chem. Soc., Perkin Trans., 2, 2757-2762 (1996).

R. Liu, R. M. Marra and T. T. Tidwell, Phenyldimethylsilyl ketenes and bisketenes, J. Org. Chem., 61, 6227-6232 (1996).

T. T. Tidwell, The Electrophilic addition to alkynes revisited, J. Chem. Ed., 73, 1081-1082(1996).

I. Egle, V. Gabelica, A. J. Kresge and T. T. Tidwell, The acid-catalyzed demetalation of 1-(tri-n-butylstannyl)-2-phenylethyne, a surprisingly small β-stannyl effect, Can. J. Chem., 74, 1366-1368(1996).

J. D. Colomvakos, I. Egle, J. Ma, D. L. Pole, T. T. Tidwell and J. Warkentin, [2+2] and [4+2] cycloaddition reactions of bisketenes with aldehydes, diazomethanes, tetramethoxyethylene and dialkoxycarbenes, J. Org. Chem., 61, 9522-9527(1996).

A. D. Allen, J. Ma, J. Liu, M. A. McAllister, T. T. Tidwell and D.-c. Zhao, Silylated Bisketenes: Accessible and reactive organic intermediates, Pure Appl. Chem., 67, 777-782(1995).

A. D. Allen, J. Ma, M. A. McAllister, T. T. Tidwell, D.-c. Zhao, Electrophilic reactivity of bisketenes: An experimental and theoretical study and photoinduced hydration, J. Chem. Soc., Perkin Trans., 2, 847-85(1995).

A. D. Allen, J. D. Colomvakos, I. Engle, J. Lusztyk, M. A. McAllister, T. T. Tidwell, B. D. Wagner and D.-c. Zhao, Time resolved infrared observation of unstabilized bisketenes and kinectics of rin closure to cyclobutenediones, J. Am. Chem. Soc., 117, 7552-7553(1995).

A. D. Allen, J. Ma, M. A. McAllister, T. T. Tidwell and D.-c. Zhao, New tricks from an old dog: Bisketenes after 90 Years, Acc. Chem. Res., 28, 265-271(1995).

R. Liu and T. T. Tidwell, A stabilized and persistent tetraketene; 1,4-bis(1',4'-dioxo-3'trimethylsily-2'buta-1',3'-dienyl) benzene, Can. J. Chem., 73, 1818-1822(1995).

A. D. Allen, M. Fujio, O. S. Tee, T. T. Tidwell, Y. Tsuji, Y. Tsuno and K. Yatsugi, Ion pairs in solvolysis of secondary systems, salt effect, ^{18}O-labeling and polarimetric studies of 1-(4-tolyl-2,2,2-trifluoroethyl) tosylate, J. Am. Chem. Soc., 117, 8974-8981(1995).

Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin 53202
Phone: 414/277-0730
Fax: 414/277-0709

A Chemist Helping Chemists

September 17, 1997

Professor William F. Reynolds
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
CANADA

Dear Professor Reynolds:

Following receipt of your fax I spent yesterday evening going through Loschmidt's voluminous hand-written notes but could not find anything about Mendel.

These notes are not easy to read but, luckily, they were transcribed. If you are interested in seeing these, I could easily bring them along. They deal very little with chemistry but a good deal with mathematics, philosophy, mineralogy, etc.

I also had to look at Hubert de Marten's Ph.D. thesis and enclose page 21 of that where de Marten refers to Mendel without, however, anywhere pointing to a meeting between Mendel and Loschmidt.

With all good wishes, I remain,

Yours sincerely,

AB/nik

Enclosure

spätere Schüler Loschmidt's und Förderer der kinetischen Gas = Theorie, welcher auch nach dem Tode seines Lehrers die geistige Richtung seiner Schule einhielt und als einer der letzten Vertreter dieser Forschungsmethode zu betrachten ist, geboren.

Die Universität Wien feierte das 500 jährige Jubiläum ihres Bestandes, zu welchem Anlaß großartige Feierstunden und mehrere Festschriften veröffentlicht wurden.- August Kekulé stellte seine berühmte Benzoltheorie auf und wenn wir unseren Blick nach Norden richten, so finden wir einen Abt namens Gregor Mendel, welcher in Brünn in einem Klostergarten an Hand von Experimenten mit Bohnen und Erbsen Resultate erhält, welche ihm das Rüstzeug zu einer mathematischen Behandlung der Erblehre liefern. Seine 33 Seiten umfassende Schrift: „Versuche über Pflanzenhybriden" ist der Beginn einer neuen Experimentiertechnik. Auch Mendel's Arbeiten ereilte ein ähnliches Schicksal, wie wir es bei Josef Loschmid vorgefunden haben. Zwanzig Jahre lang war sein Werk in Vergessenheit geraten, und wurde wiederentdeckt von de Vries, Tschermak und Correns, welch letzterer die Leistung Mendel's mit dem Hebel von Archimedes vergleicht und Lenz stellt dessen praktische Bedeutung über die der Entdeckung eines Kopernikus.-

Wenn wir unser Augenmerk nun wieder auf Loschmidt richten, so müssen wir feststellen, daß dieser sein altes Vorhaben, eine Lehrstelle an einer Hochschule zu bekommen, schärfer denn je verfolgt und zu realisieren gewillt ist. Um diese Zeit hatte er sich in wissenschaftlichen Kreisen bereits einen Namen gemacht und fand jetzt in seinem Freunde Josef Stefan einen einflußreichen und tatkräftigen Kollegen. Dieser ebnete ihm viele Wege und schaffte ihm so manche Unannehmlichkeit beiseite.

Am 28. Mai 1866 suchte Loschmidt um Zulassung zur Habilitation an. Er legte diesem Gesuche seine bisherigen wissenschaftlichen Abhandlungen sowie seinen Lebenslauf (Curriculum Vitae)

Department of Chemistry

FAX COVER PAGE

MESSAGE

IF THERE ARE ANY PROBLEMS WITH THIS TRANSMISSION PLEASE CONTACT: Blanca
(416) 978-3575 or e-mail: bgranozi@alchemy.chem.utoronto.ca

Bill Reynolds

Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin 53202
Phone: 414/277-0730
Fax: 414/277-0709

A Chemist Helping Chemists

December 31, 1997

Professor William F. Reynolds
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
CANADA

Dear Professor Reynolds:

I still remember with great pleasure our meeting and discussion in Toronto.

Professor Schiemenz's letter, clearly written by Schiemenz I, will interest you.

How is your manuscript to be submitted to the *Journal of Chemical Education* coming along?

With all good wishes for 1998, I remain,

Yours sincerely,

AB/nik

Enclosure

FAX FROM

DR. ALFRED BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone: 414/277-0730
Fax: 414/277-0709

A Chemist Helping Chemists

September 10, 1997

To: Professor William F. Reynolds
Chemistry Department
University of Toronto
Fax: 416 / 978-3563

Dear Professor Reynolds:

Thank you so much for your most interesting fax of yesterday.

It is essential that you understand clearly exactly what Loschmidt said and ideally you should be helped in your translations by someone who is both fluent in German and a chemist.

Turning to pages 58 and 59 in Anschütz's reprint, note that Loschmidt dismissed 181 and, I presume, also cyclohexatriene because "despite innumerable experiments" he could not get a saturated compound. And then he goes on to say "könnte man fast versucht sein" which means one might almost be tempted to think of benzene as 182. That sentence misled Rocke into thinking that he really thought that benzene could be 182.

Even 30 or 40 years ago I was very forgetful and I could have said "I might be tempted to think that I am becoming senile" but it would have been clear, as it is with Loschmidt, that he did not think of benzene as 182 and I did not think that I was senile. But only someone really fluent in German would understand that this is really a dismissal of 182.

You will have noted that Loschmidt places the hydrogen atoms in 185 unsymmetrically. Remember the fact pointed out so clearly in Anschütz's footnote 144 that chemists in 1861 believed that there were two isomeric benzoic acids, one called benzoic acid and the other salylic acid and hence, two benzenes - one benzene and the other parabenzene. Only in 1864 did Reichenbach and Bielstein point out that salylic is simply impure benzoic acid and therefore, parabenzene impure benzene. I presume - though Loschmidt does not state that explicitly - that he thought that benzene and parabenzene differed slightly in the position of the hydrogen atoms.

When considering isomerism, please also look at structure 191. There he describes pyrogallol as 1,2,4-trihydroxybenzene and, of course, in 1861 had no way of knowing that pyrogallol is really 1,2,3-trihydroxybenzene.

I am sure that you will already have found Anschütz's footnotes most instructive.

Look, for instance, at footnote 118 where Anschütz compares Loschmidt's correct structure 154 for cyanuric acid with Couper's first ever heterocyclic structure - heterocyclic but incorrect - and Kekulé's structure in his textbook.

In Loschmidt's 1890 paper, he refers to the cyclohexatriene structure as Kekulés. Clearly he realized that cyclohexatriene was an improvement over 185.

Schiemenz poo-poos the idea expressed by Wiswesser, and many others, that Loschmidt was a shy and self-effacing man. But, in fact, he was.

Schiemenz likes to attack most everybody, even Anschütz whom he accuses of leaving out two commas in his reprint.

I do not have to tell you how very much I look forward to your paper. I very much hope that the *Plenum* publication of all the lectures of the Loschmidt symposium in June of 1995 will appear soon. I have ordered 10 copies and as soon as I have received mine I will send you a copy.

Also, of course, I much look forward to being with you on October 30th, both to wish you a happy 60th birthday and to discuss Loschmidt.

With all good wishes, I remain,

Yours sincerely,

Alfred Bader

AB/nik

bc: Rosner, Noe

man derlei Substanzen unterwarf, niemals in einen vollstelligeren übergingen, namentlich nicht durch Wasserstoff im *statu nascendi* (nach *Zinins* neuester Publikation). Ferner bleibt es unter dieser Voraussetzung unerklärlich, warum die intermediären unvollstelligen Kerne, z. B. C_6^{VIII}, C_6^{X} u. dgl., ganz fehlen oder nur in einzelnen, zum Teil zweifelhaften Fällen vorkommen, während jene nicht nur in den Naturprodukten angetroffen werden, sondern sich auch unter den mannigfachsten Verhältnissen künstlich erzeugen lassen, z. B. Einwirkung von Glühhitze auf Alkoholdampf. Unter diesen Umständen könnte man fast versucht sein, die Unvollstelligkeit dieser Kerne nicht sowohl durch Verdichtung, als vielmehr durch Schichtung der Kohenstoffatome zu erklären und dem Kerne C_6^{VI} ungefähr das

Schema 182, 183.

Sch. 182 beizulegen. Dies wäre demnach der doppelte Allylkern, nach der Variante Sch. 68, und man könnte zugleich den Kern der Naphtalinreihe C_{10}^{VIII}, den einzigen unvollstelligen Kern von Bedeutung, dem nicht sechs Stellen fehlen [der Terpentinkern C_{10}^{XVI} dürfte eher ähnlich dem Vinylkerne anzunehmen sein], als einen verdreifachten Allylkern, mehr dem Methylkern C auffassen und ihm das Sch. 183 geben. Dies Naphtalin würde dann eine dem Toluol analoge Konstitution erhalten, welch letzteres wir als Methylo-Benzol betrachten werden. Jedenfalls ist es nach dem bis jetzt Vorliegenden unmöglich, hierüber zu einem definitiven Resultat zu gelangen, und wir können unsere Entscheidung umsomehr *in suspenso* halten, als unsere Konstruktionen davon völlig unabhängig sind. Wir nehmen für den Kern C_6^{VI} das Symbol Sch. 184 an und behandeln denselben ganz so, als ob er ein sechsstelliges Element wäre.

Schema 184, 185.

Das Benzol C_6H_6 Sch. 185 ist in der Phenylreihe, was das Sumpfgas CH_4 in der Methylreihe. Wie das letztere als Methylwasserstoff, so ist ersteres als **Phenylwasserstoff**

Department of Chemistry
University of Toronto

163 of footnote 121

footn. 144, 115

cp 191

* THUS HE WENT FROM A STRUCTURE WITH FOUR DOUBLE BONDS & NO RINGS TO A STRUCTURE WITH FOUR RINGS & NO DOUBLE BONDS WITHOUT EXPLICITLY DISCUSSING ANY INTERMEDIATE STRUCTURE WHERE THE SUM OF RINGS & DOUBLE BONDS EQUALLED FOUR. EITHER HE HAD A COMPLETE MENTAL BLOCK OR HE MUST HAVE REJECTED ALL STRUCTURES WITH C=C BONDS.

FAX FROM : 01424 222223

2A HOLMESDALE RD.
BEXHILL-ON-SEA.
E. SUSSEX
TN39 3QE

DEC 19/96

AVON MACFARLANE

FAX : 001 416 978 5102

Dear M/ MacFarlane,

Thank you for your fax of Dec 9 and the invitation to lunch with President Prichard. We have been travelling and are only just beginning to catch up on mail.

Unfortunately we do not plan to be in Canada until October, although there is some possibility of a short visit in May/June.

We hope President Prichard enjoyed his brief stay in Herstmonceux Castle in November and that he feels the centre has something to offer students.

You may be interested to know that I have promised President Runte of Victoria $10,000 U.S. (each) for the next three years to be used as bursary/grant assistance if students can be found to attend courses at the I.S.C. We have been assured that this will come under the provincial and university schemes of committed donations so that the sum will be trebled.

Naturally we hope we'll have the pleasure of seeing some U of T students at Herstmonceux before too long.

Sincerely,

Isobel K. Bader

21 King's Colle
Fax: Administratio
The Bulletin & U of T Magazine (416) 978-743

21 King's College
Fax: Administration (416) 978-3958 or (416) 978-7430 •
The Bulletin & *U of T Magazine* (416) 978-7430 •

Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin 53202
Phone: 414/277-0730
Fax: 414/277-0709

A Chemist Helping Chemists

October 30, 1995

Professor A.G. Brooks
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Professor Brooks:

It was such a pleasure to be able to chat with you during my short stay in Toronto.

You will have realized how interested I was in looking at your collection of research samples dating back to the days of Henry Gillman in the early 1950's.

I know that Aldrich would be very interested in acquiring these for the Library of Rare Chemicals. When the time comes that you would like to dispose of these, please do allow Aldrich to purchase the collection. Then please either contact the manager of the Library, Mr. Bob Wandler, at Aldrich in Milwaukee or me, and we will make arrangements to have the collection brought to Milwaukee.

In the meantime, do speak to Professor Spencer at McMaster whose collection we acquired for Aldrich last summer. I think that he will assure you that the arrangements were satisfactory. And of course, I know that your collection would help many hundreds of chemists in the years to come.

With best personal regards to you and your son, I remain,

Yours sincerely,

AB/cw
cc: Bob Wandler

Dr. Alfred Bader
924 East Juneau, Suite 622
Milwaukee, Wisconsin 53202
Phone: 414/277-0730
Fax: 414/277-0709

A Chemist Helping Chemists

October 30, 1995

Professor Martin Moskovits
Chairman, Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

I so enjoyed our chat during my all-too-brief stay in Toronto.

I very much appreciated your advice about awards to young academic chemists in Canada and in the Czech Republic.

There is already one Bader family foundation, and I enclose the last annual report of that.

In time, my son, Daniel, who is the president of the Helen Bader Foundation, will be responsible for the Isabel and Alfred Bader Foundation also, and of course, we are sharing with him what our hopes are.

We will now take counsel with the Killam Awards Committee to see how best to proceed.

With many thanks for all your help and best personal regards, I remain,

Yours sincerely,

AB/cw

Enclosure

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

A Chemist Helping Chemists

August 24, 1995

Dr. Ronald Kluger, FCIC
Department of Chemistry
University of Toronto
Toronto, ON M5S 1A1
Canada

Dear Ron:

I am so happy to have your letter of August 14th and chagrinned only by your last sentence. St. John's-Newfoundland is so far away that we will not come there, much as we enjoy coming to the CIC meetings.

Isabel and I will be in Toronto just before my 50th reunion at Queen's, specifically from October 18th to the morning of the 20th, and of course, I plan to visit the Chemistry Department of the U of T. And then, I much hope to have a chance to meet your daughter at Queen's.

I do hope that you will submit your award paper to the *Aldrichimica Acta* for publication. You will find the editor, Dr. Mark Drezdzon, very helpful, and of course, the *Acta* continues to be a great publication going to over 200,000 chemists worldwide. Please just don't mention me, for reasons that will be clear from Chapter 13 of my book.

With all good wishes, I remain,

Yours sincerely,

AB/cw

UNIVERSITY OF TORONTO
Department of Chemistry
80 St. George Street, Toronto, Ontario M5S 1A1

INTERNET: rkluger@alchemy.chem.utoronto.ca Phone and fax: 416-978-3582

August 14, 1995

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, WI 53211

Dear Alfred,

Thank you very much for your note. I am especially delighted that I will be receiving the award that has your name on it. The combination of your involvement and the significance of the honor adds to the joy of my scientific life.

The timing is especially nice since I recently finished reading your book and can now benefit from your insights and experiences. There were many places where I found a personal connection, some that are not apparent. For instance, at Columbia, Gilbert Stork used to select an undergraduate to work in his lab (it was his way of encouraging interest in organic chemistry). I was lucky enough to have that job for three years. My first task was making nitrosomethylurea. Thanks to you, DiazAld came along and I was given other things to do. Gilbert's group needed deuterochloroform (to use for samples in the new 60 Mhz nmr) but we couldn't buy it. I was given the job of making it for the group. Since there was no practical preparation I developed one that worked and later published it ("A Convenient Preparation of Chloroform-*d*", *J. Org. Chem.* **29**, 2045 (1964).). I made litres of it and supplied the whole department for a few years. Merck Isotopes then began to sell $CDCl_3$ - using my method to make it. My interest in deuterium oxide, the starting material, continued and when I moved to Toronto I found how to get it in bulk from Ontario Hydro, just as you did. I was glad to see you arrived at the same conclusion. Luckily, Hydro was my first try for a bulk source. They later paid me commissions in deuterium oxide when I sent them other customers.

I look forward to seeing you and Isabel in St. John's. Melissa looks forward to your visit to Kingston..

Best regards,

Ron

Ronald Kluger

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

A Chemist Helping Chemists

August 1, 1995

Professor Thomas T. Tidwell
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Thomas:

I am sorry that a long trip to Europe has delayed my responding to your letter of June 21st.

Tom, I am sure that you will realize that Isabel and I are asked for funds for a great many good causes, on the average two or three times daily. We try very hard to concentrate our giving to help students and truly disadvantaged people. I am sure that sending able scientists to a symposium in Hawaii is very worthwhile, but it is really outside our interests, even though I've been so involved with diketene chemistry.

The four companies that have benefitted most from this chemistry are Eastman Chemicals, Wacker, Lonza, and Union Carbide. The man in charge of bulk chemical sales at Lonza, Dr. Peter Pollak, is usually in his office in Basel, but at the moment, he is spending some time at Lonza US, and I enclose a Xerox copy of his visiting card.

With all good wishes, I remain,

Yours sincerely,

AB/cw

1995 International Chemical Congress of Pacific Basin Societies

Honolulu, Hawaii, USA ◆ December 17-22, 1995

Sponsors
Canadian Society for Chemistry
American Chemical Society
The Chemical Society of Japan
New Zealand Institute of Chemistry
The Royal Australian Chemical Institute

Symposium on Ketene Chemistry

Organizing Committee: Thomas T. Tidwell
Department of Chemistry, University of Toronto
Toronto, Ontario, Canada M5S 1A1
Tel 416-287-7217 *Fax* 416-287-7204
email tidwell@lake.scar.utoronto.ca
Rick L. Danheiser, Massachusetts Institute of Technology
Curt Wentrup, The University of Queensland
Chikara Kaneko, Tohoku University

June 21, 1995

Dr. Alfred Bader
The Astor Hotel
924 Juneau Avenue
Milwaukee, Wisconsin 53202

Dear Alfred:

This past Friday evening I had a remarkably pleasurable time reading the last chapters of your book you had autographed for me in Guelph. Chapter 19 on Efim Shapiro was especially interesting, describing his studies at St. Petersburg University and his devotion to the Hermitage Museum. This recalled my own visit to that city in 1989, when my wife and I stayed in a rat-infested apartment owned by the University with a wonderful view across the Neva of the Hermitage. We were able to visit the galleries for three days, but this was still not enough time.

The purpose of my trip was to visit the Department of Chemistry, including the laboratories of Dr. Valerij Nikolaev and his wife, Professor Ludmila Rodina. Dr. Nikolaev studies acylketenes, carrying on the tradition there of Professor Irina Korobitsyna, and this brings me to the point of this letter. I have organized a symposium "Ketene Chemistry" to be held in conjunction with Pacifichem '95 in Honolulu, December 17-22, 1995, and have an outstanding international group of speakers, including all the world leaders in ketene chemistry. This list includes three Russians, and besides Nikolaev these are Professor Yuri Andreichikov from The Pharmaceutical Faculty at Perm, who also works on acrylketenes and Professor N.V. Lukashev from Moscow, who carries on the long tradition there of Professor I.F. Lutsenko. I had counted on travel support for these individuals from the Soros foundation, but unfortunately have just learned from them that they have suspended their support of science in Eastern Europe out of frustration at the lack of matching support from governmental agencies. Despite my efforts I have also raised very little money from industry to suport this symposium.

I should like to ask your support for the travel and lodging of these three individuals, which I estimate would cost $2,000 apiece, or $6,000 for all three, although any amount would be helpful. I am familiar with your own early involvement in ketene chemistry, and have included this in my own book on the subject (pages enclosed), and see this is described in more detail on pp. 115 of your book. You may be interested that as a sequel to this study Professor Jerry Kresge in this Department and Professor Ossie Tee from Montreal have used a sample of the dioxinone **1** purchased long ago from Aldrich to generate acetylketene by flash photolysis, and have observed a fascinating cascade of reaction intermediates from the reaction with H_2O, including several enols.

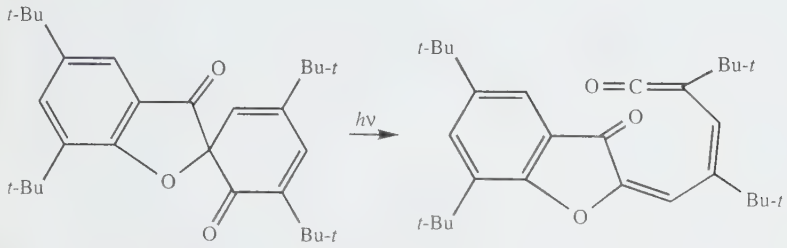
In any event I wish to thank you for the pleasure your book gave me, and the help that Aldrich Chemical has given to my work over the years.

With best wishes,

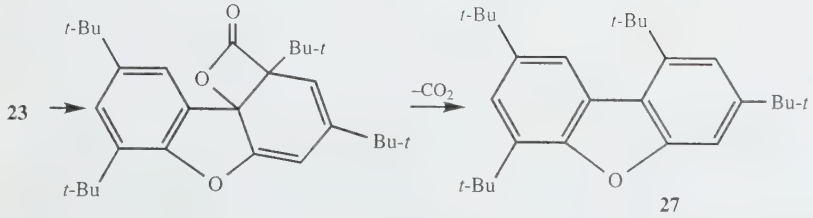
Sincerely,

Thomas T. Tidwell
Professor of Chemistry

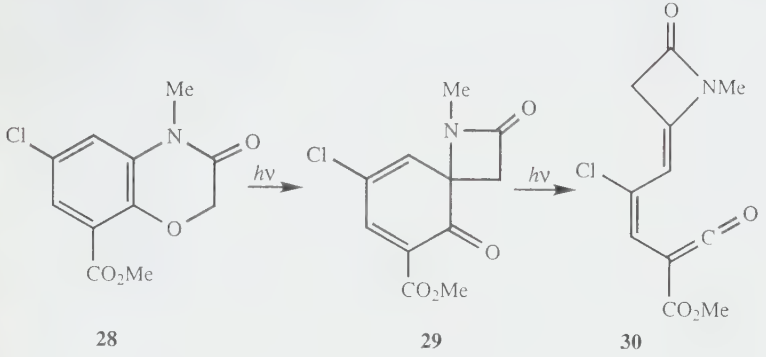
Photolysis of **25** gave a ketene (or diradical) **26** which led to **27** after decarboxylation (equation 13).[16]



(13)



Photolysis of **28** gave **29** by a bond-cleavage recyclization route. Isolation of **29** followed by further photolysis was proposed to give ring opening to **30** and its stereoisomer, and these were captured by MeOH as the esters (equation 14).[17]



(14)

References

1. Quinkert, G.; Kleiner, E.; Freitag, B.; Glenneberg, J.; Billhardt, U.; Cech, F.; Schmieder, K. R.; Schudok, C.; Steinmetzer, H.; Bats, J. W.; Zimmermann, G.; Dürner, G.; Rehm, D.; Paulus, E. F. *Helv. Chim. Acta* **1986,** *69,* 469–535.

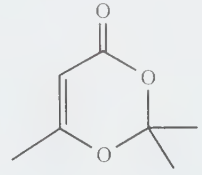
2. Quinkert, G. *Angew. Chem., Int. Ed. Engl.* **1965,** *4,* 211–222.
3. Barton, D. H. R.; Quinkert, G. *J. Chem. Soc.* **1960,** 1–9.
4. Waring, A. J. *Adv. Alicyclic Chem.* **1966,** *1,* 129–256.
5. Jerina, D. M.; Witkop, B.; McIntosh, C. L.; Chapman, O. L. *J. Am. Chem. Soc.,* **1974,** *96,* 5578–5580.
6. Capponi, M.; Gut, I.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1986,** *25,* 344–345.
7. Chapman, O. L.; Lassila, J. D. *J. Am. Chem. Soc.* **1968,** *90,* 2449–2450.
8. Baldwin, J. E.; McDaniel, M. C. *J. Am. Chem. Soc.* **1968,** *90,* 6118–6124.
9. Soelch, R. R.; Mauer, G. W.; Lemal, D. M. *J. Org. Chem.* **1985,** *50,* 5845–5852.
10. Dannenberg, W.; Perst, H. *Liebigs Ann. Chem.* **1975,** 1873–1894.
11. Hobson, J. D.; Al Holly, M. M.; Malpass, J. R. *Chem. Commun.* **1968,** 764–766.
12. Hobson, J. D.; Malpass, J. R. *J. Chem. Soc. (C)* **1967,** 1645–1648.
13. Maier, G.; Schäfer, U. *Liebigs Ann. Chem.* **1980,** 798–813.

13a. Lapinski, L.; Nowak, M.-J.; Les, A.; Adamowicz, L. *J. Am. Chem. Soc.* **1994,** *116,* 1461–1467.

14. Pirkle, W. H.; Seto, H.; Turner, W. V. *J. Am. Chem. Soc.* **1970,** 92, 6984–6985.
15. Swenton, J. S.; Saurborn, E.; Srinivasan, R.; Sonntag, F. I. *J. Am. Chem. Soc.* **1968,** *90,* 2990–2991.
16. Izuoka, A.; Miya, S.; Sugawara, T. *Tetrahedron Lett.* **1988,** *29,* 5673–5676.
17. Marubayashi, N.; Ogawa, T.; Kuroita, T.; Hamasaki, T.; Ueda, I. *Tetrahedron Lett.* **1992,** *33,* 4585–4588.

3.4.4 Ketenes from Dioxinones

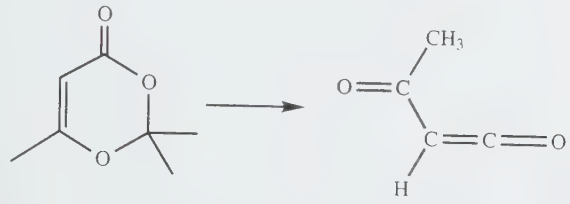
The dioxinone **1** is formed from the reaction of diketene and acetone, but even though the preparation of diketene in acetone was used industrially on a large scale, the formation of **1** was not recognized for many years. The structure of **1** was established in a collaboration by Michael F. Carroll of the A. Boake, Roberts and Company, Ltd., and Alfred Bader, founder of the Aldrich Chemical Company, using UV and IR analysis, and later NMR.[1,2] Compound **1** was one of the early offerings of the Aldrich Co., but initial sales were very slow.



1

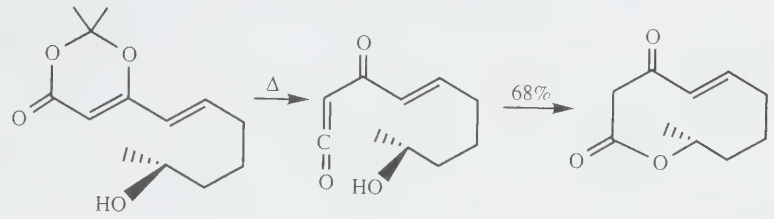
Dioxinones cleave on thermolysis or photolysis[3] with formation of acylketenes and a ketone. When **1** was pyrolyzed at 180–240 °C and the product trapped in an Ar matrix at 5–12 K the IR spectrum showed the presence of acetylketene (**2**) and acetone (equation 1).[4] Distinct ketene absorptions at 2142 and 2135 cm^{-1}

could be resolved, and it is possible that these are due to the presence of both the *s-cis* and *s-trans* rotamers of **2**, although this was not established. On the basis of MNDO calculations it was proposed that the *s-trans* form depicted is more stable.[4] As discussed in Section 4.1.6, this question has also been addressed by ab initio calculations, and for the parent formylketene the *s-cis* form is more stable.

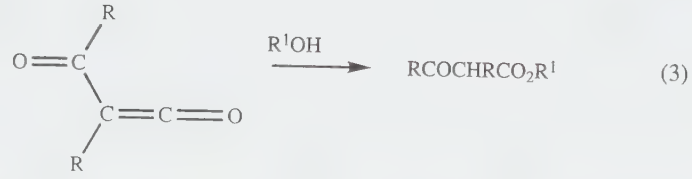


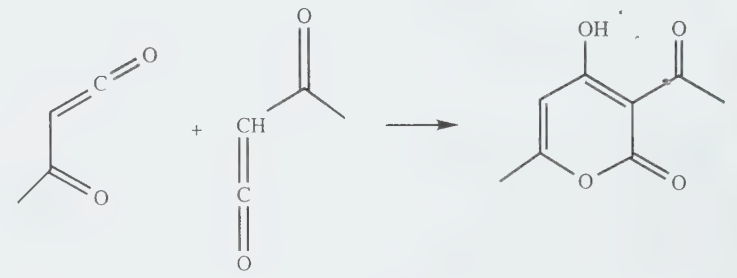
1 **2**

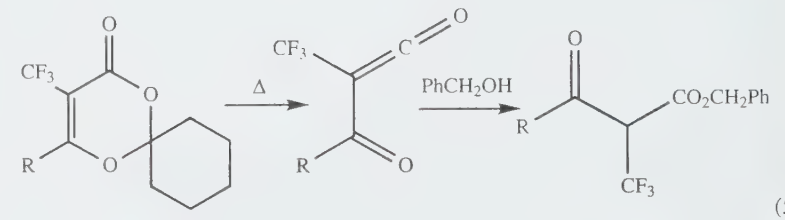
Thermolyses of a variety of dioxinones to give acylketenes have been examined. The acylketenes have been trapped intramolecularly by hydroxy groups to give ketolactones (equation 2),[5,6,15,16] intermolecularly by nucleophiles[7–11] such as alcohols (equation 3),[4] amines,[4,12] and thiols,[7] by dienophiles, including enol ethers,[12] and by dimerization (equation 4).[4] 5-Trifluoromethyl-1,3-dioxin-4-ones give trifluoromethyl acyl ketenes (equation 5).[14] 5-Halodioxinones react similarly to form α-haloacylketenes which are trapped with alcohols to give esters, or with dimethylcyanamide to give oxazinones (equation 6).[17,18] The chloroketene formed more readily than the fluoro analogue,[17] consistent with the known low stability of fluoroketenes.

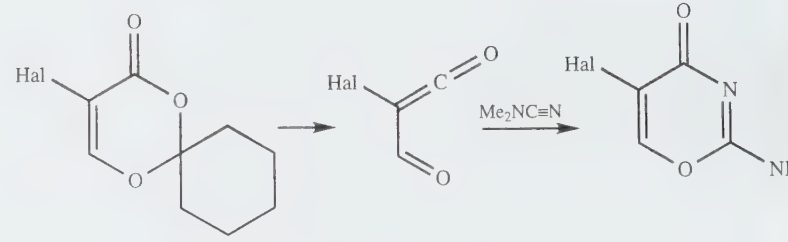


(2)[5]

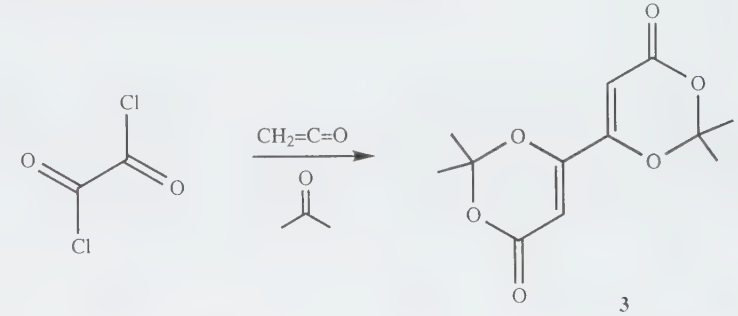




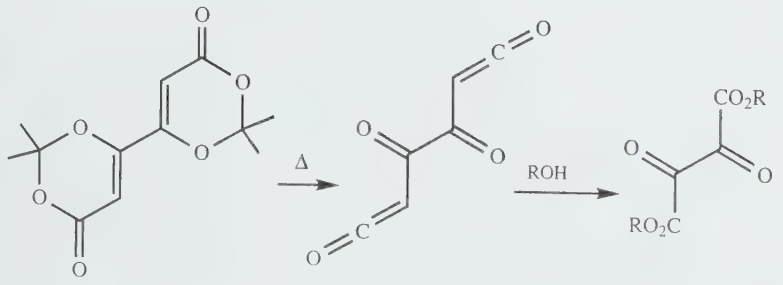




The bisdioxinone **3** was prepared from the reaction of oxalyl chloride, ketene, and acetone (equation 7) and on heating with alcohols gave the corresponding diesters.[19,20] This reaction can formally be written as proceeding through the bisketene intermediate **4** (equation 8),[19] but it is more likely that the ketenyl moieties are formed and esterified sequentially.



3



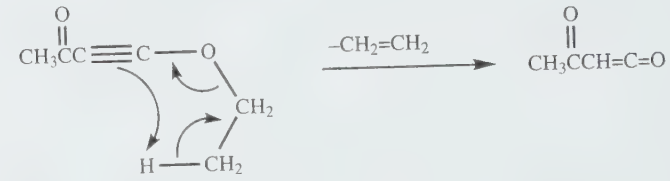
3 4 (8)

References

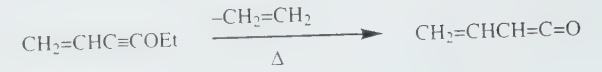
1. Carroll, M. F.; Bader, A. R. *J. Am. Chem. Soc.* **1952,** *74,* 6305; **1953,** *75,* 5400–5402.
2. Bader, A. R.; Gutowsky, H. S.; Heeschen, J. P. *J. Org. Chem.* **1956,** *21,* 821–822.
3. Kaneko, C.; Sato, M.; Sakaki, J.; Abe, Y. *J. Heterocyl. Chem.* **1990,** *27,* 25–31.
4. Clemens, R. J.; Witzeman, J. S. *J. Am. Chem. Soc.* **1989,** *111,* 2186–2193.
5. Boeckman, R. K., Jr.; Pruitt, J. R. *J. Am. Chem. Soc.* **1989,** *111,* 8286–8288.
6. Petasis, N. A.; Patane, M. A. *J. Chem. Soc., Chem. Commun.* **1990,** 836–837.
7. Sakaki, J.; Kobayashi, S.; Sato, M.; Kaneko, C. *Chem. Pharm. Bull.* **1990,** *38,* 2262–2264.
8. Clemens, R. J.; Hyatt, J. A. *J. Org. Chem.* **1985,** *50,* 2431–2435.
9. Hyatt, J. A.; Feldman, P. L.; Clemens, R. J. *J. Org. Chem.* **1984,** *49,* 5105–5108.
10. Sato, M.; Kanuma, N.; Kato, T. *Chem. Pharm. Bull.* **1982,** *30,* 1315–1321.
11. Sato, M.; Ogasawara, H.; Yoshizumi, E.; Kato, T. *Chem. Pharm. Bull.* **1983,** *31,* 1902–1909.
12. Sato, M.; Ogasawa, H.; Komatsu, S.; Kato, T. *Chem. Pharm. Bull.* **1984,** *32,* 3848–3856.
13. Coleman, R. S.; Grant, E. B. *Tetrahedron Lett.* **1990,** *31,* 3677–3680.
14. Iwaoka, T.; Sato, M.; Kaneko, C. *J. Chem. Soc, Chem. Commun.* **1991,** 1241–1242.
15. Sato, M.; Sakaki, J.; Sugita, Y.; Yasuda, S.; Sakoda, H.; Kaneko, C. *Tetrahedron* **1991,** *47,* 5689–5708.
16. Sakaki, J.; Sugita, Y.; Sato, M.; Kaneko, C. *Tetrahedron* **1991,** *47,* 6197–6214.
17. Sato, M.; Kaneko, C.; Iwaoka, T.; Kobayahsi, Y.; Iida, T. *J. Chem. Soc., Chem. Commun.* **1991,** 699–700.
18. Iwaoka, T.; Murohashi, T.; Sato, M.; Kaneko, C. *Synthesis* **1992,** 977–981.
19. Stachel, H. D. *Arch. Pharm.* **1962,** *295,* 735–744. *Chem. Abstr.* **1963,** *59,* 1582d.
20. Stachel, H. D. *Angew. Chem.* **1957,** *69,* 507.

3.4.5 Ketenes by Thermolysis of Alkynyl Ethers

Thermolysis of alkynyl ethers provides a mild and specific route to a variety of ketenes,[1–8] as in equations 1[2] and 2.[3]



(1)



(2)

For alkynyl ethers RC≡COR[1] it was found that the rate of thermolysis increased in the order R[1] = *t* − Bu > *i* − Pr > Et, as predicted by a semiempirical molecular orbital study of the reaction.[9] *tert*-Butyl alkynyl ethers *t*-BuOC≡CR undergo ketene formation at temperatures as low as 40 °C,[10,11] and provide a route to ketene itself.[10] When the ketene is thermally stable, it may be prepared and isolated from the alkyne, as in the preparation of $Me_3SiCH{=}C{=}O$ from $Me_3SiC{\equiv}COBu\text{-}t$.[11] Other ketenes were trapped by reaction with nucleophiles, or in [2 + 2] cycloadditions. The main limitations on this process are the availability of the desired 2-substituted 1-alkoxyalkynes and their stability under the conditions needed to generate the corresponding ketenes.[13] Reaction of the alkynyl ethers with the product ketene to give cyclobutenones is a common occurrence.[12] New preparative methods for such alkynes make them more available as synthetic reagents.[13] Alkynyl ether pyrolysis has been particularly useful in the preparation of silyl-substituted ketenes (Section 4.5) and phosphorous-substituted ketenes (Section 4.6). Ketenes generated from alkynyl ether pyrolysis are also useful in intramolecular cyclization to give lactones.[14]

Irradiation of the alkynyl ether **1** in methanol gave 32% yield of the ester **2,** evidently formed through the ketene **3** (equation 3),[15] along with 30–40% cyclohexanol. The corresponding reaction of the alkynyl ether of (+)-2-octanol gave 40% racemization in formation of the rearranged ester, so a mechanism involving the intermediacy of a short-lived radical pair **4** appears likely (equation 3), although some concerted 1,3-migration is also possible.[15]

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

A Chemist Helping Chemists

August 1, 1995

Professor Martin Moskovits
Chairman, Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

In response to your letter of June 27th, what a great pity that we couldn't get together in Prague in June.

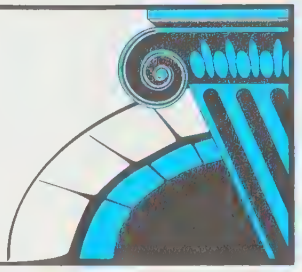
I think that the Loschmidt Symposium was a very great successand also that the many Czech chemists enjoyed it and learned a lot.

With all good wishes, I remain,

Yours sincerely,

AB/cw

Department of Chemistry
University of Toronto
150 Years of Teaching Excellence in Chemistry
1843 - 1993



27 June 1995

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin, 53211
U.S.A.

Dear Alfred:

Our journeys lately have interwoven without crossing. Although we cohabited Prague for one day, I thought it imprudent to impose upon you on the evening of your arrival when, if you are anything like me, you would have been wracked with fatigue. Interestingly, I was in Vienna on the 19th and 20th and returned to Prague at noon on the 21st, just as you were about to leave for the Loschmidt Symposium.

Coincidentally, the Conference I was attending in honour of the 400th Anniversary of the birth of Jan Marek Marci, was also attended by a Viennese Chemist named Varmuza, who advertised the Loschmidt Symposium widely and spoke peripherally in his presentation of Loschmidt's priority over Kekule, with respect to the structure of benzene. He also hung colourful posters of the Symposium all over the little town of Lonskroun, the birthplace of Marci. I felt a private joy in seeing your name listed among the speakers in that remote and anonymous corner of Eastern Bohemia.

I do hope all is well with you and Isabel and that our paths cross and intersect again soon.

With best wishes,

Yours sincerely,

Martin

/fw

Martin Moskovits
Professor and Chair.

80 St. George Street, Toronto CANADA
M5S 1A1 FAX 978-8775

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

July 10, 1995

Professor Martin Moskovits
Chairman, Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Dr. Moskovits:

Thank you for your letter of June 27th to Dr. Bader. Since speaking at the Loschmidt Symposium, Dr. Bader is staying at his home in England through the end of the month. He will reply personally upon his return to Milwaukee.

Best wishes,

Cheryl

Cheryl Weiss
Office Manager

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

A Chemist Helping Chemists

July 31, 1995

Dr. Ronald Kluger, FCIC
Department of Chemistry
University of Toronto
Toronto, ON M5S 1A1
Canada

Dear Ronald:

I have just learned that you have won the Bader Award of the Canadian Society of Chemistry to be presented to you next summer in St. John's, Newfoundland. It couldn't happen to a greater guy!

Isabel and I look forward to being at Queen's for our reunion in October, and I hope then to have a chance to get to know your daughter.

With all good wishes, I remain,

Yours sincerely,

AB/cw

bc: Steven Branca

ALFRED BADER FINE ARTS

DR. ALFRED BADER

ESTABLISHED 1961

September 21, 1994

Professor Ronald Kluger
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Ron:

I am so happy to know from your letter of September 7th that your daughter is now at Queen's.

Isabel and I plan to be there from the very end of October until the 3rd of November, giving all sorts of lectures, one of them to the Hillel Foundation. It would, of course, give me great pleasure if I could meet Melissa personally.

I am not likely ever to forget the enormous help you gave to Aldrich, Canadian universities and UPS!

All good wishes.

Sincerely,

By Appointment Only
ASTOR HOTEL SUITE 622
924 EAST JUNEAU AVENUE
MILWAUKEE WISCONSIN USA 53202
TEL 414 277-0730 FAX 414 277-0709

UNIVERSITY OF TORONTO
Department of Chemistry
80 St. George Street, Toronto, Ontario M5S 1A1

INTERNET: rkluger@alchemy.chem.utoronto.ca Phone and fax: 416-978-3582

September 7, 1994

Dr. Alfred Bader
924 E. Juneau Avenue, apt 622
Milwaukee, WI 53202

Dear Alfred,

First, my best wishes to you and Isabel for a good year.

I am writing because on Monday we took our daughter Melissa to Kingston where she is beginning her university studies at Queen's (Hillel House made arrangements for her to attend services in Kingston the next day). It was hard to relate this event to the birth 19 years ago of our first child! I was impressed with how well she was treated and how excited she was at this prospect for a new stage of education. She had been an excellent student in high school and Queen's gave her the impression that she would be in good company.

We could see the benefits of your efforts. The castle in England is mentioned in their brochures and catalogues and spoken of with excitement by student guides. One even told us that the art gallery on campus will be undergoing a major improvement with the acquisition of an important collection of early Dutch paintings. It is a special pleasure for me to see the benefits available to the young people of Ontario as a result of the vision of you and Isabel.

Sincerely,

Ronald Kluger

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

July 15, 1994

Professor J. B. Jones
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario, Canada M5S 1A1

Dear Bryan:

Thank you for your letter of July 7th.

Isabel and I very much want to establish awards not unlike the Killam awards, both in Canada and in the Czech Republic, and we are considering carefully how best to do it. One model is the Killam Awards, another, the Leibnitz Awards given by the German Chemical Society.

We think very much along your thoughts, except that I believe we should limit the awards in both countries to organic chemists and biochemists, simply because I have had very little interest in inorganic, analytical, physical and theoretical chemistry.

The amounts of money involved are very large, so we want to move very cautiously. Also, we are taking counsel with Daniel Bader, my son, who will be the president of the Isabel and Alfred Bader Foundation after we are gone.

Isabel and I look forward to being in Canada several times during the next year, and we will try to talk to you, Martin Moskovits, and Eva Kushner to share our thinking in detail.

All good wishes.

Sincerely,

c: Dr. Eva Kushner
Prof. Martin Moskovits

University of Toronto

Professor J. Bryan Jones

Tel: (416) 978-3589
Fax: (416) 978-1553

Department of Chemistry
Lash Miller Chemical Laboratories
80 St. George Street
Toronto , Ontario
Canada M5S 1A1

7 July 1994

Dr. Alfred R. Bader
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
USA

Dear Alfred:

It was very good seeing you again recently during your, and Isabel's, visit to Toronto.

I have reflected further on your question as to "what would make a difference in the Canadian chemical scene", and I always come back to the scheme I mentioned to you that would support our best young people.

What I believe would be enormously important, would be a fund to award grants to perhaps 6-10 academic chemists at a time. One could invite nation-wide applications for 3-year grants, of $50,000 per annum?, to be given to the best young applicants, on a once-only basis. This should cover all the areas of chemistry so that a broad maintenance of excellence is encouraged. On the other hand, it should be ensured that no one discipline corners the funds, so that a structure enabling support across all disciplines should be put in place, perhaps specifying at least 2 grants in each of organic/biological, inorganic/analytical, and physical/theoretical, with any remaining grants to the best in any area. An age limit of 37? for the last application for a 3-year grant would ensure that the support went to young scientists within the important development times of their careers.

I know that Martin Moskovits and you have also talked about this type of programme, and Martin and Dr. Eva Kushner are also in close touch. The Killam-like mechanism that Martin suggested for such a scheme, with peer reviews from external experts in the selection and screening, would be very appropriate and would give such a programme the high national profile and credibility it would deserve. Martin is aware of this letter, and will pass its content on to Dr. Kushner, since he and she are in frequent contact.

Another way of making a real difference, in a very targetted manner, would be for you to set up chairs in the areas that you identify as important, at the universities that you feel could best do the job. This would help to advance, or develop anew, key areas in which Canada needs more, or has little or no, strength. If such a scheme were to be attractive to you, the best location(s) would have to be selected very carefully in order for the opportunity to be exploited fully and incisively.

I know you are in Europe at this time, but I hope this letter will reach you eventually.

With very best regards to you and to Isabel.

Sincerely,

J. B. Jones

cc: Martin Moskovits

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

January 5, 1995

Professor J. C. Polanyi
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Professor Polanyi:

I am truly moved by your thoughtfulness in sending me your letter of November 26th and your talk at the gala dinner of November 3rd.

So very often talks given at dinners, no matter how important, are competent but forgettable. Yours is not. I have picked it up five times in the last three days--since returning from England--and have thought, not just about this or that facet, but about the total picture which you paint so clearly.

All good wishes for 1995.

Sincerely,

PROFESSOR J.C. POLANYI
Department of Chemistry
University of Toronto TORONTO ONTARIO M5S 1A1

Dr and Mrs Alfred Bader

Nov 26th, '94

Dear Dr and Mrs. Bader,

I was so sorry that you could not be a part of the two-day bash that Martin Moskovits mounted early this month. To give you the flavour of it I enclose some remarks that I made at the dinner.

With kindest regards,

John Polanyi

Lash Miller Chemical Laboratories 80 St. George Street Tel: (416) 978-3580; FAX: (416) 978-7580

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

May 19, 1995

Professor Martin Moskovits
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

Isabel and I spent two delightful days in Toronto earlier this week, and yesterday Isabel received her honorary doctorate from Victoria University.

I know how very much influence you had in bringing this about, and I wanted to stop by and thank you personally. However, our schedule was so crowded that I didn't know exactly when I would be able to stop by, couldn't make an appointment, and so missed seeing you.

A copy of Isabel's convocation speech is enclosed. I hope that the budding ministers graduating were listening.

With many thanks and best personal regards, I remain,

Yours sincerely,

AB/cw

Enclosure

Department of Chemistry
Office of the Chair • **University of Toronto**

80 St. George Street
Toronto, Ontario
M5S 1A1
fax • (416) 978-8775
phone • (416) 978-3564

April 3, 1995

Mrs. Isabel Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

Dear Isabel:

I was greatly touched that you included me among the guests celebrating your richly deserved honor. I look forward with anticipation to seeing you receive your honorary degree.

I do also hope that both you and Alfred are well and busily pursuing your very many valuable philanthropic projects. I think of you both often. I know that you received a copy of the address which John Polanyi composed for gala dinner in his honor. It was a very splendid event and I still regret that you were not able to attend. I am curious to know what you and Alfred thought of John's words. I have recently finished editing a small volume of the public lectures also associated with the Polanyi celebration. I will send you a copy as soon as it appears. (It will, naturally, be authographed unless you request otherwise. Some claim that it is the *un*-autographed copies of my books that are more rare.)

I had lunch recently with Eva Kushner and we spoke fondly of the Baders.

Do let me know when you're in Toronto. It would give me pleasure to see you both if you can spare the time. I will be visiting Prague again in June. Apparently the Academy of Sciences wishes honor me in some way. As before, I will be happy to communicate my impressions to you and Alfred.

All the very best to you and Alfred for the Passover season.

Sincerely,

Martin Moskovits

grad@chem.utoronto.ca • undergrad@chem.utoronto.ca • chair@chem.utoronto.ca

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

June 5, 1995

Via Facsimile: 416/978-8775

Professor Martin Moskovits
Chairman, Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

The *Leitmotiv* of your letter of May 19th, only just received, is the word *moving*. But I must tell you that what Isabel and I found truly moving is the thoughtfulness of your letter. Many thanks.

As you will be able to imagine, Isabel gave a great deal of thought to her convocation speech, and I am glad you enjoyed it.

Isabel and I will spend just three days in Prague this month, from Sunday evening, June 18th until Wednesday noon, June 21st, staying at the U Zlatého Konícka in the Husova 18. Wednesday noon, we plan to drive to Brno, where I will give four talks between Wednesday evening and Friday noon, when we will drive to Vienna to be at the Loschmidt Symposium.

I enclose a copy of the Loschmidt program; is there any chance that you might attend?

With all good wishes, I remain,

Yours sincerely,

AB/cw

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

June 5, 1995

Via Facsimile: 416/978-8775

Professor Martin Moskovits
Chairman, Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

The *Leitmotiv* of your letter of May 19th, only just received, is the word *moving*. But I must tell you that what Isabel and I found truly moving is the thoughtfulness of your letter. Many thanks.

As you will be able to imagine, Isabel gave a great deal of thought to her convocation speech, and I am glad you enjoyed it.

Isabel and I will spend just three days in Prague this month, from Sunday evening, June 18th until Wednesday noon, June 21st, staying at the U Zlatého Konícka in the Husova 18. Wednesday noon, we plan to drive to Brno, where I will give four talks between Wednesday evening and Friday noon, when we will drive to Vienna to be at the Loschmidt Symposium.

I enclose a copy of the Loschmidt program; is there any chance that you might attend?

With all good wishes, I remain,

Yours sincerely,

AB/cw

Department of Chemistry • University of Toronto
Office of the Chair

80 St. George Street
Toronto, Ontario
M5S 1A1
fax • (416) 978-8775
phone • (416) 978-3564

May 19, 1995

Dr. and Dr. Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

Dear Alfred and Isabel:

I was privileged to experience two moving events recently. The first was reading Alfred's Parson's Award address, the second was listening to Isabel's address at last night's Convocation at which she received her much deserved doctorate. You might accept the fact that the word *moving* is a fitting descriptor for Isabel's beautifully crafted and inspiring sermon. Quoting the words of Moses, filled with so much love for his people yet also suffused with the pathos of knowing that he would be denied the gratification of entering the promised land was such an apt and inspirational symbol. But why do you suppose that I chose to characterize Alfred's address as *moving*? Certainly it was informative. It was courageous. It was erudite. It was the final the final paragraph that made it moving.

I tried to come up to you both after the Convocation to give you my best wishes. The throng was so great and all but your faces (aside from those of Eva and Roseanne) were so unfamiliar that I realized that, although I was so happy for the two of you, the celebration was not mine. It belonged to you, of course, but also to that special and nurturing intellectual hearth that is Victoria College.

I was also very disappointed to have missed Alfred when he came to visit me. I had a doctor's appointment. Just the same I was very touched that Alfred made the effort. I do hope that there's another opportunity to see each other soon.

I will be spending two weeks in the Czech Republic in the middle of June. If there are any duties that you'd like me to carry out while I'm there I'd be very happy to comply. I am also glad that you enjoyed reading John Polanyi's address. I'm perfectly certain that he is flattered that you quoted him in your Parson's lecture.

Finally, I attended another moving event recently. The University of Toronto hosted a remembrance in Convocation Hall in honor of Yom Hashoa. The ceremony was preceded with a tribute by the Provincial Government of Ontario to Jewish war veterans. I enclose the program. Perhaps it's of interest to you.

With best wishes and good health to both of you.

Sincerely,

Martin Moskovits

PROFESSOR J.C. POLANYI

Department of Chemistry

University of Toronto TORONTO ONTARIO M5S 1A1

May 8, 1995

Dr. Alfred Bader
Astor Hotel Suite 622
924 East Juneau Avenue
Milwaukee Wisconsin
53202,
U.S.A.

Dear Dr. Bader,

How kind of you to send your charming Parson Award Address. I have just read an irresistible excerpt from your biography in the Queen's alumni magazine and am in the process of sending for a copy.

With all good wishes,

John

/nb

Enclosure: A recent talk in the U.K.

Lash Miller Chemical Laboratories 80 St. George Street Tel: (416) 978-3580; FAX: (416) 978-7580

UNIVERSITY OF TORONTO
Department of Chemistry
80 St. George Street, Toronto, Ontario M5S 1A1

INTERNET: rkluger@alchemy.chem.utoronto.ca Phone and fax: 416-978-3582

March 9, 1995

Dr. Alfred Bader
924 E. Juneau Avenue, apt 622
Milwaukee, WI 53202

Dear Alfred,

After I wrote to you on March 3, I called the exams office at Queen's and was told that they are investigating scheduling. The exams officer said that the concerns I expressed were being dealt with by a Senate committee. Furthermore, my daughter said she went to the exams office to request to have her exam moved from Passover and they were very fair. In light of these positive events, I withdraw my request to you to intervene. The whole story seems better than its beginning. I know that it is probably not too bad to "bother" you, since it follows your policy from the Aldrich days. Nonetheless, I will try to limit my requests.

I thank you for your continuing interest.

Sincerely,

Ronald Kluger

UNIVERSITY OF TORONTO
Department of Chemistry
80 St. George Street, Toronto, Ontario M5S 1A1

INTERNET: rkluger@alchemy.chem.utoronto.ca Phone and fax: 416-978-3582

March 3, 1995

Dr. Alfred Bader
924 E. Juneau Avenue, apt 622
Milwaukee, WI 53202

Dear Alfred,

My daughter Melissa has called my attention to an issue at Queen's for which I'd like to ask you to consider providing some help as a member of their Board of Governors (I know you were effective for UPS). Queen's schedules classes and final examinations without regard to Jewish holy days. Thus, this year, Melissa and others have been asked to write final exams on the first day of Passover. The son of a friend of ours went to the registrar to complain about the scheduling and was told that Queen's is a Christian university and the examination arrangements reflect that status. Jewish students can take make-up exams in the summer if they miss the exams to observe Passover. I think this places an unnecessary strain on these students.

The contrast with the University of Toronto is instructive. We do not hold classes or exams on Saturday and we are not permitted to give exams on Jewish or Moslem holy days. The start of our fall term was delayed until after Rosh Hashanah while Queen's was in full swing. I think the attitude my daughter feels from the Queen's administration is one of insensitivity and intolerance. Her friends who have gone elsewhere have done much better in this regard. I think Queen's might wish to emulate what we are doing here. Other students do not object to treating minority religions with sensitivity, even if it places some challenges before administrators.

Best regards,

Ronald Kluger
Professor

FAX TRANSMITTAL SHEET

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211
Telephone 414 962 5169
FAX 414 962 8322

DATE: March 1995

TO:

Prof. Ronald Kluger
Dept. of Chemistry, U. of Toronto

Dear Ronald

Please fax me the name
of the paper at Penn. Sta. under
the Statement about Durian odour
in Penicillin.

Yours always

Al

ALFRED BADER FINE ARTS

DR. ALFRED BADER

ESTABLISHED 1961

March 31, 1995

Professor John Polanyi
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Professor Polanyi:

I hope that you will not mind my quoting so liberally from your wonderful speech last November.

With all good wishes, I remain,

Yours sincerely,

AB/cw

Enclosure - Speech

By Appointment Only
ASTOR HOTEL SUITE 622
924 EAST JUNEAU AVENUE
MILWAUKEE WISCONSIN USA 53202
TEL 414 277-0730 FAX 414 277-0709

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

November 9, 1994

Professor Martin Moskovits, Chairman
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

Please accept Isabel's and my sincere thanks for your great care last Sunday. Of course we were truly sorry about the turn of events, and know that it's initiative came neither from you nor Eva Kushner.

What I have so enjoyed about Queen's University--besides their wonderful treatment of me--is that I have never, ever been asked to give anything. Isabel very much wanted to act the same way with the University of Toronto, and last year gave U.S.$25,000 to a scholarship fund without being asked, and then repeated that gift this year.

I hope that you will understand.

All good wishes.

Sincerely,

ALFRED BADER FINE ARTS

DR. ALFRED BADER

ESTABLISHED 1961

September 21, 1994

Professor Ronald Kluger
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Ron:

I am so happy to know from your letter of September 7th that your daughter is now at Queen's.

Isabel and I plan to be there from the very end of October until the 3rd of November, giving all sorts of lectures, one of them to the Hillel Foundation. It would, of course, give me great pleasure if I could meet Melissa personally.

I am not likely ever to forget the enormous help you gave to Aldrich, Canadian universities and UPS!

All good wishes.

Sincerely,

By Appointment Only
ASTOR HOTEL SUITE 622
924 EAST JUNEAU AVENUE
MILWAUKEE WISCONSIN USA 53202
TEL 414 277-0730 FAX 414 277-0709

UNIVERSITY OF TORONTO
Department of Chemistry
80 St. George Street, Toronto, Ontario M5S 1A1

INTERNET: rkluger@alchemy.chem.utoronto.ca Phone and fax: 416-978-3582

September 7, 1994

Dr. Alfred Bader
924 E. Juneau Avenue, apt 622
Milwaukee, WI 53202

Dear Alfred,

First, my best wishes to you and Isabel for a good year.

I am writing because on Monday we took our daughter Melissa to Kingston where she is beginning her university studies at Queen's (Hillel House made arrangements for her to attend services in Kingston the next day). It was hard to relate this event to the birth 19 years ago of our first child! I was impressed with how well she was treated and how excited she was at this prospect for a new stage of education. She had been an excellent student in high school and Queen's gave her the impression that she would be in good company.

We could see the benefits of your efforts. The castle in England is mentioned in their brochures and catalogues and spoken of with excitement by student guides. One even told us that the art gallery on campus will be undergoing a major improvement with the acquisition of an important collection of early Dutch paintings. It is a special pleasure for me to see the benefits available to the young people of Ontario as a result of the vision of you and Isabel.

Sincerely,

Ronald Kluger

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

August 1, 1994

Professor Martin Moskovits, Chairman
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario
Canada M5S 1A1

Dear Martin:

Thank you so much for your letter of July 11th.

It would be churlish of me to say that Isabel and I should not receive honorary degrees together, but I truly believe that Isabel is more deserving, particularly at the University of Toronto.

The more we think about how to help Canadian students and Czech students in chemistry, the more we feel that the same kind of scheme might well apply to both; namely, a substantial amount of money for young organic chemists regardless of the university at which they are.

I much look forward to discussing this with you and Dr. Kushner when we see you.

Best wishes.

Sincerely,

Department of Chemistry • University of Toronto

80 St. George Street
Toronto Ontario
M5S 1A1
fax • 978-8775
phone • 978-3564

Dr. Alfred R. Bader
2961 North Shepard Avenue
Milwakee, Wisconsin 53211
USA

July 11, 1994

Dear Alfred:

I do hope that your travels through Europe were both pleasant and successful. Thank you, also, for the delightful Chapter from your autobiography. Coincidentally, I just finished reading an article in Saturday Night regarding Herstmonceux castle. It filled in some important details concerning your adventures and accomplishments.

Dr. Eva Kushner and I met to discuss the possibility of an honorary degree. We believe that it would be most fitting if both you and Isabel were nominated for an honorary degree together. Dr. Kushner has already approached President Rob Prichard about this and I will speak with him about it in my own right.

Additionally we chatted about the possibility of participating, in some way, in your plans for supporting research and scholarship activities in the Czech Republic and the startup costs of young scientists in Canada. Perhaps when you return to North America Dr. Kushner and I can come to visit you in Milwaukee at a convenient date, or alternatively, we can meet in Toronto, if you and Isabel prefer.

Dr. Kushner made a very strong impression on me. I believe that the four of us can work effectively together. We should discuss how we can do so.

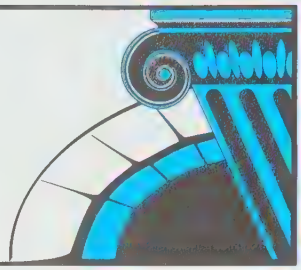
With best personal regards to you and Isabel.

Sincerely,

Martin

Martin Moskovits

Department of Chemistry
University of Toronto
150 Years of Teaching Excellence in Chemistry
1843 - 1993



June 24, 1994

Dr. Alfred R. Bader & Mrs. Isabel Bader
Suite 622, 924 East Juneau Avenue
Miiwaukee, Wisconsin
U.S.A. 53202

Dear Alfred and Isabel:

We are extremely grateful to you for taking time to participate in the Feasibility Study for our proposed extension of the Lash Miller Chemical Laboratories of the University of Toronto. The study indicated that there was overwhelming support both for the need and the possibility of realizing such a goal. In addition, many useful caveats were expressed by the participants which will help us greatly in our campaign. Your valuable time and wisdom is appreciated.

Yours sincerely,

M. Moskovits
Professor and Chair

MMo:dc
dc:\mmo\letts\thanks.bad

80 St. George Street, Toronto CANADA
M5S 1A1 FAX 978-8775

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

July 15, 1994

Professor J. B. Jones
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario, Canada M5S 1A1

Dear Bryan:

Thank you for your letter of July 7th.

Isabel and I very much want to establish awards not unlike the Killam awards, both in Canada and in the Czech Republic, and we are considering carefully how best to do it. One model is the Killam Awards, another, the Leibnitz Awards given by the German Chemical Society.

We think very much along your thoughts, except that I believe we should limit the awards in both countries to organic chemists and biochemists, simply because I have had very little interest in inorganic, analytical, physical and theoretical chemistry.

The amounts of money involved are very large, so we want to move very cautiously. Also, we are taking counsel with Daniel Bader, my son, who will be the president of the Isabel and Alfred Bader Foundation after we are gone.

Isabel and I look forward to being in Canada several times during the next year, and we will try to talk to you, Martin Moskovits, and Eva Kushner to share our thinking in detail.

All good wishes.

Sincerely,

c: Dr. Eva Kushner
Prof. Martin Moskovits

University of Toronto

Professor J. Bryan Jones

Tel: (416) 978-3589
Fax: (416) 978-1553

Department of Chemistry
Lash Miller Chemical Laboratories
80 St. George Street
Toronto , Ontario
Canada M5S 1A1

7 July 1994

Dr. Alfred R. Bader
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
USA

Dear Alfred:

It was very good seeing you again recently during your, and Isabel's, visit to Toronto.

I have reflected further on your question as to "what would make a difference in the Canadian chemical scene", and I always come back to the scheme I mentioned to you that would support our best young people.

What I believe would be enormously important, would be a fund to award grants to perhaps 6-10 academic chemists at a time. One could invite nation-wide applications for 3-year grants, of $50,000 per annum?, to be given to the best young applicants, on a once-only basis. This should cover all the areas of chemistry so that a broad maintenance of excellence is encouraged. On the other hand, it should be ensured that no one discipline corners the funds, so that a structure enabling support across all disciplines should be put in place, perhaps specifying at least 2 grants in each of organic/biological, inorganic/analytical, and physical/theoretical, with any remaining grants to the best in any area. An age limit of 37? for the last application for a 3-year grant would ensure that the support went to young scientists within the important development times of their careers.

I know that Martin Moskovits and you have also talked about this type of programme, and Martin and Dr. Eva Kushner are also in close touch. The Killam-like mechanism that Martin suggested for such a scheme, with peer reviews from external experts in the selection and screening, would be very appropriate and would give such a programme the high national profile and credibility it would deserve. Martin is aware of this letter, and will pass its content on to Dr. Kushner, since he and she are in frequent contact.

Another way of making a real difference, in a very targetted manner, would be for you to set up chairs in the areas that you identify as important, at the universities that you feel could best do the job. This would help to advance, or develop anew, key areas in which Canada needs more, or has little or no, strength. If such a scheme were to be attractive to you, the best location(s) would have to be selected very carefully in order for the opportunity to be exploited fully and incisively.

I know you are in Europe at this time, but I hope this letter will reach you eventually.

With very best regards to you and to Isabel.

Sincerely,

J. B. Jones

cc: Martin Moskovits

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

June 6, 1994

Professor Martin Moskovits, Chairman
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Martin:

You must have realized how very much I enjoyed our hour together on Friday.

As promised, please find enclosed the chapter from my autobiography. Please do keep this confidential, but feel free to quote individual passages which apply.

You know that I will value your advice how best to help Czech chemists. The most important question to be answered is which university would be helped most by the establishment of a chair.

Isabel and I are off to England tomorrow, and then to Prague on Sunday. Hence, please don't mind this hurried note.

All good wishes.

Sincerely,

Enclosure

FAX FROM

DR. ALFRED R. BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone 414-277-0730
Fax No. 414-277-0709

May 27, 1994

To: Professor M. Moskovits, Chair
Department of Chemistry
University of Toronto 416 978 8775

Dear Professor Moskovits:

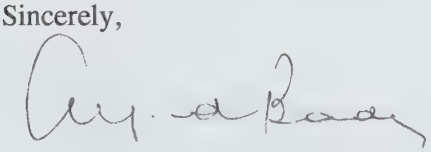
Thank you very much for your kind invitation for lunch and additional time on Friday, June 3.

Isabel and I would love to be able to accept, but we cannot because of the uncertainty of our timetable. It is Isabel's 45th class reunion at Victoria University with all sorts of festivities. Also, Principal David Smith is trying to set up a meeting with Ontario government officials to discuss building plans at Queen's. However, the time has not yet been set.

Isabel and I will not fail to visit the chemistry department on Friday to greet our many friends, but we just do not know when.

Many thanks for your understanding.

Sincerely,



Department of Chemistry
University of Toronto
150 Years of Teaching Excellence in Chemistry
1843 - 1993

May 25, 1994
Faxed May 26, 94

Dr. Alfred R. Bader
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
U.S.A.

Dear Dr. Bader:

Thank you for your letter of May 17th, 1994. I understand from Bryan Jones that you will be in Toronto on June 3rd and I have set aside that day for you and Isabel. May I suggest lunch and perhaps you would both like to meet with some of our staff during the day.

With all best wishes,

Yours sincerely,

M. Moskovits
Professor and Chair

MMo:dc
dc:\mmo\letts\bader.2

80 St. George Street, Toronto CANADA
M5S 1A1 FAX 978-8775

William Blake (English, 1757–1827)
The Ancient of Days, frontispiece from *Europe, A Prophecy*, 1821
Relief etching, pen and watercolor, heightened with gold,
304 x 236 mm

The Fitzwilliam Museum, Cambridge

150-4533 Pomegranate Publications, Box 808022, Petaluma, CA 94975
Printed in Korea

CANADA
$1.95

May 16, 1994

Dear Alfred,

I read that you will be receiving the ACS's Parsons Award for your services to chemistry. It is a very well-deserved honor, furthermore it gave C&E news a reason to write another story that told me more about your interesting background.

Congratulations!

Ron Kluger

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

May 23, 1994

Professor Ronald Kluger
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Ron,

Thank you for your gracious note.

Isabel's 45th reunion will be held at your university the weekend of June 4th, and so I look forward to being in your department on Friday the third, and it would be great if I could thank you personally.

All good wishes.

Sincerely,

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

May 20, 1994

Via Fax 416 978 1553
Confirmation by mail

Prof. J. Bryan Jones
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Bryan:

When you asked me yesterday to send you a list of my donations to Queen's University, I thought that it would be no problem at all. However, I have tried to help Queen's in many different ways over the years, and so I hope that you will understand that I have only included the highlights in the attached list. I have included the first two, even though they were very small, simply because these gifts started it all.

I also continue to give old master paintings to Queen's and can give you a copy of the 1988 catalog when I see you. Now I just enclose copies of the introduction.

Isabel and I much look forward to seeing you in two weeks.

Best regards.

As always,

Enclosures

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

May 20, 1994

Via Fax 416 978 1553
Confirmation by mail

Prof. J. Bryan Jones
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Bryan:

When you asked me yesterday to send you a list of my donations to Queen's University, I thought that it would be no problem at all. However, I have tried to help Queen's in many different ways over the years, and so I hope that you will understand that I have only included the highlights in the attached list. I have included the first two, even though they were very small, simply because these gifts started it all.

I also continue to give old master paintings to Queen's and can give you a copy of the 1988 catalog when I see you. Now I just enclose copies of the introduction.

Isabel and I much look forward to seeing you in two weeks.

Best regards.

As always,

Enclosures

GIFTS TO QUEEN'S UNIVERSITY

1948	Martin Wolff prize in civil engineering (See enclosed from my autobiography.)
1956	Aldrich Scholarship in Chemistry (Funded personally, not by Aldrich.)
1968 to date	Over 120 old master paintings, 36 of which travelled throughout Canada in 1988-89
1990	$1 million Graduate Fellowship Fund
1991	Bader Chair in Chemistry
1991	$2 million "Seed Money" for new Queen's Art Museum
1993	Gift to Queen's (£6,000,000) to purchase Herstmonceux Castle
1994	Gift to Queen's to purchase additional 250 acres adjoining Castle

Several smaller gifts not included in this list.

FAX FROM

DR. ALFRED R. BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone 414-277-0730
Fax No. 414-277-0709

May 17, 1994

To: Professor M. Moskovits, Chair
Department of Chemistry
University of Toronto 416 978 8775

Dear Professor Moskovits:

Thank you for your thoughtful letter of May 9th, received today.

Isabel and I look forward to being in Toronto the first weekend in June to attend Isabel's 45th reunion at Victoria University.

In fact, on Saturday morning we will be with Professor Eva Kushner, who knows a great deal about the Czech Republic and who is counseling us how best we can help. She is the President of Victoria University, and surely you know her.

Isabel and I have established four fellowships for Czech students to earn their PhD at Columbia, Imperial College, University of Pennsylvania, and Harvard. Surprisingly, these universities have found it difficult to attract students.

We will telephone you while we are in Toronto to see if we can get together.

All good wishes.

Sincerely,

Department of Chemistry • University of Toronto

80 St. George Street
Toronto Ontario
M5S 1A1
fax • 978-8775
phone • 978-3564

May 9, 1994

Dr. A.R. Bader
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin
53202 U.S.A.

Dear Dr. Bader:

I have just returned from the Czech republic where I participated in putting a bilateral agreement between Charles University and the University of Toronto into effect. I also met a very large group of Czech scientists and had a lengthy meeting with Professor Zahradnik the president of the Czech Academy of Science which also operates the rather extensive networks of research institutes where much of the best research in the CR is carried out. Professor Zahradnik is an old friend. I discussed with him and with others the difficulties that benefactors such as yourself are having in ensuring that funds are targeted towards students and other worthwhile causes rather than being squandered on phoney administration excercises. (Needless to say, I did not mention your name). I believe that there are ways of ensuring this.

The Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences appears to be doing very fine work. I became aware of the work of Dr. I. Rosenberg and Z. Tocík who seems to be working on forefront problems with rather poor resources. Likewise a Professor V. Fidler of Charles University seems to be doing very fine biophysical chemistry. There are many others.

I am quite interested in continuing my efforts to help Czech chemists by bringing students and young faculty to Canada for short sojourns in order to allow them to participate in modern research on modern equipment. I would be happy to keep in touch so that we can profit from each other's experience in this regard.

I understand that you will be in Toronto for spring reunion. Would it be possible for us to have lunch together?

With best regards,

Yours sincerely,

M. Moskovits
Professor and Chair

MMo:dc
dc:\

Department of Chemistry • University of Toronto

80 St. George Street
Toronto Ontario
M5S 1A1
fax • 978-8775
phone • 978-3564

April 11, 1994

Dr. Alfred R. Bader & Mrs. Isabel Bader
Suite 622, 924 East Juneau Avenue
Milwaukee, Wisconsin
U.S.A. 53202

Dear Dr. & Mrs. Bader:

Experience has shown that it is advisable to conduct a feasibility study before embarking on fund raising. We are presently contemplating an appeal for funds to upgrade the facilities for research and teaching in Chemistry at the University of Toronto, and we are most anxious to have your views, in confidence.

The situation, in brief, is this. Since we moved into our present building in 1960, the field of chemistry has been transformed (see the attached). It has invaded, or has been invaded, by physics and biology. It has moved from the study of matter in bulk to the molecular level. It has, in fact, become *molecular science*.

This academic concern for the microscopic has, as so often in the past, been accompanied by parallel changes in the world of practice. In 1960 the future of technology still seemed to lie with the very big. Now it is recognized to lie with the extremely small.

Specifically, our problem in molecular science is too little space, and the wrong sort of space. We need to build, and have formulated plans for doing so.

Timing is critical for such an undertaking. After three decades of reconfiguring, in order to adjust to transformed circumstances, we can reconfigure no more. We believe that this is the right time to build. That is our view; we would greatly value yours.

What we are hoping, is that you will agree to a fifteen-to-thirty minute confidential interview to share your perceptions with a senior member of the consulting firm of Gordon L. Goldie Co. Ltd., which we have engaged to assist in gathering opinions. A member of the project team will contact you in the next few days, in the hope of arranging a convenient time for a personal/telephone interview.

We have some notion of the pressures on your time, and would be correspondingly grateful if you could assist us in this way.

Sincerely,

Martin Moskovits
Chair
Department of Chemistry

John C. Polanyi
Professor
Department of Chemistry

/aa

Department of Chemistry
University of Toronto

THE RIGHT MIX

In 1960,

- John G. Diefenbaker was Prime Minister of Canada
- "Let's Do the Twist" was top of the charts
- The Chevrolet "Corvair" was the car of the year
- The Lash Miller Chemical Laboratories were constructed to house the Department of Chemistry at the University of Toronto.

In 1960, benzene was a common solvent used liberally with bare hands in the open laboratory. In those days, solvents were stored on shelves in bottles as were chemicals, and only the most noxious and dangerous reactions were carried out in fume hoods.

Today, almost all chemical procedures must be performed in fume hoods. Solvents must be held in special cans or in solvent cabinets, and chemicals must be housed in vent cupboards. Benzene is now recognized as a dangerous carcinogen that must only be used in a fume hood. In this instance, the current severe shortage of fume hoods fundamentally affects research and undergraduate instruction alike. This is only one example of the need to address the debilitating limitations of a 34-year-old structure on the most successful and prestigious department of its kind in Canada. And one of the top chemistry departments world-wide.

The extraordinarily high level of scholarship in the Department of Chemistry forms the basis on which graduate and undergraduate students are educated. Nobel Prize winner Dr. John Polanyi is one of Canada's best known scientists and typifies the depth of research underway within the Department. There are currently many young, top-flight scientists who, with the appropriate support, will reach new heights of research excellence.

Over the past three decades, there have been phenomenal advances in research and related technology. It has been suggested that the very term "Chemistry" is being transformed into a discipline that is better described as "molecular sciences." The Lash Miller Chemical Laboratories were never intended to take into account the large floor space areas needed for high field NMR machines, tandem mass-spectrometers, lasers, ultra-high vacuum systems used in modern surface science, the large controlled-atmosphere enclosures and ovens used to prepare novel materials, nor the fact that even preparative organic chemists now wish to have instruments such as high-performance liquid chromatographs, gas-chromatograph-mass-

spectrometers within their labs. Theorists who were connected to massive and static mainframe computers now have the flexibility of multiple work stations and mid-sized computers.

Consider for a moment these scenarios:

> (1) The undergraduate laboratory wing of the Lash Miller Chemical Laboratories was built in an era when there were no summer students. Consequently, it was not air-conditioned. The use of the laboratories nowadays is almost as heavy in the summer as during the winter and spring terms. With windows sealed and without air conditioning, the temperature in those laboratories exceeds 35°C. Last year, for example, some of the solid chemicals used in experiments melted during use! Students also had to leave the laboratory periodically, in order to continue working under those conditions.
>
> (2) In the '60's, there were approximately 20 professional research faculty and 138 research assistants (graduate students, post doctorals and research associates). Today, there are 36 professors active in research, 200 research assistants, plus other tutors, support staff and technical staff to service instrumental facilities.
>
> As the number of undergraduates and graduate students climbed, common rooms, meeting rooms and seminar rooms were slowly absorbed into desperately needed laboratory space. Safety regulations forbid occupants from eating in the labs. Regretfully, most leave the building for seminars, meetings, eating, studying and even a breath of fresh air in summer.
>
> Particularly in specialist programs, the inability to meet and create together in a team environment fragments the solidarity and departmental morale of faculty and students.

These are perplexing circumstances from the users' point of view; however, the long-term damage lies in the perceptions of prospective colleagues who see the physical facility limitations and compare them to other leading university facilities.

Clearly, after years of "making do" under deteriorating conditions, the U of T Department of Chemistry must undertake a deliberate and aggressive campaign to maintain its pre-eminence in the areas of graduate training and undergraduate teaching. Reorganization, consolidation and renovation of existing space, coupled with the building of new space, forms the basis of this capital program. Central to the campaign is formulating the appropriate academic plans and priorities which will include new undergraduate programs, new directions in the graduate area and a policy of interaction and partnership with Canadian industry and business.

The immediate academic goals for the Department include:

1. Establishing undergraduate programs in biological chemistry, materials chemistry and environmental chemistry, increasing, thereby, the number of FTE chemistry specialists by approximately 50,

2. Recruiting more and higher quality graduate students in order to enlarge our steady-state numbers to 150-160,

3. Making two industrial Chair appointments, one in the materials area, the other in biophysical chemistry. Interest has been expressed by major corporations, and candidates have been identified.

In order to achieve these goals, there is the need to rearrange existing space and to increase the laboratory space and the non-laboratory space each by approximately 20,400 square feet, gross area. The non-laboratory space will allow current administrative space to revert to laboratories and, therefore, more research space. The Lash Miller Chemical Laboratories were built in such a manner that all the space in the research area, including offices, is actually fully serviced research space.

What will it cost?

Floors #1, #2 and Roof Renovations, Air Quality, Mechanical Work	$1,300,000
Floor #3 Additional Laboratories (13) and 1 Common Room	5,100,000
Floor #4 Department Administration, Meeting, Common and Seminar Rooms	3,600,000
TOTAL	$10,000,000

SUMMARY

This capital development program will address the following issues:

(1) Safety/health hazards
(2) Space-reorganization/consolidation/renovation/creation
(3) Relevant academic programming
(4) Retaining/attracting world-class researchers
(5) Corporate relationships
(6) Providing the highest standards of undergraduate and graduate education.

Imagine, if you will, building a precision formula race car in a shop that was built over thirty years ago. It's unthinkable and no longer tenable. In fewer than six years, we will enter a new millenium. The world will not wait for Canadians. We must be ready.

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

April 4, 1994

Professor Adrian Brook
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Professor Brook:

Please accept my heartiest congratulations on winning the Killam Prize.

I have known for many years what brilliant work you do, and it is good to know that others appreciate this also.

Isabel and I look forward to being at the CIC meeting in Winnipeg, and after than at the University of Toronto for Isabel's 45th reunion, and we hope to have a chance to meet you personally to congratulate.

Best regards, also to your son.

Sincerely,

University of Toronto

Professor J. Bryan Jones

Tel: (416) 978-3589
Fax: (416) 978-1553

Department of Chemistry
Lash Miller Chemical Laboratories
80 St. George Street
Toronto , Ontario
Canada M5S 1A1

1 February 1994

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211
USA

Dear Alfred:

Many thanks for your note of January 20th - I was equally delighted with the appearance of my lecture-text in the *Aldrichimica Acta* and very pleased to know that your name is there and being noticed by the perspicacious!

Unfortunately, I won't be in Winnipeg for the CIC meeting this year. Instead I will be giving a short lecture course at the University of Florence, a long-planned commitment. However, I do plan to be back in Toronto in early June, and I will look forward to seeing you in Toronto at that time.

Best wishes to you and Isabel.

Yours sincerely,

Bryan

JBJ:hc

P.S. Stephen Branca was well aware that I had slipped the "Bader" word in ☺.

Dr. Alfred Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

January 20, 1994

Professor J. Bryan Jones
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario M5S 1A1
Canada

Dear Bryan:

I was just delighted to note that your biochemical article did appear in the latest Aldrichimica Acta; many thanks.

A number of chemists have told me that they were amused that the name "Bader" did appear in the "About the Author." They were also amused by the fact that the ship on the cover is called The Isabella. I doubt that Tom Cori reads the Acta that carefully.

Isabel and I look forward to being at the CIC meeting in Winnipeg in May, and then in Toronto for Isabel's 45th reunion during the early days of June. Of course, we hope to have a chance to see you then.

Best wishes.

Sincerely,

c: Dr. Stephen J. Branca

University of Toronto *150 Years of Chemistry 1843-1993*

Professor J. Bryan Jones

Tel: (416) 978-3589
Fax: (416) 978-1553

Department of Chemistry
Lash Miller Chemical Laboratories
80 St. George Street
Toronto , Ontario
Canada M5S 1A1

11 November 1993

Dr. A.R. and Mrs. I. Bader
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
USA

Dear Isabel and Alfred:

Just a brief note to thank you both very much for coming to visit us and for the super day we enjoyed with you. I have had many very good comments about your visit and about the splendid Loschmidt talk, which clearly elicited tremendous interest and discussion. My research group is still arguing the points, for example.

With many thanks again and with best regards.

Yours sincerely,

Bryan

JBJ:hc

J. B. Jones.

Department of Chemistry
University of Toronto
150 Years of Teaching Excellence in Chemistry
1843 - 1993

Schedule

Visit of Dr. Alfred R. and Mrs. Isabel Bader
Thursday, November 4th, 1993

12:00 noon	Bryan Jones, room 622	
12:30 PM	Lunch at the Faculty Club with	Cynthia Goh Ian Manners Martin Moskovits Bryan Jones
1:35 PM	Martin Moskovits, room 150	
2:15 PM	Ron Kluger, room 627	
2:45 PM	John Polanyi, room 262	
3:15 PM	- pick up material in room 622 -	
3:30 PM	Lecture, room 159	
	"Joseph Loschmidt, The Father of Molecular Modelling"	
4:45 PM	Coffee and Doughnuts, room 428	

80 St. George Street, Toronto CANADA
M5S 1A1 FAX 978-8775

University of Toronto *150 Years of Chemistry 1843-1993*

Professor J. Bryan Jones

Tel: (416) 978-3589
Fax: (416) 978-1553

Department of Chemistry
Lash Miller Chemical Laboratories
80 St. George Street
Toronto , Ontario
Canada M5S 1A1

7 April 1993

Dr. Alfred Bader
P.O. Box 93225
Milwaukee, Wisconsin 53203
USA

Dear Dr. Bader:

I enclose a copy of the text of my Bader Award Lecture from the Canadian Chemical Conference in Edmonton in June 1992. I am afraid that I elected to withdraw the article from Aldrichimica Acta because they asked me to delete all reference to your name. Since I feel so strongly that this is your personal gift to Canada, I clearly could not accept this very inappropriate and small-minded action. The manuscript has now been submitted to the Canadian Journal of Chemistry where the "acknowledgments" will permit me to pay the proper tribute to your contributions.

With best regards.

Yours sincerely,

JBJ:hc
Encl.

J. B. Jones,
Professor of Chemistry.

Probing the Specificity of Synthetically Useful Enzymes[1]

J. Bryan Jones

Department of Chemistry

University of Toronto

Toronto, Ontario

Canada M5S 1A1

Tel: (416) 978-3589

Fax: (416) 978-1553

---

[1]Bader Award Lecture presented at the 75th Canadian Chemical Conference, Edmonton, Alberta, 3 June 1991.

Abstract: Factors involved in controlling and predicting the structural specificity and stereospecificity of synthetically useful enzymes, including pig liver esterase, subtilisin BPN' and Carlsberg, α-chymotrypsin, and an *L*-lactate dehydrogenase, are discussed.

Enzymes are now broadly accepted as useful catalysts for a broad range of organic synthesis, with their capacities for inducing asymmetric transformations being the most exploited (1). However, despite the widespread uses of both enzymes and microorganisms in asymmetric synthesis, relatively little is known of the factors that determine the structural specificity and stereospecificity of enzymes. In view of the increasingly broad spectrum of new and unnatural substrate structures that synthetically useful enzymes are being called on to accommodate, it is becoming more and more essential to delineate the enzyme-substrate interactions that regulate and control enzyme specificity. This will then permit the selection of the enzymes that are best suited for any given chiral synthon preparation, and will facilitate the development of active site models capable of accurately forecasting whether an enzyme will accept a new structure as a substrate, and of reliably predicting what the stereochemical outcome of the reaction will be. Knowledge of the factors determining specificity will also facilitate the rational tailoring of enzyme specificity by the site-directed mutagenesis techniques of protein engineering.

The classes of enzymes most widely applied are the hydrolases and the oxidoreductases and this lecture will focus on probing the specificity of representative, synthetically useful, members of both of these groups.

Hydrolases

An Active Site Model for Pig liver Esterase.

Hydrolases are currently the enzyme group receiving the most attention, Within this group, the esterase that has seen the most extensive utilization is pig liver esterase (PLE, EC 3.1.1.1)) (2). PLE is a serine protease that catalyzes the hydrolysis of a broad range of carboxylic acid esters. It is capable of enantiomeric and enantiotopic group specificity and has been widely employed for resolving racemic esters and for producing chiral acid-ester synthons from prochiral diester substrates. Despite its proven value in asymmetric synthesis, organic chemists became somewhat uneasy in their continued use of PLE because of some uncertainty about the fidelity of its stereospecificity.

For an enzyme to receive universal approval as a routine catalyst for synthetic applications, it is important that its stereospecificity be seen to be unwavering in its absolute configuration preferences from one substrate to another. In this regard, PLE posed a dilemma in that its stereochemistry appeared to be somewhat fickle towards certain substrate groups. For example, within the homologous series of monocyclic meso diesters **1-3**, the stereoselectivity of PLE hydrolysis reverses itself. For the cyclobutane diester **1**, the *S*-ester is hydrolyzed to give **4**, while for the cyclohexane substrate **3**, the acid-ester **5** from *R*-ester cleavage is formed. Both **4** and **5** are enantiomerically pure. The cyclopentane substrate **2** represents the change-over point, with the acid-ester **5** being virtually racemic (3a). This behaviour turned out to be

general, with similar stereospecificity reversals being observed in other substrate series also (3b).

Formulae **1-6**

Initially we felt that the apparent variability of PLE's stereospecificity was due to the fact that the commercially available material was a melange of similar proteins, with some having *R*, and others *S*, stereospecificity preferences and that separating the mixture into its components would provide us with enzymes of both *R*- and *S*-types. Separation of PLE into its components by isoelectric focussing gave six distinct fractions of different isoelectric points. However, when each of these fractions was employed to hydrolyze diesters such as **1-3**, the stereospecificity results were unchanged (4), thereby demonstrating that, although commercial PLE is a mixture, it behaves as if it is a single species. Thus the stereospecificity reversal patterns observed are a fundamental attribute of PLE's active site. This stimulated us to create an active site model that would permit all PLE's specificity characteristics to be interpreted.

As with other active site model proposals (5), the lack of an X-ray structure dictated an empirical approach. We surveyed all the known literature substrates and, using computer graphics, overlaid them to determine the active site volumes and orientations that permitted each substrate to be accommodated satisfactorily in steric terms, and in accord with the experimentally observed stereospecificities. The picture that emerged was surprisingly simple (6), and is depicted in Figure 1.

Figure 1

The model is comprised of five binding loci. The boundaries of the binding pockets represent the physical restrictions which amino acids of the enzyme place on substrates binding in the active site and, with the exceptions noted below, substrates may not penetrate them. The catalytically essential region is that of the serine residue that initiates hydrolysis by its attack of the carbonyl group of the susceptible ester function. The binding regions controlling specificity are composed of four pockets, of which two are hydrophobic. Two others are more polar in character. The two hydrophobic zones, which interact with the aliphatic or aromatic hydrocarbon portions of a substrate, are designated $H_{L(arge)}$ and $H_{S(mall)}$. The larger of the two, H_L, has a volume of approximately 33 Å^3, while the smaller H_S pocket has a volume of roughly 5.5 Å^3. Polar groups such as hydroxyl, amino, carbonyl, nitro etc. are excluded from these areas. However, the hydrophobic pockets can accommodate less polar heteroatom functions such as halogen, and ether or ketal oxygen atoms, if necessary. The remaining two sectors accept groups that are more polar (P) or hydrophilic. They are located at the front (P_F) and back (P_B) of the active site, respectively. Unlike the other binding regions, the rear boundary of the P_B pocket is open, and hydrogen-bonding or similar groups may extend out beyond the back of this region. The area above the model is also open, and is completely accessible to any substrate moiety that needs to locate there. Such groups may extend in this direction without restriction.

This model reveals the structural basis for the stereospecificity reversals, in that for homologous series of substrates such as **1-3**, small hydrophobic groups bind in H_S until they become too large to do so, at which point the substrate orientation must be turned around to place the larger hydrophobic group in the H_L pocket, where there is room to accommodate it. It is this "turning over" requirement that is responsible for the *S*-to-*R* (and *vice versa*)

switches observed experimentally. The situation is exemplified in Figure 2 for the **1-3** substrate series (6).

Figure 2

The pocket sizes created in the initial Figure 1 model represented the minimum volumes. Their actual sizes have subsequently been systematically probed with substrates of varying steric requirements (7). The dimensions of H_S, P_B and P_F have been confirmed as originally identified, but H_L's capacity for large groups turned out to be greater than first specified. Its maximum dimensions have now been established (8) as 6.1 x 4.6 x 3.1Å^3. To the best of our knowledge, when applied correctly (6), this final model now permits all known PLE specificity to be satisfactorily interpreted, and also enables the stereospecificity of PLE-catalyzed hydrolysis to be correctly forecast for new substrate structures.

Probing Enzyme Specificity

Because of their simplicity, active site specifications of the Figure 1-type are presently the models of choice of organic chemists using enzymes synthetically, even when X-ray structures are available. However, they do not provide the understanding of enzyme specificity that in the long term is essential for identifying the range of substrate structures any synthetically useful enzyme can accept, and for selecting the most appropriate enzyme for transforming a given substrate structure into a desired synthon. Accordingly, in order to gain insights into the factors that control and determine enzyme specificity, we have begun to probe the nature of enzyme-substrate interactions in a systematic manner. This involves studying only synthetically useful enzymes for which

good X-ray structures are available, using graphics analyses to select substrate or inhibitor structures that address a particular specificity question most appropriately and, after kinetic studies on the selected structures, analyzing the experimental data with the aid of graphics and molecular modelling methods. The eventual goal of this approach is to maximize the synthetic potential of each enzyme. However, no natural enzyme can be expected to handle the ever increasing range of substrate structures imposed by the chiral synthon demands of asymmetric synthesis. An important corollary of this strategy is thus its potential for identifying unfavourable amino acid residues at an active site that preclude conversion of a synthetically desirable substrate structure. This opens up the possibility of using the site-directed mutagenesis techniques of protein engineering to correct unsuitable amino acid positions, and eventually to tailor an enzyme's specificity so that any given structural requirement will be accommodated.

Probing the Structural Specificity of Hydrolases

The target enzymes selected as being representative of synthetically useful hydrolases were subtilisin BPN' (SBPN, EC 3.4.21.14), subtilisin Carlsberg (SC, EC 3.4.21.14), and α-chymotrypsin (CT, EC 3.4.21.1). These serine proteases favour ester substrates possessing hydrophobic groups that bind well into the S_1 active site pocket, as represented schematically in Figure 3(a) for the ES-complex formed by SBPN and its excellent substrate N-acetyl-*L*-phenylalanine methyl ester (NAPME). In this ES-complex, the hydrophobic benzyl group of NAPME fits nicely into the S_1 pocket, which in this case provides an appropriate environment as a result of the hydrophobic amino acid residues that form it. However, the unnatural substrates that SBPN may in the future be called on to hydrolyze could well include polar residues, towards which the

natural S_1 environment would be hostile. We therefore decided to see if the S_1 pocket of the wild-type (WT) enzyme could be protein-engineered to be more accommodating of polar groups.

Figure 3

N-Tosyl-*L*-argininine methyl ester (TAME) was selected as a substrate structure whose positively charged side chain was much more polar than that of NAPME, and for which a poor interaction was anticipated between its guanidinium group and the hydrophobic S_1-environment of WT-SBPN if binding in the Figure 3(b) manner took place. We therefore explored the prospect of making the S_1 trough more receptive to TAME-like side chains by changing the Gly166 residue at the bottom of S_1 to amino acids such as Asn or Ser whose side chains are capable of hydrogen bonding to polar groups such as guanidinium. The results obtained supported the validity of this strategy, with the effectiveness of TAME binding being increased by up to 2.4-fold, as reflected by the improvement in K_m from 34 mM for WT-SBPN to 21 mM and 14 mM for the Gly166Asn and Gly166Ser mutants respectively. The G166S enzyme was the most effective catalyst of this series for TAME hydrolysis, and graphics analysis indicated it to be the optimum 166 mutant for this substrate (9).

The S_1' site is also an important region in terms of specificity control. It is the zone in which the leaving groups of amide and ester substrates locate prior to, and during, the acylation step. In SBPN, the S_1' site is not very large, having at its end a bulky hydroxybenzyl side chain of Tyr217 (Figure 3) with the potential to restrict its ability to accept large leaving groups. In such situations, replacement of the relatively large Tyr217 at the end of the S_1' region of SBPN by the smaller Leu residue (as present in subtilisin Carlsberg) should increase

the space available for accommodating leaving groups. This was confirmed for the Tyr217Leu mutant, prepared by the Genencor International group (10), using the tetrapeptide substrates **7a,b**. For **7a**, its *p*-nitroanilide leaving group is still present in the rate-determining acylation step, and the catalytic constant k_{cat} is increased by a factor of 5.6 when the volume of S_1' is increased by substituting the smaller Leu side chain for that of Tyr217 of the WT-SBPN. In contrast, for the ester substrates such as TAME or **7b**, for which leaving groups have already departed prior to the deacylation rate-determining step, the k_{cat} values for the Tyr217Leu and WT enzymes are virtually identical, as expected, with the differences in size between the thiobenzyl and methoxy functions being without effect on the catalytic constant (9).

Formulae **7a,b**

Mutation of Met222 to Phe represents the converse situation in that the volume of S_1' is markedly reduced by the substitution of the benzyl side chain for that of methionine. The rate of hydrolysis of the amide substrate **7a**, with its medium-sized leaving moiety, is now reduced by this mutation, with the k_{cat} value observed for hydrolysis of **7a** with the Met222Phe being 14-fold lower than for the WT-enzyme. Once again, as expected because deacylation is rate-determining for esters, the k_{cat}'s for WT- and Met222Phe-catalyzed hydrolyses of TAME and **7b** are unaffected. While reducing catalytic effectiveness is seldom a worthwhile goal, in this case the combination of the sharply reduced amide hydrolysis efficiency and unchanged esterase activity of SBPN Met222Phe is of particular synthetic interest. This mutant should be an excellent catalyst for the preparation of peptides by coupling of amino acid ester

components in that the ester-to-acyl enzyme steps will proceed normally, but little subsequent hydrolysis of the newly formed peptide bond can occur. The potential thus exists for practical peptide synthesis in aqueous solution.

Probing Hydrolase Stereospecificity

So far, with some exceptions, the use of enzymes in asymmetric synthesis has been largely confined to the creation of chiral synthons with only one stereocentre. However, in principle, the large chiral environments provided by enzymes have the capacity to discriminate and control many stereocentres concurrently, potentially providing access to any multiple-stereocentre combination desired in syntheses of chiral targets. We have begun to explore this with the two-stereocentre substrates **9** and **10**, in which the natural *L (S)*-configuration preferred by esterases is maintained at the α-amino position, but with either an *S* (**9**) or *R* (**10**) configuration at C-3. These *p*-nitro compound were selected because of their synthetic potential as chloramphenicol precursors (11). The question was: will serine proteases such as subtilisin Carlsberg (SC) or α-chymotrypsin (CT) discriminate the second, C-3, centre?

Formulae **8-10**

The kinetic results, together with those on the *p*-nitrophenylalanyl parent **8** of **9** and **10**, showed that the replacement of either the pro-*R* or pro-*S* C-3-H by an OH-group caused a $>10^4$-fold reduction in the hydrolysis rates, as reflected by the specificity constants, k_{cat}/K_M, for both SC- and CT-catalyzed reactions. While the rates of SC and CT hydrolyses of **9** and **10** were low, they remained preparatively viable. However, for SC, the hydrolysis rates of **9** and **10** were about the same, being 126 and 360 $M^{-1}s^{-1}$ respectively, showing that the

enzyme did not distinguish significantly between a C-3 *S* or *R* centre and that separation of a diastereomeric mixture of **9** and **10** could not be achieved using SC hydrolysis. On the other hand, while the rate of CT hydrolysis of **9** was also low (k_{cat}/K_M 70 $M^{-1}s^{-1}$), **10** was not a substrate at all so that CT could very effectively be applied to separate the individual diastereomers from a mixture of **9** and **10**.

The reasons for the dramatic rate reductions for both SC and CT on introducing a C-3 OH substituent of either configuration, and for the differences in the abilities of the two enzymes to distinguish between the two C-3 configurations, were revealed by molecular modelling. The acyl enzyme intermediates derived from the *p*-nitrophenylalanyl parent compound **8** for each of SC and CT were minimized by molecular mechanics and molecular dynamics using the BioSym *Discover* program. For the SC-complex, the C-3 hydrogens of **8** were located in the bottom of the S_1 pocket in environments of about equal steric constraints that are large enough to accept either an *S*- or *R*-centre hydroxyl group, but not without engendering some unfavourable steric interactions, specifically with Ala152 and Asn155 for an *S*-OH and with Ser 125 for an *R*-OH. Thus the consequences of replacing either the C-3 *pro-S* or *pro-R* hydrogens by hydroxyl, as in **9** or **10** respectively, both result in reduced hydrolysis rates, and to approximately the same degree. On the other hand, while the situation for the *pro-S* C-3-H of **9** in the CT-complex parallels closely that of the SC situation, the *pro-R* C-3-H of **10** is already in van-der-Waals contact with Cys191, Met192, Gly193 and Asp194 and this site cannot accommodate anything bigger than hydrogen.. Thus when the *pro-R* C-3-H is replaced by OH, as in **10**, formation of an acyl enzyme is precluded and the *S,R*-diastereomer **10** is a non-substrate. In fact, **10** does not bind at all to CT, as demonstrated by its ineffectiveness (K_I > 150 mM) as a competitive inhibitor.

Exploiting Electrostatic Contributions to Binding

When the electrostatic potential surfaces of SC and CT are calculated using the BioSym *Delphi* programme, the patterns for the two enzymes are very different. We wondered if such electrostatic differences could be exploited to improve the strength or selectivity of binding to enzymes for appropriately designed substrates or inhibitors. For example, the calculations showed that, at the bottom of the S_1 pocket of SC, there was a region of positive potential which could contribute to increased binding strength of a substrate or inhibitor possessing a group of negative potential capable of interacting with this positive enzyme locus. The initial evaluations of this concept were carried out with the boronic acid inhibitors **11**. When bound to serine proteases, boronic acids of this type are transition state inhibitors that form EI-complexes of the type represented in Figure 4, in which the aromatic group binds in S_1.

Formulae **11**

Figure 4

In such orientations, the *para*-substituents should then project into the positive region at the base of S_1. The results observed with the series of inhibitors **11a-f** support this concept, as shown in Figure 5, with the strength of binding increasing, as reflected by the decreasing K_I values, as the negative potential character of the *para*-substituent increases (12). For the *p*-chloro-inhibitor **11f**, with the most negative *para*-group and thus the greatest electrostatic attraction with the base of S_1, binding is 13.5-fold stronger than for the parent compound **11a**. The possibility that the observed trends simply

reflected desolvation energy differences between the inhibitors on forming the respective EI-complexes was excluded by calculations and from literature tabulations of experimental solvation data.

Figure 5

Oxidoreductases

Oxidoreductases, such as horse liver alcohol dehydrogenase (HLADH) have proven of considerable value in asymmetric synthesis. Illustrative examples of HLADH use include resolution, combined with diastereotopic face selectivity, of racemic ketones such as **12**, and additionally of regioselectivity, as in the oxidation of **13**, and of the enantiotopic group and face distinctions involved in the conversions of **14** and **15**. (1c)

Formulae **12-15**

With the potential of a broad specificity oxidoreductase like HLADH well documented, we decided to examine an enzyme of this group with narrower specificity, with the intent of probing the factors determining structural and stereospecificity. The oxidoreductase selected was the *L*-lactate dehydrogenase of *Bacillus stearothermophilus* (BSLDH). BSLDH is an excellent candidate for such exploratory studies since it is a very stable, thermophilic, enzyme of known protein sequence and its properties have already been the subject of several studies (13). Also, its gene has been cloned and the protein very efficiently overexpressed, thereby enabling large quantities of BSLDH to be produced inexpensively from small fermentation volumes (14). Furthermore, the feasibility

of altering the specificity of the native enzyme by site-directed mutagenesis of key active-site amino acid residues has been established (13).

On the Structural Specificity of BSLDH

BSLDH is an NAD/H-coenzyme dependent, fructose-1,6-diphosphate (FDP) activated, enzyme whose *in vivo* function is to catalyze pyruvate $\rightleftharpoons$ *L*-lactate oxidoreductions of the type

$$\underset{\mathbf{16}}{RCOCOOH} + NADH + H^+ \rightleftharpoons \underset{\mathbf{17}}{RCH(OH)COOH} + NAD^+$$

While its strongly preferred substrate is pyruvate (**16,** R = Me) with its small R-group, BSLDH will accept as substrates a broad range of α-ketoacids, albeit with substantial rate penalties for large or branched R-groups. Nevertheless, preparative-scale reactions to produce a range of enantiomerically pure *L*-α-hydroxyacids **17** are feasible, as illustrated in Figure 6 (13).

Figure 6

Figure 7

Much is known about the structure of the active site of BSLDH (15). The key features are represented in Figure 7. The narrow substrate specificity is due, at least in part, to the fact that the 98-110 and 235-248 loops close over the ketoacid substrate during the formation of the active ES-complex, thereby leaving only a restricted volume for the R-side chains. Graphics analyses revealed that, in the productive ES-complex, large R-groups would engender a bad steric interaction with the loop residue Gln102 and indicated that these adverse interactions with bulky, especially branched-chain, substrates could be

diminished by reducing the size of the 102-position amino acid side chain. The validity of this analysis was tested by using site-directed mutagenesis to replace Gln102 by Asn, an amino acid of similar hydrophobicity but having one fewer CH_2-groups in its side chain and thus providing more room for bigger side chains. The results obtained supported the application of such protein engineering approaches to expand the structural specificity of enzymes, with the Gln102Asn mutant now being a better enzyme than WT-BSLDH for substrates such as **16,** R = $CH_3(CH_2)_{2\text{-}5}$-, $(CH_3)_2CH$-, $(CH_3)_2CHCH_2$-, $CH_3CH_2CH(CH_3)$-, and C_6H_5- (16).

Probing BSLDH Stereospecificity

The stereospecificity of enzymes is their most important property for asymmetric synthetic applications. However, as noted already, little is known about the factors that determine and control enzyme stereospecificity. With *L*-LDH's being so committed to *Re*-face carbonyl attack to give (S)-α-hydroxyacids, BSLDH provides an excellent instrument for beginning to identify and understand important stereospecificity determinants, initially of oxidoreductases, but eventually of all enzymes. Among the methods of probing the factors controlling enzyme stereospecificity, evaluating how effectively an enzyme resists attempts to change this capability is potentially one of the most powerful. The natural *L*-stereospecificity of BSLDH is determined by the orientation of 2-ketoacids, such as pyruvate (**16,** R = CH_3), in the ES-complex such that the hydride-equivalent from NADH is delivered to the *Re*-face of the carbonyl group. This is depicted schematically in Figure 8(a). An important interaction helping to maintain this pyruvate orientation is that between the substrate's COO^- and Arg171. As one measure of BSLDH's commitment to the *L*-pathway, we elected to evaluate its resistance to being induced to catalyze *D*-lactate formation. Reduction of

pyruvate to *D*-lactate requires delivery of the NADH-"hydride" to the *Si*-face of pyruvate. One of the ways that can be envisaged of inducing this *Si*-face attack would be via an ES complex in which the orientation of pyruvate was reversed, as illustrated in Figure 8(b).

Figure 8

Towards this goal, Arg171 was replaced by Tyr and Trp. Despite the elimination of the key Arg171-COO^--binding orientation, the Arg171Trp/Tyr mutants were still completely *L*-stereospecific (17). In a subsequent study, the WT-Arg171 was retained but a second COO^--binding Arg residue was introduced in place of Gln102, thereby providing a competitive possibility between the Figure 8(a) and 8(b) pyruvate orientations and the prospect of formation of racemic products. As expected (18), the best substrates for this mutant were dicarboxylic α-ketoacids that concurrently exploit both the Arg171 and 102Arg binding sites. However, once again, this Gln102Arg mutation did not disturb the *L*-proclivity of BSLDH in any preparatively significant way, with only *L*-α-hydroxyacids being produced in preparative-scale reactions. Nevertheless, this mutant provided the first indication that it was possible to disturb the natural *L*-stereospecificity of BSLDH in that, in contrast to the WT-situation for which oxidation of *L*-malate was much faster than for the *D*-enantiomer, the rates of oxidation of *L*- and *D*-malate for the Gln102Arg mutant had become approximately equal (13). In the latest experiments, the 171Trp/Tyr and 102Arg mutations were combined in order to eliminate any prospect of the natural Arg171-COO^- interaction and at the same time to provide the opportunity for a reversal of pyruvate orientation via 102Arg-COO^- binding. Furthermore, the formation of the natural, Arg171-directed, Figure 8(a) type complex is clearly impossible for the Arg171Trp/Tyr;Gln102Arg double mutants. Despite the

binding constraints designed into these double mutants, their fidelity with respect to *L*-stereospecificity remained dominant, with preparative-scale reductions of α-ketoacids affording only the *L*-hydroxyacids.

The question of how the above BSLDH-mutants maintain their control of *L*-stereospecificity is thus an intriguing one. The X-ray structure of the 171Trp/102Arg/97Gly triple mutant that is now being refined should provide new insights into these questions. Already it is clear that Arg171Trp replacement is not wholly benign, and that the 171Trp side chain shifts out of the active site (19). Because none of the 171 or 102 mutations disturbs the natural stereospecificity of BSLDH, it is evident that there must be fail-safe, *L*-directing, interactions that take over when Arg171 is not present. One such fail-safe candidate is Thr246. Other X-ray data (15) indicate that the Thr246 side chain is close enough to the substrate carboxylate function for effective hydrogen bonding (Figure 7), although explaining how such a secondary, hydrogen-bonding, interaction could override carboxylate binding to 102Arg-containing mutants in the productive ES-complexes remains a quandary. This is particularly true for small substrates such as pyruvate for which, other than the carbonyl group being reduced, the carboxylate group is the only function capable of binding strongly to the enzyme.

Figure 9

We have started to investigate the role of Thr246 by studying the catalytic properties of several 246 mutants, including Thr246Ala/Val/Leu/Ser. Although none of the mutants was as effective an oxidoreductase as WT-BSLDH, they did exhibit some interesting catalytic properties with respect to substrate inhibition. Substrate inhibition is a common phenomenon in enzyme-

catalyzed reactions and can be a major problem in preparative-scale applications because of the very high substrate concentrations that are employed in large-scale transformations. In fact, substrate inhibition can be very serious for BSLDH, particularly with pyruvate as substrate, and can result in reductions being brought to a virtual standstill. However, when no hydroxyl group is present in the 246 side chain, as for Thr246Val/Ala, substrate inhibition is virtually eliminated, as shown by the constant V_{max} values at high [S] for these two mutants (Figure 9). Substrate inhibition of BSLDH arises from the strong complexation of pyruvate with the E.NAD$^+$ complex in the catalytic cycle. This does not occur with Thr246Val/Ala because pyruvate no longer binds effectively to E.NAD$^+$, as reflected by the dramatic increases in apparent K_I for pyruvate for this step for these two mutants (Figure 10) (20). The effect is especially evident for the smaller 246Ala side chain where, with a K_I(app) of almost 800 mM, pyruvate is clearly not binding at all to E.NAD$^+$ Also, for WT-BSLDH, the rate determining step (k 250 s^{-1} (14)) for pyruvate reduction is closure of the 98-110 loop. Mutation of Thr246 to Ala slows the loop closure rate such that the hydride transfer process becomes at least partially rate limiting, as reflected by the k_H/k_D kinetic isotope effect of 2.4.

Figure 10

Although the Arg171 and Gln102 mutations did not disturb the stereospecificity of the enzyme, there were serendipitous benefits to these changes in that thermal stability of BSLDH was further increased, dramatically so for the Arg171Tyr enzyme, for which the T_m (app) was increased by 9.4 ^oC over that of WT-BSLDH. The greatest increase in T_m (app) was 10.7^oC for Arg171Tyr, Gln102Arg. At high ionic strength, even higher thermal stabilization

was manifest. Notably, in the presence of 100 mM K_2SO_4, the Arg171Tyr, Gln102Arg mutant retains 30% activity even after heating for 30 minutes at 100°C, conditions under which the already moderately thermostable WT-enzyme is completely inactivated in less than 2 minutes (19). This has considerable potential synthetic benefits since preparative-scale BSLDH-catalyzed reactions at temperatures of up to 100°C can now be contemplated, subject to NAD-coenzyme survival for sufficient time. The reason for the increased thermal stabilizations on replacing the Arg171 by hydrophobic residues such as Trp seems due to more favourable hydrophobic subunit contacts. This view is supported by preliminary X-ray structural evidence for a mutant BSLDH containing tryptophan in 171-position. In this structure, the 171W-side chain is rotated around the C_a-C_b-bond, relative to the wild-type arginine side chain. The mutant indolyl-group is thus located completely outside of the active site, and it projects into the space occupied by the other subunit in the BSLDH-dimer in a manner that increases the hydrophobic subunit interface area (21).

While the data presented in this lecture represent a beginning towards identifying the factors that determine enzyme specificity, it is evident that much needs to be done before enzymes and substrates can be tailored with confidence to permit optimum results in all asymmetric synthetic applications, and to maximize their performance and stability as catalysts. However, in view of the tremendous progress now being made in protein research, many exciting new insights into enzyme catalysis and specificity can be anticipated in the next few years.

Acknowledgments

I am grateful to have this opportunity to acknowledge the many excellent students and postdoctoral fellows who have contributed, either directly or

indirectly, to the body of knowledge on which the work described was built, and with whom it has been such a privilege to work. Most of the results presented were obtained by Pierre Bonneau, Jim Hogan, Helmut Kallwass, Tom Keller, Valeri Martichonok, Wendy Parris, Louis Provencher, Roman Sakowicz, Peter Seufer-Wasserthal, and Eric Toone. The subtilisin-mutants work was done in collaboration with Dave Estell and Tom Graycar of Genencor International and the BSLDH mutant X-ray structures by Michael James and R. Kodandapani at the University of Alberta. I am particularly indebted to my colleague and long-term collaborator, Marv Gold, without whose protein and molecular biology insights and expertise the BSLDH work would not have been possible . I also thank the Natural Sciences and Engineering Research Council of Canada and the Protein Engineering Network of the Canadian Centres of Excellence for generous financial support. Finally, I express my appreciation to Dr. Alfred Bader for setting up the Bader Award of the Canadian Society for Chemistry, for which I feel very privileged and honoured to have been selected. This is also an appropriate occasion to recognize the long-standing commitment and support by Dr. Bader of Canadian, and world, chemistry in other areas, not the least of which is the huge range of routine and state-of-the-art research chemicals that the Company that he founded, Aldrich, has made available over the years and without which our research could never have been done.

References

1. (a) H. G. Davies, R. H. Green, D. R. Kelly, S. M. Roberts. *In* Biotransformations in Preparative Organic Chemistry. Academic Press, London. 1990. (b) D. H. G. Crout, M. Christen. Biotransformations in Organic Synthesis. *In* Modern Synthetic Methods. Vol. 5. *Edited by* R. Scheffold, Spronger-Verlag, Berlin, 1989, pp.1-114. (c) J. B. Jones, Tetrahedron, **42**, 3351 (1986).

2. (a) M. Ohno, M. Otsuka. Organic Reactions, **37**, 1 (1989). (b) L.-M. Zhu, M. C. Tedford. Tetrahedron, **46**, 6587 (1990).

3. (a) G. Sabbioni, J. B. Jones. J. Org. Chem., **52**, 4565 (1987). (b) L. K. P. Lam, R. A. H. F. Hui, and J. B. Jones. J. Org. Chem., **51**, 2047 (1986).

4. L. K. P. Lam, C. M. Browne, B. DeJeso, L. Lym, E. J. Toone, and J. B. Jones. J. Am. Chem. Soc., **110**, 4409 (1988).

5. (a) P. Mohr, N. Waespe-Sarcevic, C. Tamm, K. Gawronska, J. K. Gawronski. Helv. Chim. Acta, **66**, 2501 (1983). (b) M. Ohno. *In* Enzymes in Organic Synthesis (Ciba Foundation Symposium 111). *Edited by* R. Clark, S. Porter. Pitman, London. 1985. p 171. (c) L. K. P. Lam, R. A. H. F. Hui, and J. B. Jones. J. Org. Chem., **51**, 2047 (1986). (d) J. Boutelje, M. Hjalmarsson, P. Szmulik, T. Norin, K. Hult. *In* Biocatalysis in Organic Media. *Edited by* C. Laane, J. Tramper, M. D. Lilly. Elsevier, Amsterdam. 1987.

6. E. J. Toone, M. J. Werth, and J. B. Jones. J. Am. Chem. Soc., **112**, 4946 (1990).

7. E. J. Toone, and J. B. Jones. Tetrahedron Asymm., **2**, 207, 1041 (1991).

8. A. Krawczyk, H. Wynn, E. J. Toone, L. R. Provencher. Unpublished results.

9. P. R. Bonneau, T. P. Graycar, D. A. Estell, and J. B. Jones. J. Am. Chem. Soc., **113**, 1026 (1990).

10. J. A. Wells, B. C. Cunningham, T. P. Graycar, D. A. Estell. Proc. Natl. Acad. Sci. USA. **84**, 5167 (1987).

11. R. Chenevert, and S. Thiboutot. Synthesis, 444 (1989).

12. T. Keller, P. Seufer-Wasserthal, and J. B. Jones. Biochem. Biophys. Res. Commun., **176**, 401 (1991).

13. H. K. W. Kallwass, M. A. Luyten, W. Parris, M. Gold, C. M. Kay, and J. B. Jones. J. Am. Chem. Soc., **114**, 4551 (1992) and references therein.

14. (a) J. J. Holbrook, A. Liljas, S. J. Steindal, M. G. Rossmann. *In* The Enzymes, 3rd ed. *Edited by* P. D. Boyer. Academic Press, New York. 1975. pp. 191-292. (b) D. A. Barstow, A. R. Clarke, W. N. Chia, D. B. Wigley, A. S. Sharman, J. J. Holbrook, T. Atkinson, N. T. Mington. Gene, **46**, 47 (1986). (c) D. Stangl, F. Wiederkehr, F. Suter, H. Zuber. Biol. Chem. Hoppe-Seyler. **368**, 1157 (1987).

15. (a) D. B. Wigley, S. J. Gamblin, J. P. Turkenburg, E. J. Dodson, K. Piontek, H. Muirhead, J. J. Holbrook. J. Mol. Biol., **223**, 317 (1992). (b) K. Piontek, P. Chakrabarti, H.-P. Schaer, M. G. Rossmann, H. Zuber. Proteins, **7**, 74 (1990).

16. M. A. Luyten, D. Bur, H. Wynn, W. Parris, M. Gold, J. D. Friesen, and J. B. Jones. J. Am. Chem. Soc., **111**, 6800 (1989).

17. M. A. Luyten, M. Gold, J. D. Friesen, and J. B. Jones. Biochemistry, **28**, 6605 (1989).

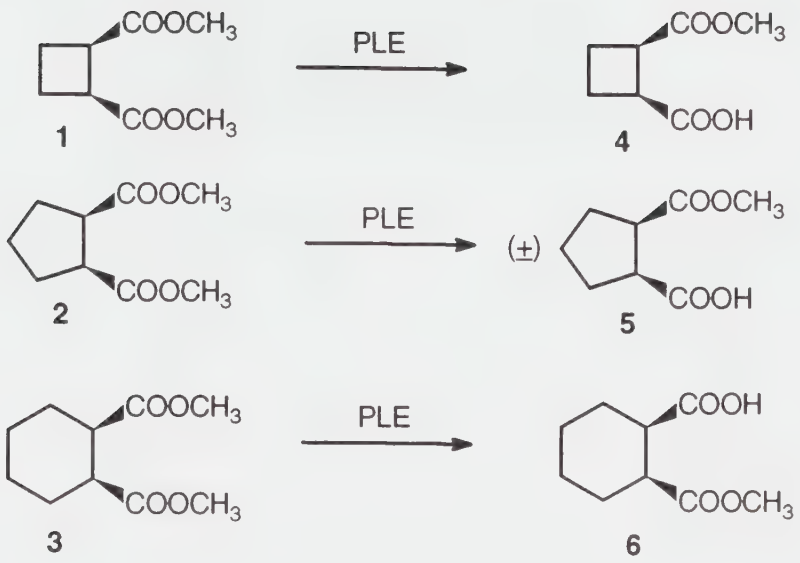
18. H. Wilks, K. Hart, R. Feeney, C. Dunn, H. Muirhead, W. Chia, D. Barstow, T. Atkinson, A. Clarke, and J. J. Holbrook. Science, **242**, 1541 (1988).

19 H. K. W. Kallwass, W. K. Surewicz, W. Parris, E. L. A. Macfarlane, M. A. Luyten, C. M. Kay, M. Gold, and J. B. Jones. Prot. Eng., **5**, 769 (1992).

20. R. Sakowicz, H. K. W. Kallwass, W. Parris, M. Gold, and J. B. Jones. Biochem. Biophys. Res. Commun., **182**, 1305 (1992).

21. (a) K. Huang, R. Kodandapani, H. K. W. Kallwass, J. K. Hogan, W. Parris, J. D. Friesen, M. Gold, J. B. Jones, and M. N. G. James. Proteins, **13**, 158 (1992). (b) R. Kodandapani, M. N. G. James. Unpublished results.

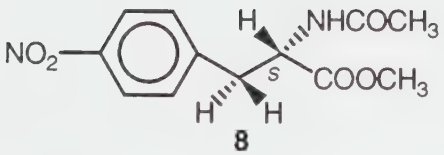
Formulae


COOCH3
COOCH3
PLE
COOCH3
COOH
1
4
COOCH3
COOCH3
PLE
(±)
COOCH3
COOH
2
5
COOCH3
COOCH3
PLE
COOH
COOCH3
3
6

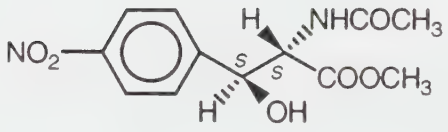
Formulae (contd.)

Succinyl-*L*-Ala-*L*-Ala-*L*-Pro-*L*-Phe-X
7a, X = p-nitroanilide; **7b,** X = thiobenzyl

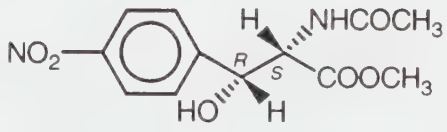
Formulae (contd.)



8

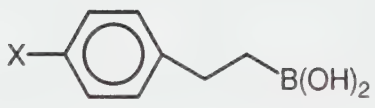


9



10

Formulae (contd.)



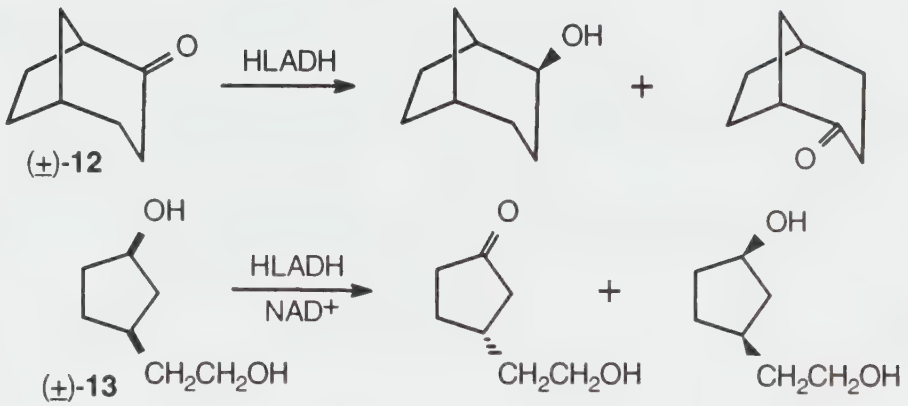
11

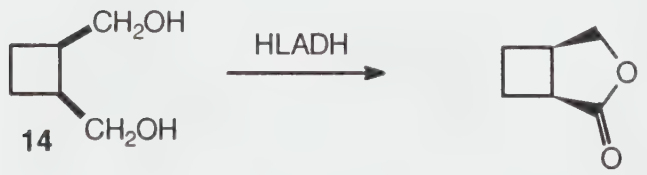
a, X = H **d, X = OCH_3**

b, X = CH_3 **e, X = F**

c, X = CF_3 **f, X = Cl**

Formulae (contd.)





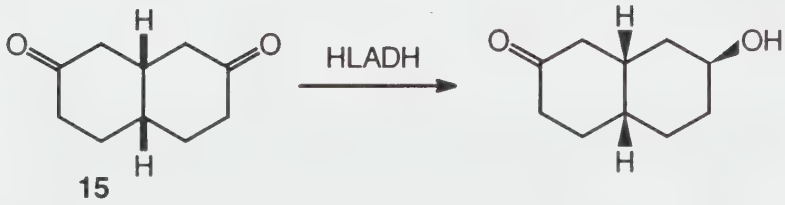


Figure Legends

Figure 1. Active Site Model for PLE

Figure 2. The top-perspective view of the active site model is used to illustrate the binding mode selections for diesters **1-3**. Hydrolysis of an ester group can only occur when it locates within the spherical locus of the catalytically active serine function. **Dimethyl cyclobutane-1,2-dicarboxylate** (**1**). The S-centre ester hydrolysis orientation shown in (a) permits all substrate groups to be accommodated in the active site binding pockets, with the cyclobutane ring fitting cleanly into, and filling, the H_S pocket. The alternative binding mode required for hydrolysis of the R-centre ester would place a portion of the cyclobutane ring in the H_L pocket (Figure 2(b)). Since binding of hydrophobic groups must occur in the H_S rather than the H_L site if sterically possible, substrate-binding as in (a) is preferred, in accord with the observed formation of the 2S-acid product **4**. **Dimethyl Cyclohexane-1,2-dicarboxylate (3).** The binding depicted in (c) shows the preferred ES-complex for hydrolysis of the R-center ester to the 2R-acid **6**, with the cyclohexane ring bound in the large hydrophobic pocket. Hydrolysis of the S-ester would require the orientation shown in (d). This is clearly precluded since the H_S pocket is clearly too small to accept the six-membered ring. **Dimethyl Cyclopentane-1,2-dicarboxylate (2)**. In this instance, both R- and S-centre ester functions can be acceptably located in the serine sphere, as shown in (e) and (f) respectively. The cyclopentane group is marginally too large for optimum fit into H_S, ensuing in a slight preference for hydrolysis via (e) that translates into a 17%ee of the corresponding 2R-acid **5**.

Figure 3. Schematic representation of the active site of subtilisin BPN'. In **(a)** the non-polar benzyl group of NAPME binds well in the hydrophobic S_1 pocket, which has a Gly166 located at its end. The S_1' region that accommodates the leaving group is not very large, being blocked off at the end by Tyr217. S_1' also contains the serine residue of the catalytically vital Ser221-His64-Asp32 serine protease triad. In **(b)** TAME is depicted in an orientation that site-directed mutagenesis of Gly166 to Asn or Ser should promote by creating a favourable hydrogen bonding environment for the guanidinium function, thereby ameliorating the inhospitality of the hydrophobic milieu of S_1 towards polar groups.

Figure Legends (contd.)

Figure 4. Schematic representation of boronic acid inhibitor binding to subtilisin Carlsberg.

Figure 5. *Para*-substituent Effects on Phenylboronic Acid Inhibitors of Subtilisin Carlsberg.

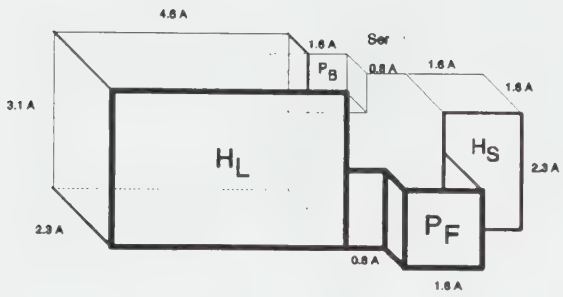
Figure 6. Preparative-scale BSLDH-catalyzed reductions.

Figure 7. Important Active-site Amino Acid Residues of BSLDH.

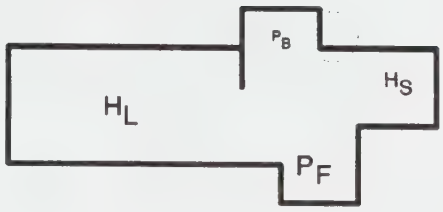
Figure 8. Schematic representation of pyruvate bound at the active site of BSLDH in orientations leading to *L*- or *D*-lactic acid formation. Part **(a)** represents the natural binding mode that results in *L*-lactate formation. Part **(b)** illustrates a reversal of the natural binding orientation of pyruvate that might be induced by mutations such as Arg171Trp/Tyr, Gln102Arg, and combinations thereof, that would lead to *D*-lactate as the product.

Figure 9. Elimination of Substrate Inhibition by pyruvate by T246V/A Mutations.

Figure 10. Apparent K_I's for Pyruvate inhibition of 246 Mutant BSLDH's.



Top Perspective



(Figure 1)

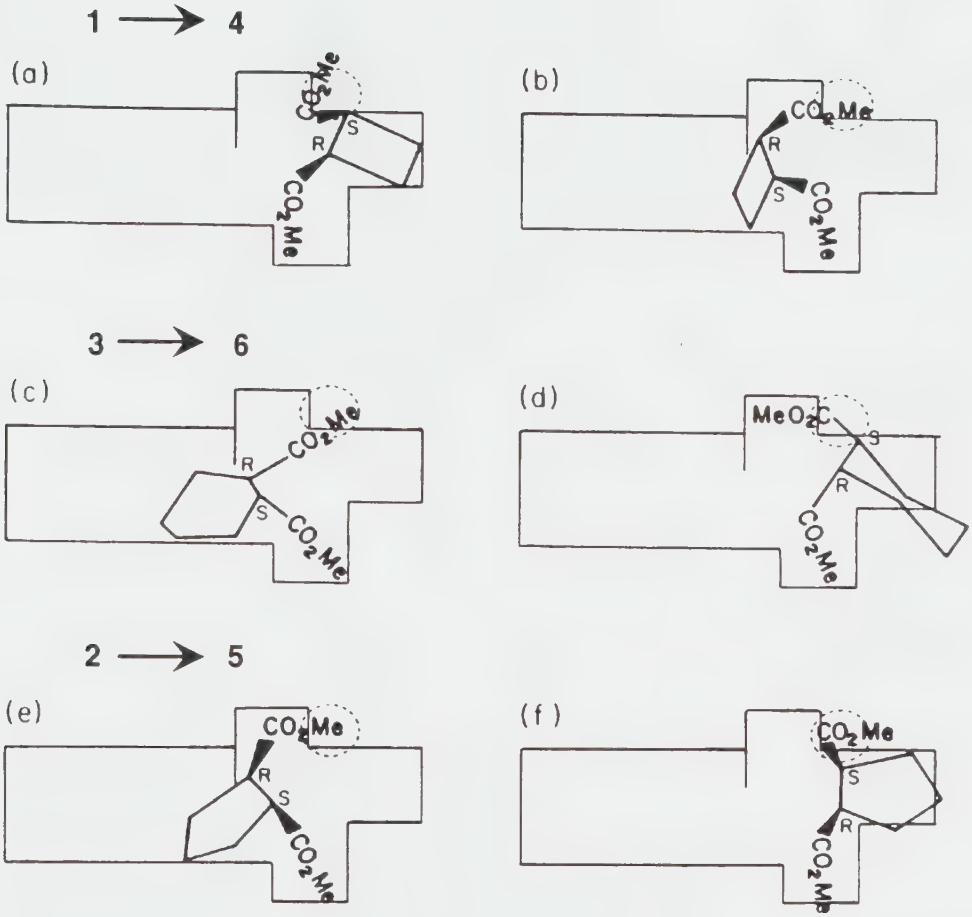
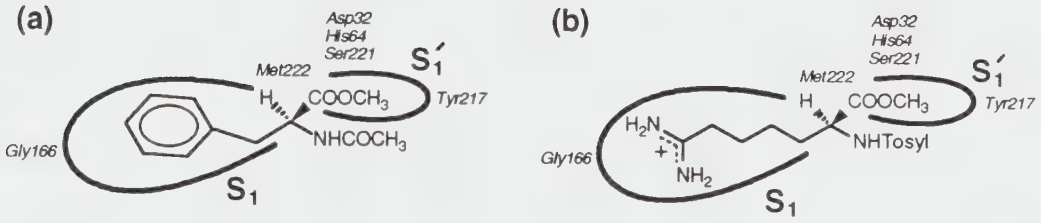
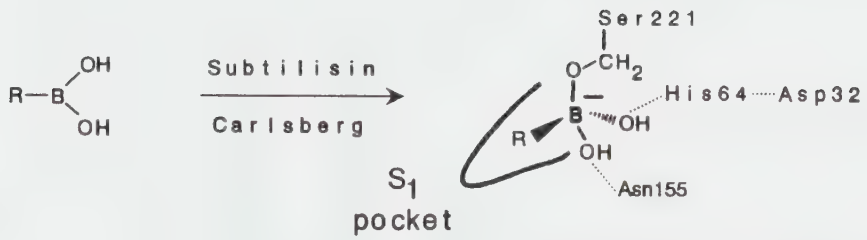


Figure 2


(a)
Asp32
His64
Ser221
S1´
Met222
H
COOCH3
Tyr217
NHCOCH3
Gly166
S1
(b)
Asp32
His64
Ser221
S1´
Met222
H
COOCH3
Tyr217
H2N
+
NH2
NHTosyl
Gly166
S1

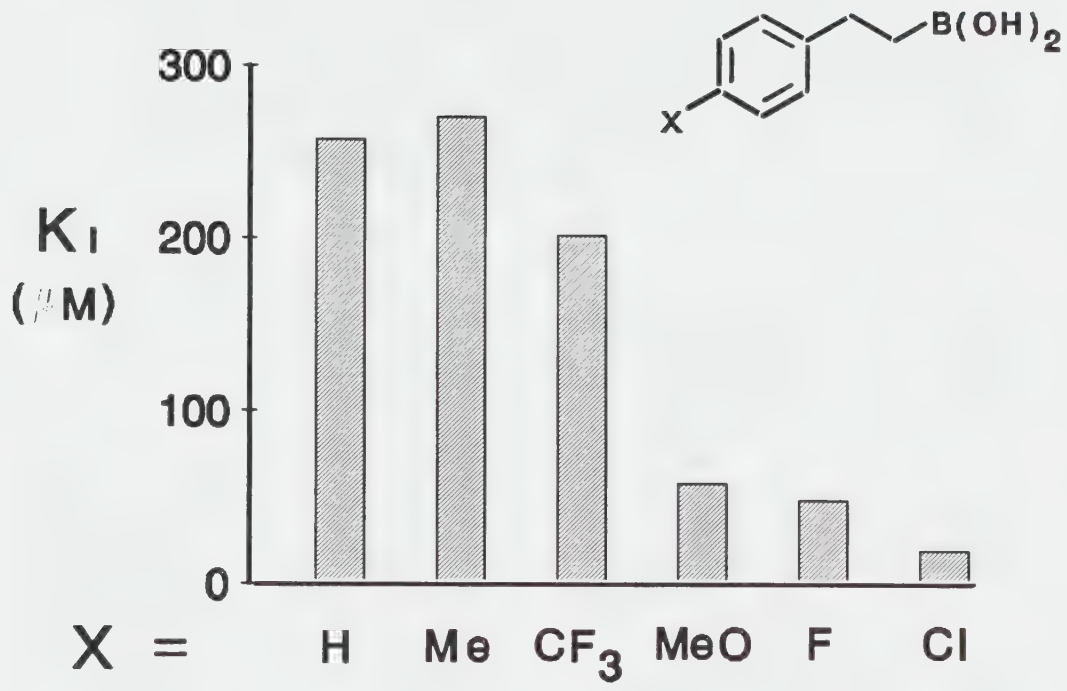
(Figure 3)



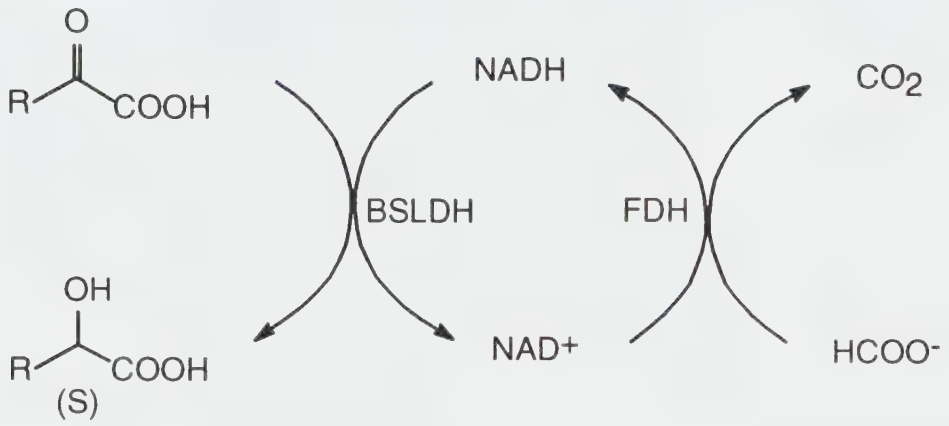
Tetrahedral Intermediate

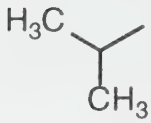
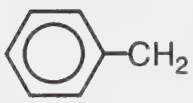
Transition-state like Inhibitor

(Figure 4)

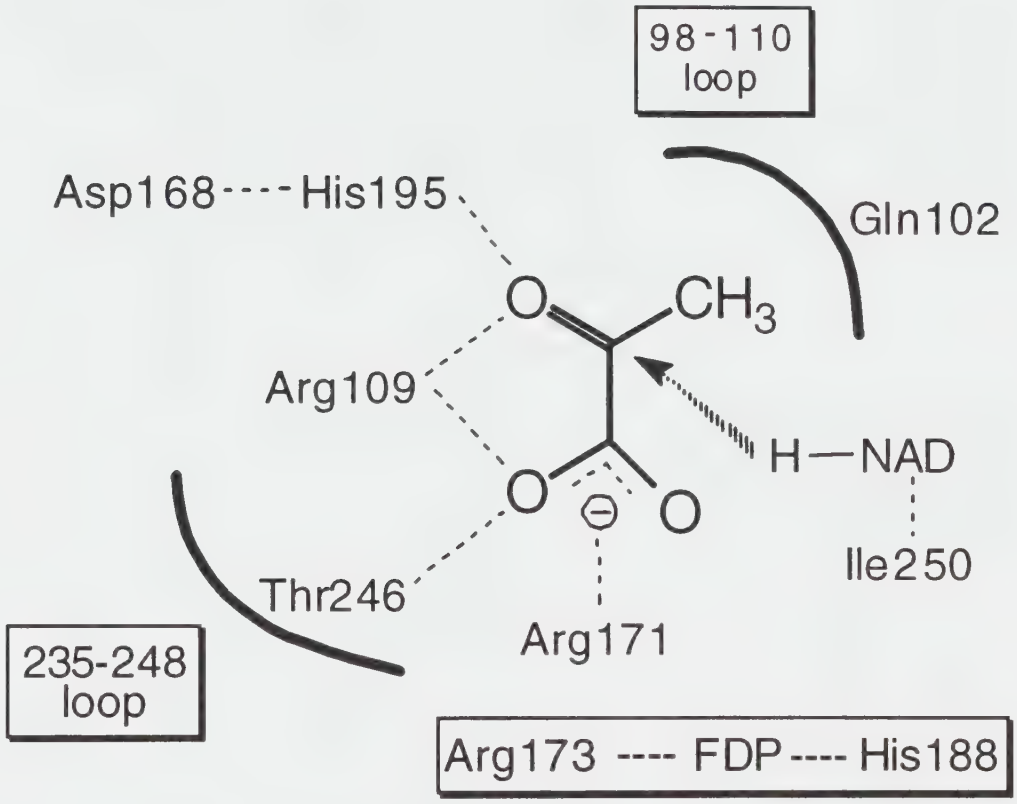


(Figure 5)

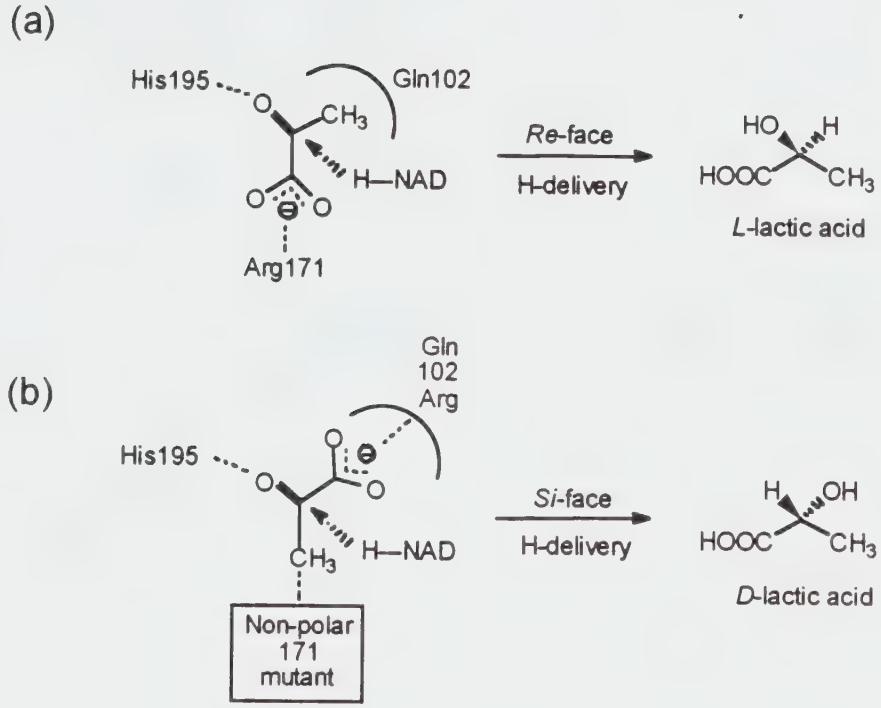


R	Rel. Rate	%Yield	% ee
CH_3	++++		
CH_3CH_2	+++	88	>99
$CH_3(CH_2)_2$	+	89	>99
	<+	88	>99
	+	89	>99
	++	90	>99

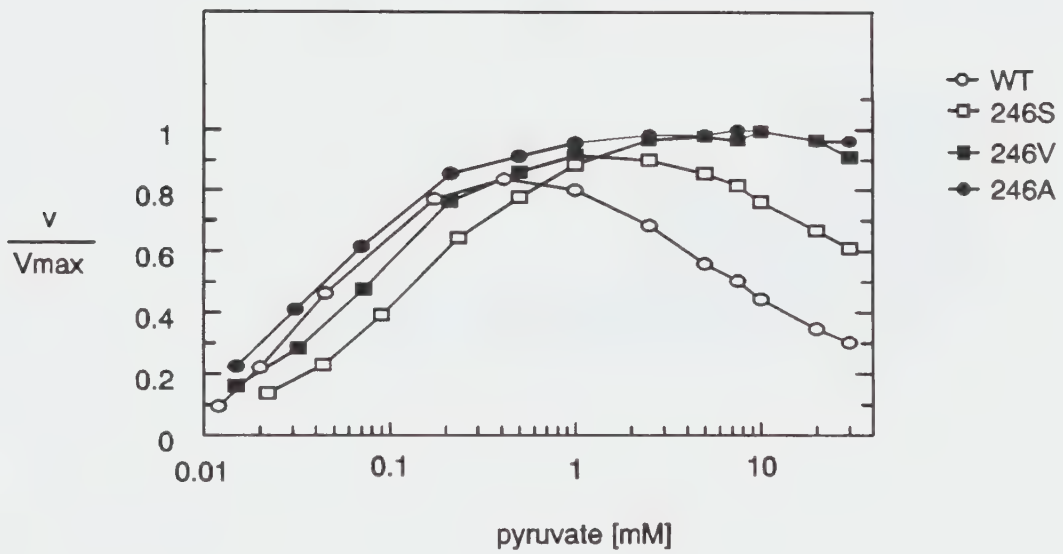
(Figure 6)


98-110 loop
Asp168 ---- His195
Gln102
O
CH3
Arg109
H—NAD
O
O
Ile250
Thr246
Arg171
235-248 loop
Arg173 ---- FDP ---- His188

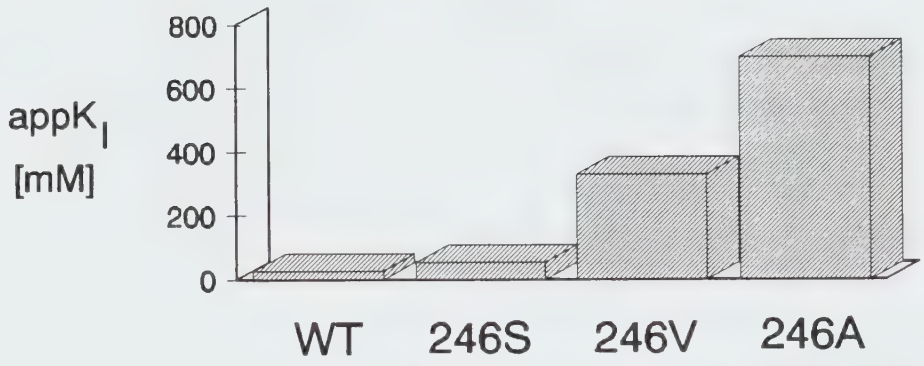
(Figure 7)


(a)
His195
Gln102
CH3
H—NAD
Arg171
Re-face
H-delivery
HO
H
HOOC
CH3
L-lactic acid
(b)
Gln
102
Arg
His195
H—NAD
CH3
Non-polar
171
mutant
Si-face
H-delivery
H
OH
HOOC
CH3
D-lactic acid

(Figure 8)



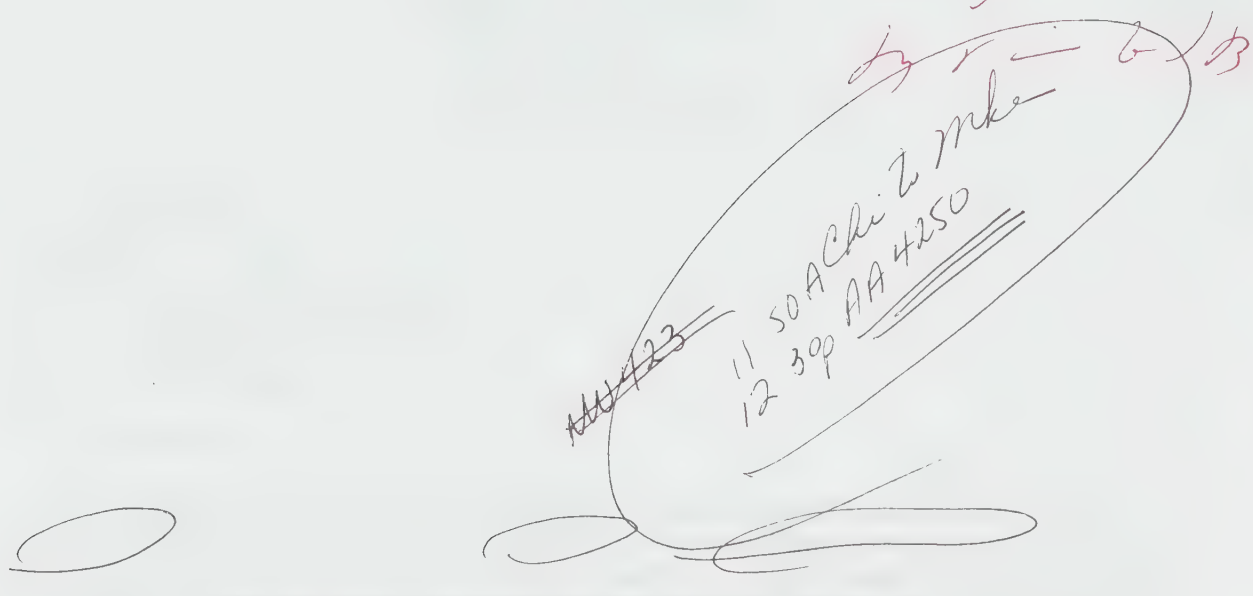
(Figure 9)



(Figure 10)

American 4250

3/27 Rez



FAX FROM

DR. ALFRED R. BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone 414-277-0730
Fax No. 414-277-0709

March 3, 1993

To: Professor Thomas T. Tidwell
Department of Chemistry
Unviersity of Toronto

FAX 416 287 7642

Dear Professor Tidwell:

As requested in your fax, we have made a reservation for you at the Astor Hotel for the night of Saturday, March 27th, at the special rate of $45/night, plus tax.

The telephone and fax numbers for the gallery are shown above. The telephone and fax numbers for Dr. Bader's home are:

Telephone 414 962 5169
Fax 414 962 8322

If you need anything further, please contact us.

Cordially,

Marilyn Hassmann
Secretary to Dr. Bader

FAX FROM

DR. ALFRED R. BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone 414-277-0730
Fax No. 414-277-0709

February 26, 1993

To: Professor Thomas T. Tidwell
Department of Chemistry
University of Toronto 416 287 7642

Dear Prof. Tidwell:

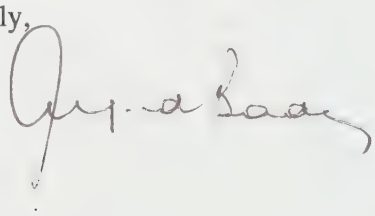
I am happy to know from your fax of today that you will be in Milwaukee on Saturday, March the 27th, and I would love to meet you.

I believe on that day three art historian friends, all from the Fogg Museum of Harvard, will be visiting us to look at our paintings. They are very pleasant people, and you will enjoy meeting them. I will be able to take some time off to tell you about my friendship with the late Michael Carroll. If you wish, I will take a photograph off my wall and loan it to you.

Should you stay overnight in Milwaukee, the Astor Hotel has a special rate of $45 per night for visitors to my gallery. The hotel is very pleasant and close to downtown and my home.

I look forward to meeting you.

Sincerely,



FAX FROM

DR. ALFRED R. BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone 414-277-0730
Fax No. 414-277-0709

September 21, 1993

To: Professor Bryan Jones
Department of Chemistry
University of Toronto

416 978 1553

Dear Bryan:

Isabel (a graduate of the U of T '49) and I look forward to being with you the morning of Thursday, November 4th.

We will be staying with Dr. Eva Cuschner, the President of Victoria College, and Prof. Cuschner, at 63 Albany Avenue, not far from the campus.

I hope that you will find the following 10 pages sufficient.

Do you know the Aldrich Story which appeared in the Canadian Chemical News 44, 23 (1992), written by Professor J. T. Edward.

Best wishes.

As always,

Enclosures

FAX FROM

DR. ALFRED R. BADER
Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin 53202
Telephone 414-277-0730
Fax No. 414-277-0709

3 pages

To:

Prof. Bryan Jones

Best wishes

Alfred Bader

Dr. Alfred R. Bader
2961 North Shepard Avenue
Milwaukee, Wisconsin 53211

August 5, 1993

Professor J. B. Jones
Department of Chemistry
University of Toronto
80 St. George Street
Toronto, Ontario, Canada M5S 1A1

Dear Professor Jones:

I am sorry that a very long trip to Europe has delayed my thanking you for your truly moving letter of April 7th with the paper you presented to the CIC in June.

Of course I am really touched by your very kind words, but I am also truly sorry that you decided to submit the paper to the Canadian Journal of Chemistry, rather than to the Aldrichimica Acta.

Perhaps you know that the decision to dismiss me was not made by anyone at Aldrich in Milwaukee, but by only one man, Dr. Tom Cori in St. Louis. I very much hope that many of us will survive Tom Cori and that Aldrich, Sigma-Aldrich and the Aldrichimica Acta will continue to do well. Dr. Cori has decreed that my name may never be mentioned in the Acta, but I would very much prefer to have great papers such as yours published in the Acta without reference to me, than not to have them published in the Acta. The Acta goes to over 250,000 scientists worldwide, presents the papers really well, and is often cited in the literature.

Would it be possible for you to consider whether the Acta might also publish your paper with your kind remarks on page 20 deleted.

Over the years we have tried to have more excellent papers which combine Sigma's biochemical with Aldrich's organic interests, and your paper is truly one of the best of these.

Again, many thanks for your kindness.

Sincerely,

c: Dr. Stephen Branca

FAX TRANSMITTAL SHEET

FROM: DR. ALFRED BADER

2961 North Shepard Ave.
Milwaukee, Wisconsin 53211

PHONE: (414) 962-5169

FAX: (414) 962-8322

TO: Ms. Jane Stirling, Editor
The Bulletin
University of Toronto
Department of Public Affairs

DATE: April 19, 1993

Dear Ms. Stirling:

I must correct an error in Nicholas Pashley's column "On the Other Hand" in your March 29 issue.

He states that Allan Arlete, our university's new fund raiser is really good, although perhaps not as good as his Queen's counterpart who convinced an alumnus to donate an English castle.

I know quite a few Queen's people, and the Queen's fund raiser wouldn't be there if he weren't good. But I know that he had nothing to do with persuading my husband to donate Herstmonceux to Queen's. That was purely Alfred's and my idea, and what littler persuasion was needed came from us to persuade Queen's to accept Herstmonceux.

Ever since Alfred inherited $1,000 in 1948 and used that to establish an award in Civil Engineering at Queen's he has prided himself on making gift after gift to his university without anyone at Queen's ever asking for anything. It is the wonderful way he was accepted at Queen's in 1941, not the ability of any fund raiser that has resulted in his many gifts.

Incidentally, Alfred applied to Queen's in November 1941 after McGill and Toronto had turned him down.

Sincerely,

Isabel Overton Bader
B.A. 1949
University of Toronto

letter from Isabel