Alfred Bader fonds

Correspondence

British Columbia, Univ. of

QUEEN'S UNIVERSITY ARCHIVES
LOCATOR 5095.5
BOX 4
FILE 23

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

A Chemist Helping Chemists

May 7, 1997

Professor Larry Weiler
Department of Chemistry
University of British Columbia
Vancouver, BC V6T 1Z1
Canada

Dear Larry:

Thank you for your gracious letter of April 18.

I am indeed honoured to become a Fellow of the Canadian Society for Chemistry.

Unfortunately Isabel and I come to Canada relatively seldom even though most of her family now lives in and around Vancouver.

But I very much look forward to giving four talks in Toronto at the end of this month and then a few on my annual visit to Queen's late in October.

With all good wishes, I remain,

Yours sincerely,

AB/nik

Canadian Society for Chemistry
Société canadienne de chimie

April 18, 1997

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

Dear Alfred ~~Dr. Ba~~der:

It is a pleasure to welcome you to the Canadian Society for Chemistry. As a member of the CSC you are also a member of the Chemical Institute of Canada. Some of the benefits of membership in the CSC are outlined in the package sent from Head Office. You should also be receiving the Canadian Chemical News which provides news about Canadian chemists, along with reports about activities within the CSC and the CIC.

Our Society is the professional organization for chemists in Canada. However, we are also a volunteer organization. As a result our strength and impact are very much dependent on the input and involvement of our members. The demands on us as professional chemists or scientists increase daily. As a result we often look to professional organizations to provide up-to-date information on both the political and scientific changes around us. I hope the CSC, mainly through CCN, meets these needs for you. However, for the CSC to be effective, it needs an informed and active membership. This is particularly the case for relatively small societies such as our own.

There are three major activities of the CSC that I would like to point out to you. The first is National Chemistry Week that is held every October. The major thrust is our Local Sections. The Membership Chair of your Local Section has received your name and address, and will add your name to the mailing list for notification of activities at the local level. When the call comes for support and assistance for National Chemistry Week, please consider responding however you can. It is a good opportunity to meet other chemists in your community and to publicize the benefits and excitement in chemistry small groups who are often very interested and open to learning about chemistry. The second major activity of the CSC is the national conference. This year we meet in Windsor from May 31 - June 4. The third major activity of the CSC is informing politicians and the public about the importance of chemistry in a modern society.

I would certainly welcome your input into any of the CSC's activities. If you have suggestions as to how the CSC can better meet your needs or those of chemists in Canada, please let me know. You can contact me through our Head Office using the address on our letterhead or at the Department of Chemistry, University of British Columbia, Vancouver, BC, V6T 1Z1. In this age of electronic communication, feel free to contact me at my e-mail address at lsw@chem.ubc.ca. We also hope to have e-mail postings to our membership available very shortly and I would also encourage you to visit our web site at http://fox.nstn.ca/~cic_adm/.

I hope you will have a long and rewarding association with our Society. I look forward to meeting you and participating with you in activities of the CSC.

Yours truly,

Larry Weiler

Larry Weiler
President-Elect

A Constituent Society of The Chemical Institute of Canada • Une société constituante de l'Institut de chimie du Canada

130 Slater Street, Suite 550 • Ottawa, Ontario K1P 6E2 • Tel: 613-232-6252 • Fax: 613-232-5862
e-mail: cic_adm@fox.nstn.ca • URL: http://fox.nstn.ca/~cic_adm/

FAX TRANSMITTAL SHEET

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

June 6, 1994

TO: Professor Ed Piers
Department of Chemistry
University of British Columbia 604 822 2847

Dear Professor Piers:

I so enjoyed your award lecture; it was one of the finest I have ever heard.

I very much hope that you will submit the manuscript to the *Aldrichimica Acta*. You may have noticed that Professor Bryan Jones submitted his paper which was published recently. There is no need to mention that this is the Bader Award address.

Almost all of the chemists at Aldrich have remained my very good friends, and I am still the largest individual stockholder and so of course want the company to do well.

One of our ablest chemists, Dr. Stephen Branca, who has recently been promoted to vice president of Aldrich, is in charge of the Acta and I know that he will assure that great care is taken with your manuscript. Of course, the very nature of the manuscript makes it of such importance to Aldrich: how many other manuscripts have discussed such exciting new synthetic tools?

All good wishes.

Sincerely,

c: Dr. Stephen Branca

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C. Canada V6T 1Z1
Tel: (604) 822-3266
Fax: (604) 822-2847

June 14, 1994

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

Dear Alfred:

Thank you very much for your letter of June 6 and for your gracious words regarding my lecture in Winnipeg. I plan to send a manuscript to *Aldrichimica Acta* later this year.

You may recall that we spoke in Winnipeg about the possibility of you and Isabel visiting UBC at some time during the Spring of 1995. I would now like to extend to you a "formal" invitation to do so. I have two questions. 1. When would you like to come and how many days would you like to spend in our Department? From our perspective, some time during the last half of March would be preferable. 2. How many lectures would you be prepared to give? If I recall correctly, you mentioned that you have three "prepared" talks that you could give. Is this correct? In any case, my colleagues and I, along with our graduate students and postdoctoral fellows, would be delighted to welcome you and Isabel to UBC again. We have fond memories of your previous visits.

I look forward to hearing from you.

With very best regards,

Yours sincerely,

Ed

Edward Piers
Professor

SB: NB

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

July 15, 1994

Professor Edward Piers
Department of Chemistry
University of British Columbia
2036 Main Mall
Vancouver, British Columbia
Canada V6T 1Z1

Dear Edward:

I am sorry that a trip to Europe has delayed my thanking you for your kind letter of June 14th.

I know that Dr. Stephen Branca, editor of the *Aldrichimica Acta,* looks forward to your manuscript.

There may be one logistical problem about visiting the UBC. Of course, I don't accept honoraria from universities, but Isabel and I would like to be reimbursed for our travel expenses, which we try to keep as modest as possible.

Flying from here to Vancouver could be quite costly, but as we do plan to attend the A.C.S. meeting in Anaheim early next April, anyway, there probably are reasonable ways of flying from Anaheim to Vancouver. Also, we would have no housing expenses in Vancouver, as I am sure that Isabel's brother and family would welcome us as they always have.

Enclosed is a "menu" of my lectures. I would be happy to give three or four talks in two days. The most suitable for chemists is the one on Josef Loschmidt. The history of Sigma-Aldrich would be of interest to chemists and students in business administration. The various lectures on art would be of interest to your art museum. If you have a substantial Jewish community, it might be interested in the talk "The Bible through Dutch Eyes", which has a subtitle--Rembrandt and the Jews.

By next April I hope to have copies of my autobiography--*The Adventures of a Chemist Collector.*

Sincerely,

Enclosure

ack &
C: SB
6-15-94

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

June 15, 1994

Professor Edward Piers
Department of Chemistry
University of British Columbia
2036 Main Mall
Vancouver, British Columbia V6T 1Z1
Canada

Dear Professor Piers:

Your fax to Dr. Bader has been received while he is out of the country until the 10th of July.

In the meantime, enclosed is what Dr. Bader calls a "menu" of his talks. Would it be possible for Dr. Bader to lecture at other universities in the Vancouver area? Also, is there a local art museum which might be interested in a lecture?

In connection with your manuscript for the *Aldrichimica Acta*, I have taken the liberty of forwarding a copy of your letter to Dr. Stephen Branca at Aldrich.

Cordially,

Marilyn Hassmann
Secretary to Dr. Bader

Enclosure

c: Dr. Stephen Branca

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C. Canada V6T 1Z1
Tel: (604) 822-3266
Fax: (604) 822-2847

August 30, 1994

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

Dear Alfred:

Greetings from Vancouver!

From our previous correspondence and from your letters to Dr. Cooley in Edmonton, it is my understanding that you and Isabel will be available to visit UBC on April 6 and 7, 1995, after you have attended the ACS meeting in Anaheim. These proposed arrangements are fine with us. We note that you are willing to give three or four lectures during your visit and I will give you our lecture preferences later this fall, after I have consulted further with my colleagues. We will make sure that your talks are widely advertised on campus.

We will be happy to reimburse you and Isabel for your travel costs. I assume that these will be related to your travelling from Anaheim to Milwaukee via Vancouver and Edmonton and that they will be shared with our colleagues in Edmonton.

It will be a pleasure for us to have you visit UBC again.

With very best regards,

Yours sincerely,

Ed

Edward Piers
Professor

FAX FROM

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

April 6, 1995

Page 1 of 2

To: Professor Edward Piers
Department of Chemistry
University of British Columbia
Fax: 604/822-2847

From: Cheryl Weiss
Assistant to Dr. Bader

Dear Dr. Piers:

Following are some more documents for Dr. Bader. I don't know if they are still timely, but would you please give them to him anyway?

Thank you for your help.

Sincerely,

NOTE TO AB:

The bios are from Ivanka Franjkovic at Queen's, Dept. of Alumni Affairs. She apologizes for the delay in getting this information to you.

Also, Nicholas Lambourne from Christie's called re: tomorrow's sale. He just returned from 5 weeks abroad and wanted to remind you of the sale and inquire about your wishes. You may fax him at 171-389-2209 or call him at his home this evening (London time) at 171-376-7614 if you have any instructions for him.

Thanks!

FAX FROM

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

January 23, 1995

To: Professor Edward Piers
Department of Chemistry
University of British Columbia 604 822 2847

Dear Ed:

Thank you so much for your fax of today.

Isabel and I much look forward to being in Vancouver, but I must tell you that I am disappointed that you have chosen only one talk per day.

Of all the talks, the one of greatest interest to chemists is the one entitled "Josef Loschmidt--the Father of Molecular Modelling". Would it not be possible for you to scheduled that talk either as a second talk on either day or preferably schedule two talks on each day.

The talks "Adventures of a Chemist Collector" and "The Bible through Dutch Eyes", would also be of great interest to students in art history. The talk on the history of Aldrich might also be of interest to business students.

We very much look forward to joining you for dinner, and Friday evening, April 7th, is fine.

All good wishes.

Sincerely,

Alfred

P.S. For the talks on Loschmidt, the Bible and Chemist Collector, I will need two projectors and two screens. I will bring my own packed Kodak Carousels.

UNIVERSITY OF BRITISH COLUMBIA
DEPARTMENT OF CHEMISTRY

2036 Main Mall
Vancouver, B.C.
Canada V6T 1Z1

FAX #: (604)822-2847
Telephone: (604)822-3266

TO: [illegible]
Date: [illegible]

FAX #: [illegible]
Time: ______ AM/PM

COMPANY/DEPARTMENT: ______

FROM: [illegible]
Telephone: [illegible]

SUBJECT: ______

[illegible]

[illegible]

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THE UNIVERSITY OF BRITISH COLUMBIA

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[illegible]

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C. Canada V6T 1Z1
Tel: (604) 822-3266
Fax: (604) 822-2847

January 26, 1995

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

Dear Alfred:

Thank you for your recent fax. In accord with your desire to give more the two lectures during your visit to UBC, we will do our best to schedule three talks, with, probably, one to be given on Thursday and two on Friday. Thus, a "revised" proposal would be as follows:

April 6 - The Adventures of a Chemist Collector
April 7 - 1. Josef Loschmidt - The Father of Molecular Modelling
2. History of the Aldrich Chemical Company

I hope this proposal is OK with you. Do you have any suggestions regarding the order in which the lectures are given? I will let you know the specific times later.

We will plan on taking you and Isabel out for dinner on Friday evening, April 7.

With very best regards,

Yours sincerely,

Ed

Edward Piers
Professor

FAX FROM

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

April 5, 1995

Page 1 of 7

To: Professor Edward Piers
Department of Chemistry
University of British Columbia
Fax: 604/822-2847

From: Cheryl Weiss
Assistant to Dr. Bader

Dear Dr. Piers:

Following are a few items which I believe Dr. Bader would like to see. Would you please deliver them to Dr. B when you see him on Thursday?

Thank you for your help.

Sincerely,

Cheryl

FAX TRANSMISSION

DEPARTMENT OF ALUMNI AFFAIRS

Summerhill
Queen's University
Kingston, Ontario
K7L 3N6

To: **Dr. Alfred Bader**
Fax: 414-277-0709

From: **Ivanka Franjkovic**
Branch Development Coordinator
Department of Alumni Affairs
Queen's University
Kingston, Ontario
K7L 3N6
Phone: (613) 545-2060 or 1-800-267-7837
Fax: (613) 545-6777

Date: March 31, 1995

Number of Pages: (including this one) 4

Dear Dr. Bader,

Following our recent telephone conversation, I have prepared an itinerary for you regarding all the Queen's alumni events we have arranged for you and Mrs. Bader on your travels to various Canadian cities in the next couple of months. You have already discussed all of these events with Florence Campbell. The details have been arranged for all but the Toronto event. Toronto alumni are excited about having you come to speak on the evening of Wednesday, May 17. The evening has been reserved but the details have yet to be worked out. We will consult with you once those become available.

Everyone in the Office of Advancement at Queen's is very excited about the radio interview we have arranged for you in Vancouver. CBC Radio producers have requested that it take place on Friday, April 7. Vicki Gabereau is a very well known CBC Radio host and her show is aired across the country. You will have nation-wide exposure with this interview. I have spoken with Dr. Piers and he will take care of getting you to the studio following your afternoon lecture at UBC. Since this show will get national coverage, if the opportunity presents itself, it would be wonderful if you could mention the Toronto and Guelph lectures you will be giving to Queen's alumni. You could give my telephone number (1-800-267-7837) to be used for anyone who is interested in attending these events and wants more information.

Because of the publishing schedule, copies of your book will not be available for the Vancouver event, however we will have advance order forms there for any guests interested in ordering one. We will ensure that copies of the book will be available for sale and for signing at the Toronto and Guelph events.

I hope this answers all the questions you might have about the Queen's alumni events. If you should have any more questions please feel free to contact me. Best wishes to you and Mrs. Bader on your upcoming travels.

Sincerely,

Ivanka Franjkovic

Ivanka Franjkovic
Branch Development Coordinator

P.S. On Monday I will fax you information about your alumni hosts at the various alumni events.

Itinerary for Queen's Alumni Events
For Dr. Alfred and Mrs. Isabel Bader

Vancouver

Thursday, April 6, 1995

5:30 pm Mrs. Katie Hill, Arts'50, and her husband Jim Hill will pick up Dr. and Mrs. Bader at the home of Mrs. Bader's brother, Mr. Clifford Overton. Mrs Hill will telephone Mr. Overton to confirm the final arrangements. The reception will take place at the Reception Centre of the UBC Botanical Gardens.

6:00 pm Wine and Cheese Reception at UBC Botanical Gardens Reception Centre, 6804 S.W. Marine Dr. Non-alcoholic beverages will also be provided.

7:00 pm Dr. Bader's presentation followed by a further opportunity to mingle with the guests.

8:30 pm Dr. and Mrs. Bader will be taken to dinner by Mr. and Mrs. Hill who will also drive them back to Mr. Overton's house at the end of the evening. This departure time is flexible and is at the discretion of Dr. and Mrs. Bader and Mr. and Mrs. Hill.

Friday, April 7, 1995

2:30 pm Professor Edward Piers will drive Dr. and Mrs. Bader to the CBC Radio Studio.

3:30 pm Dr. Bader will be interviewed by CBC Radio Host, Vicki Gabereau. (Interview should last 20 to 30 minutes)

Saturday, April 8, 1995

1:00 pm Brenda and David McLean will pick up Dr. and Mrs. Bader at the home of Mr. Overton and host them to lunch. Afterwards they will take Dr. and Mrs. Bader to the Vancouver Art Gallery (VAG) where Mr. Brian Foreman, Coordinator of General Programs will give them a private tour of the Gallery. The VAG will be exhibiting a small collection of still life and landscape Dutch paintings from 1600 and 1700 which might be of interest to Dr. and Mrs. Bader.

Edmonton

Because the schedule arranged by Jean Cooley of the Canadian Society of Chemistry is very full

there is no opportunity to arrange a special reception with Queen's alumni during this visit. An arrangement has been made with Jean that Queen's alumni living in Edmonton will be invited to attend the two public lectures to be presented at the Edmonton Art Gallery and at King's University College.

The Branch Development Unit of the Department of Alumni Affairs has sent an invitation to alumni living in Edmonton. Alumni in attendance at the public lectures will wear a Queen's University Alumni Association name tag showing the Queen's flag.

Toronto

Wednesday, May 17, 1995

The Toronto Branch is very interested in having Dr. Bader speak to alumni. Details are still being worked out and we will consult with Dr. Bader as more information becomes available.

Guelph

Monday, May 29, 1995

The Guelph Branch and the Kitchener/Waterloo Branch have planned to jointly host a coffee and seasonal dessert reception for Dr. and Mrs. Bader on the evening of Monday, May 29, 1995. Upon discussion with Professor Oakley we arranged that Professor Oakley will take Dr. and Mrs. Bader to their hotel in mid-afternoon on Monday.

5:00 pm	Branch Development Coordinator, Ivanka Franjkovic will pick up Dr. and Mrs. Bader for dinner with the presidents of the two alumni branches and their spouses. She will also drive them to the reception and finally back to their hotel at the end of the evening.
7:30 pm	Reception featuring coffee/tea and seasonal dessert.
8:00 pm	Dr. Bader's presentation followed by a further opportunity to talk with the guests.
9:30 pm	Ivanka Franjkovic will take Dr. and Mrs. Bader to their hotel. The departure time as indicated is flexible and is at the discretion of Dr. and Mrs. Bader.

University of Alberta
Edmonton
Canada T6G 2J9

Dr. Roderick D. Fraser
President and Vice-Chancellor
3-1 University Hall, Telephone: (403) 492-3212
Fax: (403) 492-1438
E-mail: rod.fraser@ualberta.ca

March 28, 1995

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

Dear Alfred:

Thank you for your recent note. I am pleased you enjoyed the speech, and I look forward to talking with you about what I know is an outstanding Chemistry Department. I intend to keep it that way and thus am looking for the best advice on how to do so.

Ron Kratchovil has told me you and Isabel will be here on April 10 and 11. Judith and I would be pleased to have lunch with you both on April 11, perhaps with a tour of the University of Alberta's costume collection afterwards.

Sincerely,

Rod

Dr. Roderick D. Fraser
Principal and Vice-Chancellor

RDF/cbd

From Jere McGaffey –

A favorable vote of the majority of the outstanding shares voting will be required for approval of the adoption of the 1995 Option Plan.

The Board of Directors recommends a vote FOR approval of the 1995 Option Plan.

SHAREHOLDER PROPOSED RESOLUTION CONCERNING EARNINGS ANNOUNCEMENTS

The Company has been informed that Dr. Alfred Bader, 2961 North Shepard Avenue, Milwaukee, Wisconsin 53211, the beneficial owner of more than 2,500,000 shares of the common stock of Sigma-Aldrich Corporation, intends to present the following resolution for adoption at the meeting.

Proposed Resolution

RESOLVED, that the shareholders recommend to the Board of Directors that the Board (or a Committee of outside directors of the Board) review the Company's internal financial statements monthly to determine whether in their judgement the Company's performance for the quarter is likely to differ materially from the current consensus or mean earnings estimate published by recognized financial sources for that quarter. If they differ, the Board or the Committee shall determine whether it is appropriate to make disclosure well in advance of the normal quarterly announcement.

Statement in Support of the Proposal

After the market closed on July 20, 1994, the Company reported earnings for the second quarter of $.54 per share, which was only equal to the second quarter's earnings for 1993. This was the first time that the Company had not reported an increase in earnings over the prior year's quarter. The results were below the consensus estimate of $.60 per share. The next day, the stock price fell approximately 15% from the close on the prior day.

Investors are naturally disappointed by unfavorable results. Their disappointment increases when the results are also a surprise. Much of the Company's stock is held by institutions and institutional investors are particularly concerned with surprises.

Analysts that make predictions on a company's stock typically are in contact with that company to determine whether their estimates are reasonable. While the Company should not provide one investor with "inside information", it may make public announcements to inform the market when earnings estimates made by others are unrealistic.

In the situation which occurred, either the Company was unaware of the likely earnings for the second quarter or failed to warn the market that earnings estimates were unrealistic. The Board should implement procedures to guard against either situation occurring again.

THE BOARD OF DIRECTORS RECOMMENDS A VOTE AGAINST THIS PROPOSED RESOLUTION FOR THE FOLLOWING REASONS:

First, the proposed resolution, in the Board's view, lacks clarity as it does not define when the Board should determine to issue a public announcement; instead, the proposed resolution simply calls for an assessment as to when disclosure is "appropriate". Although the proposed resolution could be construed to leave the Board with discretion in making such a determination, the Board believes adoption of such a resolution is ill advised in light of its ambiguity which carries the risk that others might seek to construe it to create a standard independent of the Board's exercise of its best judgment.

Second, if the proposed resolution is construed simply to require the Board to consider periodically when public announcements are, from time to time, appropriate, the Board does not believe the resolution prescribes a new standard of conduct for it to follow. Rather, the resolution merely requests that the Board continue what it is in large measure already doing. Thus, contrary to the inferences in the proponent's statement, the Board believes that had the proposed resolution, so construed, been in effect during the past year, the market performance of the Company's common stock would not have been different.

The Board already periodically reviews the Company's disclosure practices and the manner in which it communicates the Company's business to the public. Each month every member of the Board reviews the Company's internal financial statements and copies of analysts' reports received by the Company. In connection with such review, each member of the Board is expected to consider whether it is appropriate to make any public disclosures, even if the Board does not formally meet that month. Additionally, the Company complies with the rules and requirements of the federal securities laws and the Nasdaq National Market (on which the Company's common stock is traded) relating to prompt disclosure to the public of material information. Judgment must be exercised in the timing of disclosures as premature, incomplete announcements can simply introduce uncertainty which can be detrimental to the stock price and the shareholders. The Board has demonstrated its willingness to exercise judgment and to announce financial results ahead of schedule from time to time when it deems it appropriate.

Further, shareholders should be aware that the proponent is a former member of the Board of Directors and was not renominated to the Board in 1992 by unanimous vote of the continuing directors.

ACCORDINGLY, YOUR BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS A VOTE AGAINST THE PROPOSED RESOLUTION, AND PROXIES WILL BE SO VOTED UNLESS SHAREHOLDERS SPECIFY IN THEIR PROXIES EITHER A CONTRARY CHOICE OR A DESIRE TO ABSTAIN.

' FAX FROM

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

April 7, 1995

To: Professor Edward Piers
Department of Chemistry
University of British Columbia
Fax: 604/822-2847

From: Cheryl Weiss
Assistant to Dr. Bader

Dear Dr. Piers:

I am sorry to bother you again, but this matter is rather urgent. Would you please see that Dr. and Mrs. B. receive the following? Thank you <u>again</u> for <u>all</u> your help.

Sincerely,

Cheryl

Dear Alfred and Isabel:

Gerry Waxman called today to advise you that Isabel's immigration hearing is scheduled for May 9th. As Isabel should pass the test with flying colors, the only remaining step will be her swearing in as a citizen. <u>However</u>, INS does not permit travel outside the U.S. between the hearing and the swearing in (since they will take the green card at the hearing).

Gerry would like to discuss the pros & cons of this situation if you have time and has provided her home telephone number (305/472-7458). She also suggested investigating locally, and I have put in a call to Jere McGaffey to see if he or one of his associates knows the usual time lapse between these events and/or if a special swearing in could be arranged for Isabel prior to the Toronto trip on the 17th. (I have not yet received a response from him, but I will forward any information he provides when I receive it.)

Gerry indicated that she thinks you may be able to discuss the matter with INS at the hearing appointment and work out some arrangement, and she thinks that is probably preferable to trying to request a new hearing date, as Murphy's Law suggests that would most likely fall in the middle of your European excursion.

P.S. Deborah wanted to know if there were any additions to the grocery list for next week.

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C. Canada V6T 1Z1
Tel: (604) 822-3266
Fax: (604) 822-2847

April 24, 1995

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

Dear Alfred:

Thank you for your letter of April 17 and for the information that it contained.

The lectures that you presented in our department were extremely well received. In fact, I cannot think of another series of lectures that produced as many enthusiastically favorable comments from faculty, postdoctoral fellows, and graduate students in our department. Thanks again for taking the time to visit us and I hope that you and Isabel will be able to come again at some future time.

I just received today from the UBC bureaucracy the cheque ($404.66 US) representing our share of your travel expenses. The cheque is enclosed.

With very best regards,

Yours sincerely,

Ed

Edward Piers
Professor

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C. Canada V6T 1Z1
Tel: (604) 822-3266
Fax: (604) 822-2847

March 10, 1995

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

Dear Alfred:

The times of your lectures at UBC have now been finalized. The schedule is as follows.

Thursday, April 6, 10:30 am	The Adventures of a Chemist Collect
Friday, April 7, 10:30 am	Josef Loschmidt - The Father of Molecular Modelling
Friday, April 7, 1:30 pm	History of the Aldrich Chemical Company

I hope that these arrangements are OK with you.

I heard recently from Don Kossuth, a representative of the Queen's Alumni Association. Mr. Kossuth told me that the Association would try to arrange for you to give a talk for them on Thursday evening. Have you been contacted about this? If not, please let me know and I will try to contact Mr. Kossuth.

I look forward to hearing from you.

With very best regards,

Yours sincerely,

Ed

Edward Piers
Professor

FAX FROM

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

April 6, 1995

Page 1 of 2

To: Professor Edward Piers
Department of Chemistry
University of British Columbia
Fax: 604/822-2847

From: Cheryl Weiss
Assistant to Dr. Bader

Dear Dr. Piers:

Following are some more documents for Dr. Bader. I don't know if they are still timely, but would you please give them to him anyway?

Thank you for your help.

Sincerely,

NOTE TO AB:

The bios are from Ivanka Franjkovic at Queen's, Dept. of Alumni Affairs. She apologizes for the delay in getting this information to you.

Also, Nicholas Lambourne from Christie's called re: tomorrow's sale. He just returned from 5 weeks abroad and wanted to remind you of the sale and inquire about your wishes. You may fax him at 171-389-2209 or call him at his home this evening (London time) at 171-376-7614 if you have any instructions for him.

Thanks!

Brenda and David McLean

David is Chairman and Brenda is Vice-Chairman of The McLean Group (a Vancouver Real Estate Investment Firm). Brenda graduated from Queen's with a BA in 1968. David is not a Queen's graduate, however, one of their sons, Sasha, is currently in his second year at Queen's studying Geography.

Brenda is a member of the Queen's University Council. The McLeans have set up an entrance scholarship for a high school student from British Columbia to attend Queen's. They are benefactors also to the University of British Columbia and the University of Alberta.

The McLeans are supportive of and involved in community issues. Brenda is a member of the Board of the Vancouver Art Gallery. In November of 1994 David was appointed Chairman of the Canadian National Railway Company, a five year appointment.

Following are more detailed biographies of both Brenda and David McLean.

Mrs Katie Hill

Born Katie Beaumont, Mrs Katie Hill is married to James Hill. Together they have three children, Brian, Ross, and Nancy. Mrs. Hill is a Queen's graduate (Arts'50) as are each of the three children, although Mr. Hill is not.

Mrs. Hill grew up in Calgary but has spent her adult life living in Vancouver. There she and her husband have a large clothing store in Kerrisdale, a section of the city. The Hills are long time friends of former Queen's Chaplain, Reverend Marshall Laverty. They have kindly hosted visiting Queen's speakers (including Padre Laverty) to Vancouver on numerous occasions.

For the past 14 years Mrs. Hill has been a volunteer with the Vancouver Art Gallery where she donates her time working at the front desk. Mrs. Hill has been an enthusiastic supporter of Queen's over the years.

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C.
Canada, V6T 1Z1

G.S. Bates Associate Professor
Telephone (604) 822-2834
FAX (604) 822-2847
E-Mail FLIP@CHEM.UBC.CA

April 18, 1995

Dr. Alfred Bader
c/o Alfred Bader Fine Arts
Astor Hotel Suite 622
924 East Juneau Avenue
Milwaukee, Wisconsin
USA 53202

Dear Dr. Bader:

I am writing to you, at your suggestion, to follow-up on our recent conversation regarding the International Chemistry Olympiad. We met following your series of lectures in early April at the Department of Chemistry of the University of British Columbia. As we discussed at that time, I would like to solicit your assistance regarding funding for the Canadian involvement in the Olympiad. This international competition has been ongoing for over twenty five years and Canada is now in its tenth year as a participating nation. The Olympiad is an excellent method of reaching out to some of the brightest young scientific minds that we have in Canada. I would like to use much of the balance of this letter to outline the operation of the programme and would be most happy to provide any additional information that you might wish.

This past July something quite amazing happened. While the newspapers were reminding us of the sad state of Canadian education, Canada continued its solid effort in the International Chemistry Olympiad winning a silver, and a bronze medal in addition to an honorable mention. While it is true that Canada spends more per student on education than just about any other nation, it is also true that the general proficiency of Canadian science students as compared to their peers from around the world is sadly lacking. The Canadian school system is working to improve itself but it has a long way to go before it can offer top Canadian students the ability to compete with the world for science excellence. The recent Canadian medal winners all worked very hard, some for years, outside of school on a programme developed by The Canadian Chemistry and Physics Olympiad which coordinates our efforts in both the chemistry and physics competitions.

The Canadian Chemistry and Physics Olympiad was founded to provide world-class opportunities to our top science students, in both official languages, and in all regions of Canada. The Olympiads are not a blanket solution to bring a general appreciation of the sciences to young Canadians; we target bright prospects, convince them that their skills and abilities are rare and valuable, and we do all we can to encourage them to pursue science as a career. Canada needs these students for leadership in research and development. There is never any guarantee that as Canadian science and technology industries face increased global competition, there will be the science elite ready to take up the challenge. Canada has a relatively small population when compared to the United States or Japan. Smaller numbers means we must work harder and be smarter in preparing for the future.

continued...

We encourage students to train for the International Science Olympiads, events which are very similar to the sporting Olympics but are of an academic nature. Students from around the world congregate for a week of friendly competition, social, and cultural events. The goal is to bring together small numbers of our best students at provincial, national and international gatherings and to convince them that their talents are appreciated by an important network of future colleagues. Students glimpse the life of research science through their contact with the scores of volunteers running the Olympiads at home and abroad and make long term friendships with like-minded individuals from around the world. Over forty nations now take part in these competitions.

It works! Virtually all of the students we have trained since our beginnings in 1985 have continued on to university studies in science or engineering at major universities including one close to your own heart — Queen's University. Of those students who have finished their undergraduate degrees, nearly all of them have started graduate studies. The achievements of Olympiad students are staggering, both in terms of scholarships and research activities. During their work terms, past Olympiad students have worked for TRIUMF, Noranda, Bell Northern Research and Fermi-Labs just to name a few. Each summer, Merck-Frosst Canada in Montreal employs a number of chemistry Olympiad students. They believe that the Olympiad program helps to ensure that elite students will eventually become elite researchers, a resource that Merck-Frosst and other Canadian research and development intensive corporations must have. Our student's research activities have ranged from studies of the polar cap, synthesis of new drugs, and laser tooling to medical imaging, stellar explosions, and zinc purification processes. Invariably these students credit the Olympiad experience with giving them the start and the motivation to pursue these heights.

This success does not come easily and we must work very hard to train Olympiad competitors. Students taking part in the Olympiad program work throughout the year (and in most cases, over a period of two or three years) to learn chemistry to a level well beyond what is taught in even our most enriched schools. Canadians should stop complaining about our "low standards". Rather we should start taking notice of the opportunities available to good students to play on the world stage and to promote and reward excellence.

The Science Council of Canada outlines eight priorities for the direction of Canada's science education in the publication *Science for Every Student.* One of their top priorities is to challenge our high achievers and science enthusiasts. The Olympiads provide a powerful way to meet that need. Indeed, towards this end, The Natural Sciences and Engineering Research Council of Canada (NSERC) has promised an annual sponsorship of up to $30,000 for the Olympiads. The support will be provided as matching funds that are raised from the private sector. This kind of support is unprecedented in Canada. Traditionally, NSERC funded only post-secondary projects and research but now, NSERC agrees that to provide Canada with future talent we need to start earlier — at the high school level. The importance of this programme was recognized in a somewhat round-a-bout manner in the past few weeks — funding for the programme was initially cut completely by NSERC as a consequence of the recent federal government budget. However, vigorous lobbying by our organization and with assistance from industry-based researchers resulted in the reversal of the original decision. In times of considerable financial restraint, to have our funding fully restored speaks highly of the standards of our programme. The Olympiad organization has received the endorsement and the support of two national scientific societies — the Chemical Institute of Canada and the Canadian Association of Physicists. Both of these bodies are represented on our board of directors.

continued...

The Canadian Chemistry and Physics Olympiad organization is looking forward to 1997 when it will be hosting both the International Physics and Chemistry Olympiads. This will be the first time that both events will be held simultaneously in the same country. The 29th International Chemistry Olympiad will be held at McGill University in Montréal, in conjunction with Bishop's University, and The 28th International Physics Olympiad will be held at Laurentian University in conjunction with Science North, both of Sudbury, Ontario. Participants from perhaps fifty nations will be treated to the charm of the Québec Eastern Townships and to the beauty and geology of the Canadian Shield.

The purpose of this letter is to ask for your assistance with the The Canadian Chemistry and Physics Olympiads. The Canadian Olympiad movement would be heavily indebted to you if you could devote even a fraction of your well-known and formidable generosity to our programme. I have enclosed a copy of the budget for our 1994 – 95 operation for your perusal and will send you our fund-raising proposals for 1997 shortly. (They are in the final approval stages by the board.) As you can see, our annual budget is quite modest. Virtually everyone involved donates their time and expertise to the programme. Additional indirect financial contributions to the Olympiads are made from various universities by way of meeting the operating expenses of regional programmes which lead on to the National Olympiad Finals. These contributions amount to several tens of thousands of additional dollars. To promote excellence in Canadian education will take participation and money, not just from our federal and provincial governments but from industrial and investment corporations and individuals with an interest in the strength of Canada's scientific and technological competitiveness. Any sector which foresees a need for well-trained chemists, physicists, or engineers should be concerned about the current trends. The Olympiads represent an especially effective way of seeding the future with talent.

As you mentioned to Miss Gabareau on the CBC radio interview which you taped during your visit to Vancouver, you now devote one third of your life to helping chemists. I would ask you to please consider seriously becoming involved with the Olympiad programme and thus to helping the Canadian chemists of the future either on an ongoing basis or specifically for the exciting but fast approaching events of 1997. I would be quite pleased to hear from you to further discuss the operation of this excellent and exciting programme.

Thank you for your consideration of our effort.

Yours sincerely

Gordon S. Bates
Associate Professor
Team Leader — Canadian Chemistry Olympiad

PS: You suggested to me that being able to operate in some manner through Queen's University might be beneficial. Our organization has very close contacts with some of the faculty at Queen's University, and we are currently investigating how best to handle the manner should you become involved in the support of our programme.

CANADIAN CHEMISTRY AND PHYSICS OLYMPIAD

A non-profit corporation under the Canada Corporations Act., Incorporated October, 1985
Registered number: 0736819-20

Purpose:

The organization exists to select and train young Canadians in their later years of high school or CEGEP to compete in the International Chemistry and Physics Olympiads. Each year more than 40 countries from all continents take part in the International Olympiads. The overall objective is a wider appreciation of chemistry and physics as a career for young people, and improved Canadian standards in these disciplines.

The Canadian Olympiad thus works through high schools and universities in all regions and both official languages, with the high schools doing the initial selections, and volunteer professors at the universities doing both the final training and selection. Since 1986, the Canadian Olympiad has increased rapidly both in scope and reputation, and since then, twenty three medals, including three golds and three silvers, have been achieved. The Canadian Chemistry and Physics Olympiad has the endorsement of the Canadian Association of Physicists (CAP) and the Chemical Institute of Canada (CIC).

Olympiad Sponsors:

The main financial sponsors of the Canadian Olympiads are:

Inco Limited
Merck-Frosst Canada Inc.
The Natural Sciences and Engineering Research Council of Canada
The Toronto French School (Founding Organization)

Recognition is extended to the following for their major financial support of the Olympiads:

AECL Research
Bell Canada
Canadian Association of Physicists
Canadian Society for Chemistry
Celanese Canada Inc.
Ciba Geigy Canada
Dow Chemical
Du Pont Canada
Glaxo Canada
Imperial Oil Ltd.
Investors Group Inc.
John Wiley & Sons Canada
Power Corporation of Canada
Royal Bank of Canada
Shell Canada Limited
Spar Aerospace Ltd.
The Boland Foundation
The McLean Foundation
The Government of British Columbia
The Government of Ontario
The Government of Québec

The following universities support the Olympiads through their extensive training and selection programmes for Canadian students:

Bishop's University
Dalhousie University
McGill University
Memorial University of Newfoundland
Royal Military College
University of British Columbia
University of Manitoba
University of Toronto

Board of Directors:

President	Douglas Firth	Hill & Knowlton Canada
Vice President	Harry Giles, C.M., Q.C.	Founder, Toronto French School
Secretary-Treasurer	John Wylie, Ph.D.	Toronto French School
Member	Alan MacDonald Ph.D.	Merck-Frosst Canada Inc.
CIC Liaison	George Brown, M.C.I.C.	Toronto Section Chair
CAP Liaison	Napoleon Gauthier, Ph.D.	Royal Military College

Academic Committees:

Physics
J. De Bruyn, Memorial University
N. Gauthier, Royal Military College
D. Goble, Dalhousie University
R. Harris, McGill University
A. Kotlicki, University of British Columbia
J. Sipe, University of Toronto
C. Waltham, University of British Columbia
J. Wylie, Toronto French School

Chemistry
L. Barton, Toronto French School
G. Bates, University of British Columbia
R. Cook, Bishop's University
D. Farrar, University of Toronto
P. Georghiou, Memorial University
K. Grundy, Dalhousie University
G. Hickling, University of Manitoba

Team Leaders:

Physics
C. Waltham, University of British Columbia
J. Wylie, Toronto French School

Chemistry
G. Bates, University of British Columbia
R. Cook, Bishop's University

Budget 1994/95:

National Office		*International Participation*		*National Olympiad Finals*	
Salary	$27,000	Travel Expenses	$40,000	Travel Expenses	$15,000
Mailing	$3,000	Gifts for Exchange	$2,000	Room and Board	$20,000
Printing	$6,000			Social Events	$2,000
Telephone, Courier	$1,000			Honoraria	$1,000
Miscellaneous	$3,000				
Subtotal	$40,000	Subtotal	$42,000	Subtotal	$38,000

COMBINED TOTAL **$120,000**

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

A Chemist Helping Chemists

August 1, 1995

Professor John Sherman
Department of Chemistry
University of British Columbia
2036 Main Mall
Vancouver, BC V6T 1Z1
Canada

Dear Professor Sherman:

I am sorry that a long trip to Europe has delayed my responding to your most interesting letter of June 6th.

Obviously, you are a very competent researcher, highly thought-of at the UBC.

Isabel and I are planning to set up research awards in Canada, but I hope that you will understand that we would not like to be in the position to decide who should get these awards.

With all good wishes, I remain,

Yours sincerely,

AB/cw

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Chemistry
2036 Main Mall
Vancouver, B.C. Canada V6T 1Z1
Tel: (604) 822-3266
Fax: (604) 822-2847

6 June 1995

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

Dear Dr. Bader:

We met this past April when you visited the Department of Chemistry at UBC. Your "Collections" talk brought back vivid memories of my undergraduate days at Haverford College in Pennsylvania, where I took an art course that changed the way I look at art (and chemical structures) forever. You revitalized the creative spirit within me, which has been discouraged by the current climate in research funding. These feelings were rekindled when I saw you at the CSC conference at Guelph.

As you know, funding for basic research is on the wane and is particularly difficult for young professors like myself. I am being forced to pursue industrial collaborations, which forces a change in the direction of my research. As you can see from the enclosed preprints, my interests lie in the understanding of non-covalent interactions such as those that drive the self-assembly of biomolecules as well as synthetic materials. (I hesitate to suggest to an art collector that we think the molecules and assemblies that we are making are somewhat aesthetically pleasing.) Academicians in my research area find my work exciting and daring, not to mention accessible and novel. Thus, I am reasonably confident that my work will continue to flourish. But this will only happen if I have the resources. I have support from NSERC and PRF, the only agencies that still truly support basic research, and I am confident that my NSERC support will increase. But the next 1-2 years are looking somewhat bleak: With my present funding, I will not be able to take any new graduate students in the fall. Since I took no students this year, this could break up the continuity of students that is essential to maintaining a strong research program.

I was wondering if you have any interest in supporting a researcher such as myself by means of a Young Investigator Award. Needless to say, you have been a leader in many respects and I think this type of support for basic research and young professors would be a noble effort that would provide yet another example of your foresight. Perhaps funding agencies and other philanthropists or foundations will catch on to the wisdom of such support.

You can probably tell from this letter that I am a neophyte at "fundraising". I simply hope that you are committed to support and encourage basic research, especially creative and innovative visions by young investigators. I would be happy to discuss my research or provide any other information that you might require. Please feel free to contact references, e.g., Ed Piers, Larry Weiler or Steve Withers. Thank you for reading this letter.

Sincerely,

John Sherman
Assistant Professor of Chemistry
604-822-2305
sherman@chem.ubc.ca

Curriculum Vitae – John C. Sherman

I. Personal and Professional Vita

Education and Employment

Assistant Professor	University of British Columbia	Chemistry	1991-present
Postdoctoral Research Fellow (N. R. Kallenbach)	New York University	Chemistry	1989-1991
Postdoctoral Research Associate (E. T. Kaiser)	The Rockefeller University	Bioorganic Chem.	1988-1989
Ph.D. (D. J. Cram)	U. of California, Los Angeles	Chemistry	1988
B.A.	Haverford College	Chemistry	1983

Awards

Ichikizaki Award for Young Chemists, 1995
Ichikizaki Award for Young Chemists, 1994
National Institutes of Health Postdoctoral Research Fellowship, 1989-1991.
Damon Runyon-Walter Winchell Cancer Fund Postdoctoral Fellowship (declined).
American Cancer Society Postdoctoral Fellowship (declined).

Professional Affiliations

American Chemical Society
American Association for the Advancement of Science
American Peptide Society
Protein Society
Canadian Society for Chemistry (Chair, Biological and Medicinal Chemistry Division 1994-95)

Group members

Graduate Students:	Ashley Causton (Ph.D.) Robert Chapman (Ph.D., holds an NSERC Graduate Fellowship) Naveen Chopra (Ph.D.) Adam Mezo (Ph.D., holds an NSERC Graduate Fellowship) Frank Tsai (Ph.D., holds an NSERC Graduate Fellowship)
Postdoctorates:	Janet Fraser Bruce Gibb

Funding

NSERC Research Grant (P.I.)	$34,352 p.a. (1994-96)
NSERC Equipment (MALDI, group)	$198,000 (1994)
NSERC Equipment (Workstation, group)	$28,000 (1994)
PRF Type AC Grant (P.I.)	$25,000 p.a. (US$, 1993-95)
NSERC Equipment (Peptide Synthesizer, P.I.)	$79,312 (1993)
NSERC Research Grant (P.I.)	$27,800 p.a. (1992-94)

II. Publications

a) Refereed Journal Publications

1. *Host-Guest Complexation. 48. Octol Building Blocks For Cavitands and Carcerands.* Linda M. Tunstand, John A. Tucker, Enrico Dalcanale, Jurgen Weiser, Judi A. Bryant, John C. Sherman, Roger C. Helgeson, Carolyn B. Knobler and Donald J. Cram *J. Org. Chem.* **1989**, *54*, 1305-1312.

2. *Carcerand Interiors Provide a New Phase of Matter.* John C. Sherman and Donald J. Cram *J. Am. Chem. Soc.* **1989**, 111, 4527-4528.

3. *Synthesis and Properties of Soluble Carceplexes.* John C. Sherman, Carolyn N. Knobler and Donald J. Cram *J. Am. Chem. Soc.* **1991**, *113*, 2194-2204.

4. *Alpha Helix Stabilization by Natural and Unnatural Amino Acids with Alkyl Side Chains.* Pingchiang Lyu, John C. Sherman, Amy Chen and Neville R. Kallenbach *Proc. Natl. Acad. Sci.* **1991**, *88*, 5317-5320.

5. *A Scanning Tunneling Microscopy Study of the Formation and Chemical Activation of Step Defects on the Basal Plane of Pyrolytic Graphite.* Victor N. Morozov, John C. Sherman, Neville R. Kallenbach, Shou Ming Du and Nadrian C. Seeman *J. Microscopy* **1993**, *170*, 237-245.

6. *Circular Dichroism Analysis of a Synthetic Peptide Corresponding to the α,α–Corner of Hemoglobin.* Frank C. S. Tsai and John C. Sherman. *Bioch. Biophy. Res. Comm.* **1993**, *196*, 435-439.

7. *Carceplex Formation: Scope of a Remarkably Efficient Encapsulation Reaction.* Robert G. Chapman, Naveen Chopra, Eileen D. Cochien and John C. Sherman *J. Am. Chem. Soc.* **1994**, *116*, 369-370.

8. *An Asymmetric Carceplex and a New Crystal Structure Yield Information Regarding a One Million Fold Template Effect.* Janet R. Fraser, Bozena Borecka, James Trotter and John C. Sherman *J. Am. Chem. Soc.* **1995**, *60*, 1207-1213.

9. *Carceplexes and Hemicarceplexes: Molecular Encapsulation From Hours to Forever.* John C. Sherman *Tetrahedron* **1995**, *51*, 3395-3422.

10. *Templation Effects on a Hemicarceplex Reaction.* Naveen Chopra and John C. Sherman *J. Supramol. Chem.* **1995**, in press.

11. *Efficient Coupling of Amino Acid Derivatives to Rigid Organic Scaffolds: Model Syntheses for de novo Proteins.* Bruce C. Gibb, Adam R. Mezo, Ashley S. Causton, Janet R. Fraser, Frank C. S. Tsai and John C. Sherman *Tetrahedron* **1995**, accepted.

12. *Study of Templation and Molecular Encapsulation Using Highly Stable and Guest-Selective Self-Assembling Structures.* Robert G. Chapman and John C. Sherman *J. Am. Chem. Soc.* **1995**, submitted.

13. *Prototype for a New Family of De Novo Proteins.* Bruce C. Gibb, Adam R. Mezo and John C. Sherman *Tetrahedron Lett.* **1995**, submitted.

14. *A Deuterium NMR Study of Guest Dynamics in Carceplexes.* James Polson, Naveen Chopra, Robert G. Chapman, Jenny Chuang, John C. Sherman and E. Elliot Burnell, *J. Chem. Soc., Faraday Trans. II* **1995**, submitted.

b) Invited Presentations

1. Molecular Recognition and Supramolecular Chemistry Symposium at the 76th Canadian Chemical Conference, Sherbrooke, Quebec, June, **1993**.
2. Bio-Mega Boehringer Ingelheim Research Inc., Laval, Quebec, April **1994**.
3. Cram Symposium, Los Angeles, CA, March **1994**.
4. NATO Advanced Research Workshop on Supramolecular Stereochemistry, Iceland, September **1994**.
5. UBC-Ritsumeikan Symposium in Biology and Chemistry, Vancouver, November, **1994**
6. Canadian Workshop in Organic Chemistry, Guelph, May **1995**
7. UBC-Ritsumeikan Symposium on Chemistry, Bioscience and Biotechnology, Japan, May, **1995**
8. Symposium on Molecular Recognition and Supramolecular Assemblies, Pacifichem, Hawaii, December, **1995**

c) Conference Presentations

1. *Synthesis and Properties of the First Soluble Carceplexes.* John C. Sherman and Donald J. Cram, Presented at the 198th National Meeting of the American Chemical Society, Miami Beach, FL; September, **1989**; Paper ORGN 201. (oral presentation)
2. *Design of Stable Alpha Helices* Frank C. S. Tsai and John C. Sherman, Presented at the a) Volcano Conference, Pack Forest, WA, February **1992**, b) 75th Canadian Chemical Conference, Edmonton, Alberta, June **1992**, c) Protein Engineering-1992 Symposium (PENCE), Montreal, Quebec, June **1992** and d) International Protein Engineering Conference, Montreal, Quebec, June **1992**. (poster presentation)
3. *Carceplexes: Molecular Prisons* Robert G. Chapman, Naveen Chopra and John C. Sherman, Presented at the Volcano Conference, Pack Forest, WA, February **1992**. (poster presentation)
4. *Stabilization of Alpha Helices Using Synthetic Peptides* Frank C. S. Tsai and John Sherman, Presented at The 13th American Peptide Symposium, Edmonton, Alberta, June, **1993** and the Volcano Conference, Pack Forest, WA, February **1993**. (poster presentation)
5. *Carceplexes, The Inside Story* Robert G. Chapman and John C. Sherman, and *Synthesis and Applications of New Carceplex Molecules* Naveen Chopra and John C. Sherman, Presented at the Volcano Conference, Pack Forest, WA, February **1993**. (poster presentation)
6. *Carceplexes, The Inside Story.* Robert G. Chapman, Janet R. Fraser, Naveen Chopra, Eileen D. Cochien, and John C. Sherman, presented at the Volcano Conference, Pack WA, February **1994**, the Cram Symposium, Los Angeles, CA, March **1994** and the 207th National Meeting of the American Chemical Society, San Diego,CA, March **1994**, poster #98.
7. *The Power of Preorganization: Investigation of a Hemicarceplex Reaction.* Naveen Chopra and John C. Sherman, presented at the Volcano Conference, Pack WA, February **1994**, the Cram Symposium, Los Angeles, CA, March **1994** and the 207th National Meeting of the American Chemical Society, San Diego,CA, March **1994**, poster #99.

8. *Organization of Peptides with Organic Templates*. Ashley S. Causton, Bruce C. Gibb, Janet R. Fraser, Frank C. S. Tsai and John C. Sherman, presented at the Volcano Conference, Pack WA, February **1994**, the Cram Symposium, Los Angeles, CA, March **1994** and the 207th National Meeting of the American Chemical Society, San Diego,CA, March **1994**, poster #97.

9. *Templation Effects on Formation of Carceplexes and Hemicarceplexes.* Robert G. Chapman, Janet R. Fraser, Naveen Chopra, Eileen D. Cochien, and John C. Sherman, presented at the 207th National Meeting of the American Chemical Society, San Diego,CA, March **1994**, paper ORGN 458. (oral presentation)

10. *Two Shells About a Nut: Highly Stable Ternary Complexes and their Relevance to Templation of Carceplex and Hemicarceplex Formation.* Robert G. Chapman, Janet R. Fraser, Naveen Chopra and John C. Sherman, presented at the International Symposium on Recognition Processes, Birmingham, UK, July **1994** and the International Symposium on Molecular Recognition and Inclusion, Ottawa, Canada, August **1994**. (poster)

11. *A Highly Stable Ternary Complex and Some Proposed Self-Assembling Structures.* John C. Sherman, presented at the International Symposium on Recognition Processes, Birmingham, UK, July **1994**. (oral presentation)

12. *Physical Characterization of the Association of Ca^{2+} to Mixed and Unmixed Half Molecules of Calbindin D_{9k}.* D. W. Kupke, J. C. Sherman, F. C. S. Tsai, K. Alessi and L. A. Marky, presented at the Biophysical Society Meeting, San Francisco, CA, February **1995**. (poster presentation)

13. *Two Shells About a Nut: Carceplexes, Hemicarceplexes and Highly Stable Ternary Complexes.* Robert G. Chapman, Janet R. Fraser, Naveen Chopra and John C. Sherman, presented at the Volcano Conference, Pack Forest, WA, February **1995**. (poster presentation)

14. *Studies Toward A Model Beta-Sheet.* Ashley S. Causton and John C. Sherman, presented at the Volcano Conference, Pack Forest, WA, February **1995**. (oral presentation)

15. *A New Family of Switchable Self-Assembling Structures.* Robert G. Chapman and John C. Sherman, presented at the 78th Canadian Chemistry Conference, Guelph, Canada, May **1995**. (oral presentation)

16. *A New Family of De Novo Proteins.* Adam R. Mezo, Bruce C. Gibb, Ashley S. Causton, Janet R. Fraser, Frank C. S. Tsai and John C. Sherman, presented at the 78th Canadian Chemistry Conference, Guelph, Canada, May **1995**. (poster presentation)

d) Work in Progress

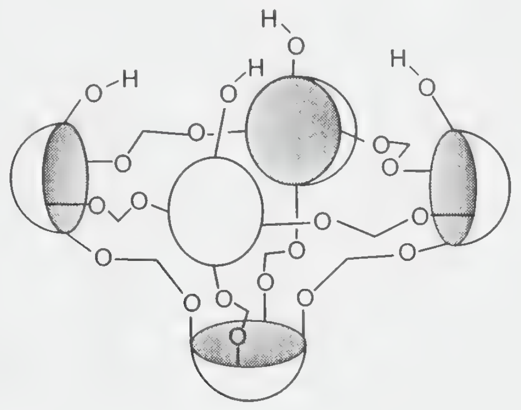
1. *Synthesis of the First Cavitand "Bowl" with Hydroxyls in the Pendant Groups.* Bruce C. Gibb, Robert G. Chapman and John C. Sherman, in preparation for *J. Org. Chem* .

2. *Carceplexes and Hemicarceplexes.* In *Large Ring Molecules*; Semlyen, J., Ed.; John Wiley & Sons, Ltd., Sussex, **1995**; invited chapter, in preparation.

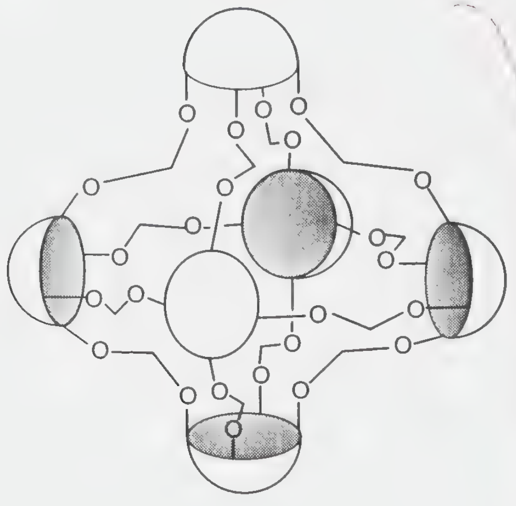
3. *Carceplexes, Circumplexes and Templation.* Robert G. Chapman and John C. Sherman, in preparartion fo *J. Am. Chem. Soc.*

4. *Effect of linker Group on the Stability of Four-Helix Bundle Caviteins.* Adam R. Mezo, Bruce C. Gibb and John C. Sherman, in preparation for *J. Am. Chem. Soc.*

5. *Beta-Sheet Caviteins.* Ashley S. Causton and John C. Sherman, in preparation for *J. Org. Chem.*
6. *Self-Assembly of Three or More Cavitands.* Naveen Chopra and John C. Sherman, in preparation for *J. Org. Chem.*
7. *Cooperativity Between Site I and Site II of Calbindin D_{9k}.* D. W. Kupke, J. C. Sherman, F. C. S. Tsai, K. Alessi and L. A. Marky, in preparation for *Biochemistry.*

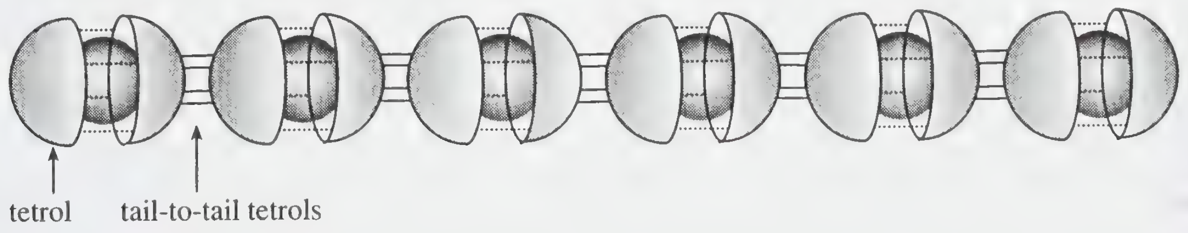


Cookie Jar

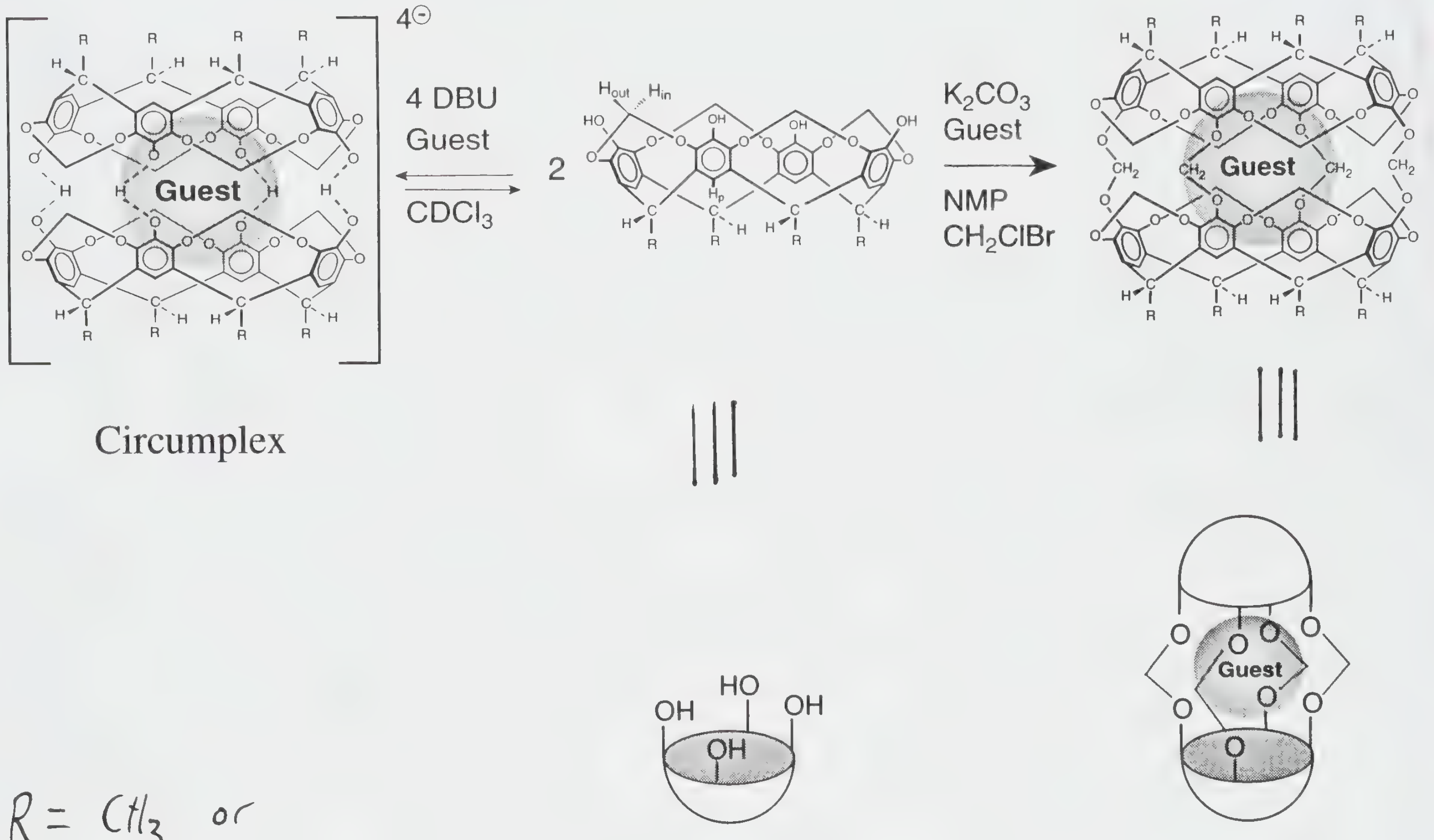


Super-carceplex

We are
trying !
make this/



Tail to Tail Self-Assembling Rod



Circumplex

Tetrol

Carceplex

$R = CH_3$ or

$PhCH_2CH_2$

We have

finally

[illegible]

these.

Prototype for a New Family of *De Novo* Proteins

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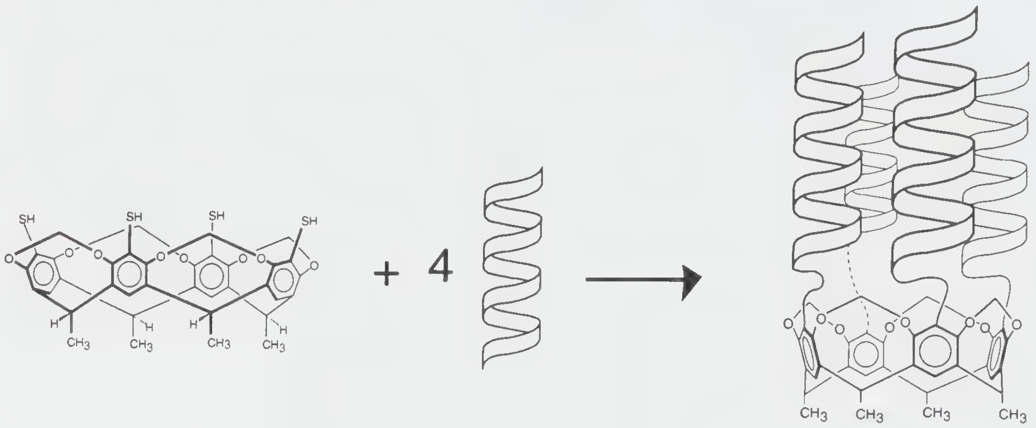
Abstract: We report the design, synthesis, and preliminary structural analysis of a four-helix bundle affixed to a rigid organic macrocycle.

Protein folding remains a seminal problem in biophysical chemistry.[1] One approach to elucidating the interactions that govern protein structure is to design and characterize simple synthetic proteins, which retain the crucial interactions of natural proteins, but are greatly reduced in complexity. We report here a prototype (**1**) for a new family of *de novo* proteins, which we call *caviteins* because they are composed of cavitands (rigid organic macrocyles that contain enforced cavities)[2] and proteins. We hope that caviteins will provide easy access to protein folding information that will be relevant to natural as well as nonnatural protein systems.

The four-helix bundle is a common motif in natural proteins and has been chosen for the design of a variety of *de novo* proteins due to its relative simplicity. Synthetic four-helix bundles have been prepared by aggregation of isolated peptides,[3] and by covalent linkage of peptides to: peptide turns,[4] branched amino acids,[5] linear[6] and cyclic peptides,[7] porphyrins,[8] and metal complexes.[9] We decided to incorporate this well-studied motif into a cavitein using tetrathiol cavitand **2**,[10] which would space peptides at nearly ideal distances for a four-helix bundle.[11] We chose methyls as the pendant groups on the cavitand because of their synthetic viability and because we have found that a tetraphenoxide cavitand containing pendant methyl groups is soluble in water and produced concentration independent ^{1}H NMR spectra in D_2O.[12] Eventually, we hope to make use of the enforced hydrophobic cavity[13] as a binding site for drugs and/or substrates.

Recently, there has been great interest in the ligation of peptides both with other peptides and with various templates. Ligation methods include the formation of amides,[5, 6a, 6d, 7a, 7b, 8a, 8b, 9] thioesters,[6b] thioethers,[8c] and oximes.[6c, 7c, 14] We recently reported the synthesis of tetrathiol **2** in 84% yield from its tetrabromo analogue and demonstrated the alkylation of tetrathiol **2** with amino acid derivatives such as $BrCH_2CO$–Phe–OEt (Phe–OEt = the ethyl ester of L-phenylalanine) in 76% yield.[10] We selected this method of ligation for three main reasons. First, it is synthetically viable: both tetrathiol **2** and the unprotected peptides, activated at their N-terminus, are readily available, and the coupling of the two components is selective and efficient. Second, the linkage maintains the natural amide backbone of the peptide. Third, the short linkage takes advantage of the rigidity of the cavitand as follows. The linkage between the cavitand and the first carbonyl of the peptide is only two atoms (SCH$_2$) and thus, there are few degrees of freedom that must be frozen for the helices to bundle. Futhermore, we have successfully linked Phe derivatives to tetrathiol **2** with two, three and four methylenes between the sulfur and the carbonyl.[10] We hope to incorporate these linkers into peptide **3** (see below), so we can probe the effect of flexibility in the linker group on the stability of the bundles.



2 **3** **1**

We designed peptide **3** with an amino acid sequence that favors an amphiphilic α-helix such that hydrophobic side chains will bundle to form a hydrophobic core, while water solubilizing groups will remain on the exterior of the bundle (see Fig. 1). In addition, we designed the sequence to allow the formation of salt bridges between lysine and glutamic acid side chains. The C-terminal glycine was incorporated as a C-cap[15] and was amidated to minimize both charge-charge repulsion between the helices, and charge-dipole repulsions within each helix.

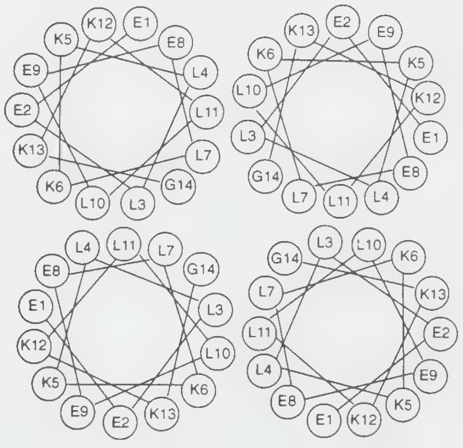


Fig. 1. Helical wheel diagram for peptide **3**. In this diagram, one is looking down the helical axis of four molecules of peptide **3** (E$_1$ is going into the page and G$_{14}$ is coming out of the page). The sequence of peptide **3** is: ClCH$_2$CO–(EELLKKLEELLKKG)–NH$_2$. The linkage to the cavitand becomes ArSCH$_2$CO–peptide. Abbreviations: E = glutamic acid; K = lysine; L = leucine; G = glycine.

We synthesized peptide **3** by standard methods using Fmoc chemistry, where the last cycle entailed coupling of ClCH$_2$COCl with the free N-terminus of the peptide. Peptide **3** was then cleaved from the resin and purified by reversed phase (C$_{18}$) HPLC and coupled to tetrathiol **2**, at 25 °C for 16 h, in dimethylacetamide as solvent, using diisopropylethylamine as the base. Cavitein **1** was obtained after removal of solvent *in vacuo*, followed by purification by reversed phase (C_{18}) HPLC. The HPLC chromatograph for the crude cavitein is shown in Fig. 2. The electrospray mass spectrum of purified cavitein **1** is shown in Fig. 3.

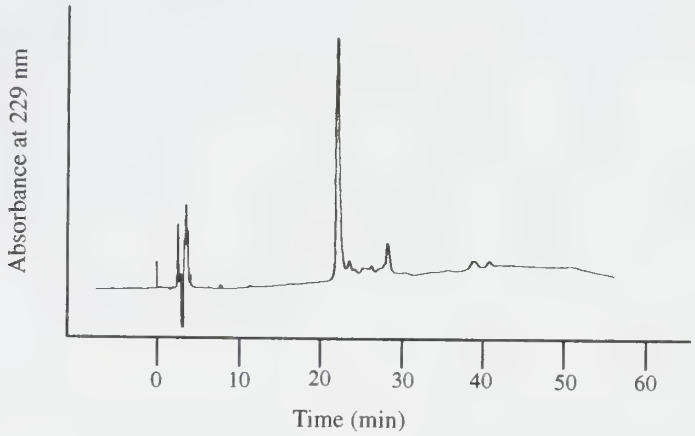


Fig. 2. Reversed phase analytical HPLC chromatograph of crude cavitein **1**. The gradient was 58-45%A, 45 min; 45%A 10 min (A = 0.1% TFA in water; B = 0.05% TFA in acetonitrile).

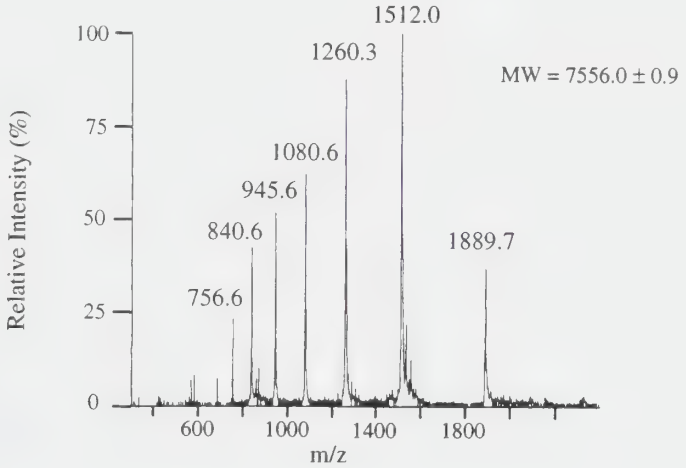


Fig. 3. Electrospray MS of cavitein **1** using a PE-Sciex API III triple quadrupole spectrometer. The calculated mass for (M + H) is 7557.18.

We investigated the presence of α-helical structure in cavitein **1** by circular dichroism (CD) as shown in Fig. 4. The spectrum shows the typical maximum (197 nm) and minima (208 & 222 nm) for an α-helix. In conclusion, we have prepared a prototype for a new family of *de novo* proteins. This *cavitein* was efficiently prepared and exhibits α-helicity, as designed. We are currently investigating the stability of this cavitein and exploring the effect of more flexible linker groups on both the amount of helicity and on the stability of the helical bundles.

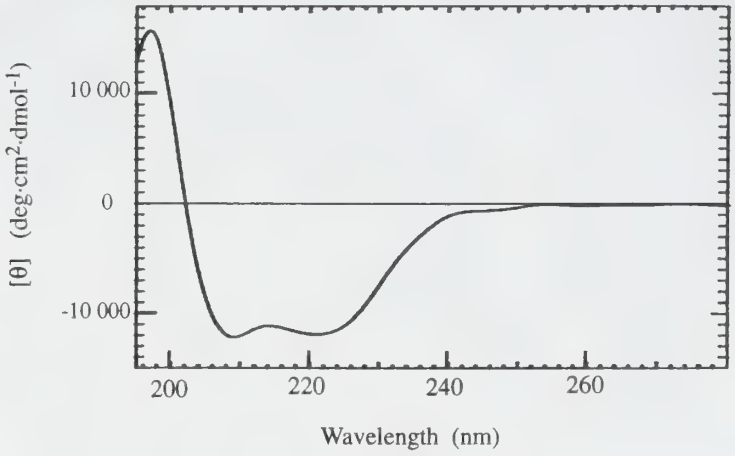


Fig. 4. Circular dichroism spectrum of cavitein **1** at 5 μM, 25 °C in 50 mM sodium borate at pH 7.5. Concentration was determined by amino acid analysis.

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11. According to a crystal structure, the distance between adjacent bromines when Br's replace the SH's of **2** is 6.8 Å and the distance between opposing Br's is 9.6 Å. See: Cram, D. J.; Karbach, S.; Kim, H.-E.; Knobler, C. B. Maverick, E. F.; Ericson, J. L.; Helgeson, R. C. *J. Am. Chem. Soc.* **1988**, *110*, 2229-2237. Typical interhelical distances in four-helix bundles are about 8 Å. See: Reddy, B. V. B.; Blundell, T. L. *J. Mol. Biol.* **1993**, *233*, 464-479.
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Study of Templation and Molecular Encapsulation Using Highly Stable and Guest-Selective Self-Assembling Structures.

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Abstract

We report the encapsulation of seven different guest molecules by two concave host molecules to yield a prototype for a new family of assemblies that we name *circumplexes*. For the circumplexes reported, the hosts are linked by four charged hydrogen bonds and the guests encounter van der Waals and electrostatic interactions with the walls of the host molecules. Free energies of binding as high as 11 kcal/mol were determined and were extremely sensitive to the guest molecules. The binding energies correlate with *template ratios* for formation of a carceplex, which indicates that the circumplex is a good model for the transition state of the guest-determining step in formation of the carceplex.

The phenomenon of self-assembly is common to both the biological and physical sciences, from the formation of cell membranes to the formation of monolayers, and thus, it is of widespread interest. We have been interested in the role of self-assembly in the formation of carceplexes, which are closed surface compounds that permenantly entrap smaller molecules within their confines,[1] and have demonstrated a one million-fold range in the template effect on the formation of carceplex **2a**⊙guest (Scheme 1).[2] We report here a self-assembling structure (**3**) that entails the encapsulation of a guest (template) molecule by two molecules of tetrol **1b**, which is the starting material for formation of carceplex **2b**⊙guest. We name assembly **3**⊙guest[2] a *circumplex*[3] for any assembly in which two or more concave molecules reversibly wrap around and encapsulate a guest molecule in solution. We have determined the stabilities of circumplexes **3**⊙guest, with seven different guest molecules, and discuss the correlation of the guest selectivities with the *template ratios*[2] obtained in the formation of carceplex **2a**⊙guest. We think these circumplexes will provide an unusual opportunity to study noncovalent interactions in general, as subtle variations in guests are manifested by large changes in the energies of binding.

[Insert Scheme 1]

During the one-pot synthesis of carceplex **2a**⊙guest, eight covalent (C–O) bonds are formed and seven molecules are brought together, including the guest (Scheme 1).[1b] The reaction requires a suitable guest/template molecule as illustrated by the range in yields of carceplex **2a**⊙guest from 0% in the presence of no suitable templates to 87% in the presence of the best template molecule, pyrazine.[2] The template ratios (TR's) for 24 guest/template molecules range from one (for *N*-methyl-2-pyrrolidinone, NMP) to one million (for pyrazine).[2] One approach to understanding the driving forces for this dramatic template effect is to explore the potential for association of the starting tetrol "bowls" with the template molecules; such a circumplex could serve as a model for the transition state of the guest-determining step (GDS, the step beyond which no guest exchange occurs) in the formation of carceplex **2**⊙guest.

The walls that line the interior of carceplex **2**⊙guest are rich with π-electrons and provide the most facile handle for characterization of these compounds: Incarcerated guest protons are typically shifted 2 – 4.5 ppm upfield from their chemcial shift when free in solvents such as $CDCl_3$.[1b] To probe the formation of a circumplex between two molecules of tetrol **1b**[4] and pyrazine, we obtained a ^1H NMR spectrum of a mixture of tetrol **1b** and pyrazine in $CDCl_3$, which showed no evidence for complexation in terms of changes in the chemical shifts of host or guest. However, upon addition of the base 1,8-diaza[5.4.0]bicycloundec-7-ene (DBU) to this mixture, the formation of a complex, circumplex **3**◌pyrazine, was striking (Fig. 1).[5] Circumplex **3**◌pyrazine undergoes slow exchange on the ^1H NMR timescale at ambient temperature as is evident by the two sets of host and guest signals. Integration of the circumplex host ("bowls") and guest signals yields a ratio of two bowls to one pyrazine. The chemical shift for complexed pyrazine is shifted upfield 4.3 ppm from its uncomplexed position in $CDCl_3$, which is similar to the 4.6 ppm upfield shift observed for entrapped pyrazine in carceplex **2b**⊙pyrazine.[2, 4] Thus, the magnetic environment formed around the guest in circumplex **3**◌pyrazine resembles that found in the carceplex, which indicates that the circumplex and the carceplex have similar geometries as represented schematically in Scheme 1.

[Insert Figure 1]

We next probed the interaction between the two bowls. When a $CDCl_3$ solution of tetrol **1b** and pyrazine was titrated with DBU, the fraction of circumplex **3**◌pyrazine[6] increased until 1/2 equivalent of DBU per hydroxyl of tetrol **1b** had been added, which indicates that half of the phenolic hydroxyls are deprotonated in circumplex **3**◌pyrazine. Thus, we suggest that four charged hydrogen bonds are formed between the two bowls as depicted in structure **3** (see Scheme 1).[7]

To probe the potential of circumplex **3**◌guest as a transition state model for the GDS in the formation of carceplex **2**⊙guest, we needed to determine the relative stabilities of the circumplexes to compare with the TR's. To calculate stability constants (K_s's) for circumplexes **3**◌guest, we needed to determine the form of the "free" host, which, in $CDCl_3$, could be monomeric tetrol or tetroxide, an empty dimer, or circumplex **3**◌$CDCl_3$. Since K_s = [**3**◌G] / [**1b**]^2[G], we need to know [**1b**], which could be all, or just a component, of the "free" species that is observed in the ^1H NMR spectra. We titrated tetrol **1b** with DBU in $CDCl_3$ and followed the change in chemical shift of the protons (H_p, Scheme 1, structure **1**) that are para to the four hydroxyls of tetrol **1b**. At 323 K and 0.0472 mM tetrol **1b**, we observed only a very small change in the chemical shift of H_p. This indicates that at high temperature and low concentration of tetrol **1b**, monomer predominates and it is mostly tetrol **1b** since we would expect a large upfield shift in H_p upon deprotonation of the phenolic hydroxyl. In contrast, at 263 K and 1.07 mM tetrol **1b**, the chemical shift of H_p moved upfield significantly (0.29 ppm total) until 1/2 equivalent of DBU per hydroxyl of tetrol **1b** was added. This indicates that the "free" species at low temperature and high concentration of tetrol **1b** contains either an empty "circumand"[3] or circumplex **3**⊙$CDCl_3$, where, in either case, four of the eight phenolic protons are removed. We next obtained ^1H NMR spectra of tetrol **1b** with DBU in a 1:1 mixture of $CDCl_3$ and $CHCl_3$, and suppressed the $CHCl_3$ signal at 7.24 ppm.[8] At 273 K,[9] a new signal appeared at 4.6 ppm, which we assign to complexed chloroform. The integration is imprecise in this type of supression experiment,[8] but agrees qualitatively with the "free" species consisting of a mixture of tetrol **1b** and circumplex **3**⊙chloroform;[9] the ratio of these two components can be determined as described below.

Knowing that the free species consists of ([**3**⊙$CDCl_3$] + [**1b**]) and knowing the initial concentrations of host and guest ($[\mathbf{1b}]_o$ and $[G]_o$, respectively), we can use the integration of the free and complexed species along with the chemical shift of H_p for ([**3**⊙$CDCl_3$] + [**1b**]) to calculate the K_s's for circumplexes **3**⊙$CDCl_3$ and **3**⊙G.[10] Thus, the K_s's for circumplexes **3**⊙guest for seven guests were determined and are listed in Table 1 along with the corresponding values of $-\Delta G°$ for each circumplex. The K_s's were found to be smaller at lower initial concentrations of tetrol **1b** and thus are reported as apparent K_s's. The cause for this concentration dependence is not as yet clear, but may be due to an aggregation of the circumplexes and the conjugate acid of DBU in the apolar $CDCl_3$ solvent.[11] Nevertheless, the overall magnitude of the binding energies are quite large. Moreover, the relative stability constants, K_{rel}, reported in Table 1 are independent of [**1b**] and are thus most useful in relating to the template effect in the carceplex reaction as discussed below. The remarkable stability of these circumplexes is further demonstrated by the formation of **3**⊙DMSO[12] as well as **3**⊙pyrazine in DMSO-d_6

as solvent. DMSO is a strong hydrogen bond acceptor and is notorious for precluding the formation of complexes that rely on hydrogen bonds for their formation.[13]

To probe the relationship between the guest-selectivity of the circumplexes and the TR's for carceplex formation (see Table 1),[2] we plotted the ln(template ratio) versus ln(K_{rel}) for six of the guests. This plot relates the relative free energies of complexation for circumplexes **3**⊙guest with the relative activation energies for the GDS in formation of carceplex **2b**⊙guest (all at ambient temperature). The correlation of the plot is $r^2 = 0.97$. This agreement implies that the interactions that govern the formation of carceplex **2b**⊙guest are similar to those that drive the formation of the circumplexes and thus, these circumplexes provide simple and useful transition state models for the GDS in the formation of carceplex **2b**⊙guest.

In conclusion, for the combination of self-assembly and molecular encapsulation, we have introduced a new term, circumplexes, that may be useful for a whole class of assemblies.[13, 14] We have demonstrated highly stable self-assembling circumplexes that are reversible and strongly guest-selective. We have used a simple transition state model to show that the one million-fold range in template ratios found in the formation of carceplex **2b**⊙guest is largely due to charged hydrogen bonds between the bowls, and van der Waals and electrostatic interactions between the guests and the walls of the cavity formed by the two bowls. We believe the large energy changes with small perturbations in the guests (cf. pyrazine and pyridine) make circumplex **3**⊙guest a useful system to study noncovalent interactions and thus, we are further probing these circumplexes by theoretical as well as experimental means. We are also expanding on prototypical circumplex **3**⊙guest by creating both larger assemblies, with potential as drug delivery devices, and higher order circumplexes (tail-to-tail and side-to-side covalently linked bowls), which may provide new materials such as linear rods or two-dimensional bilayers.

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2. Chapman, R. G.; Chopra, N.; Cochien, E. D.; Sherman, J. C. *J. Am. Chem. Soc.* **1994**, *116*, 369-370. The symbol ⊙ is used to denot permanent entrapment in a carceplex (see: Helgeson, R. C.; Knobler, C. B.; Cram. D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 307-308). The symbol ⦾ will be used to denote encapsulation in a circumplex, where the exchange rate is minutes or less. The guest-determining step (GDS) is likely the formation of the second or third methylene bridges. Template ratios reflect the relative rates of the GDS in the reaction to form carceplex **2**⊙guest. They were determined by measurement of the product ratios from competition reactions to form carceplex **2**⊙guest in the presence of two or more guests. The template ratios for carceplex **2b**⊙guest reported in Table 1 were determined as described in the above reference, but at ambient temperature using tetrol **1b**.
3. Circum is Latin for "around". Circumplex refers to a complex with a guest molecule; circumand refers to an empty dimer of bowls, with no guest.
4. Fraser, J. R.; Borecka, B.; Trotter, J.; Sherman, J. C. *J. Org. Chem.* **1995**, *60*, 1207-1213.
5. Upon addition of 1/2 equivalent of trifluoroacetic acid per hydroxyl to the complex, tetrol **1b** and free pyrazine were regenerated, demonstrating that formation of the complex is reversible and can be switched by adjustment of pH.
6. The fraction complex represents the fraction of bowls that are involved in circumplex **3**⦾pyrazine and was determined by integration of the corresponding free (I_f) and complexed (I_c) host signals (typically H_{in}, see Scheme 1) in the ^{1}H NMR spectrum: fraction complex ($f_{\mathbf{3}⦾G}$) = $I_c / (I_c + I_f)$.

7. The $(ArO{-}H{-}OAr)^-$ protons appear at 15.6 ppm in the ^1H NMR spectrum, which is consistent with "low-barrier" hydrogen bonds. See: (a) Frey, P. A.; Whitt, S. A.; Tobin, J. B. *Science* **1994**, *264*, 1927-1930. (b) Perrin, C. L. *Science* **1994**, *266*, 1665-1668. (c) Brzezinski. B.; Szafran, M. *Org. Magn. Reson.* **1981**, *15*, 78-82. (d) Gunnarsson, G.; Wennerström, H.; Egan, W.; Forsén, S. *Chem. Phys. Lett.* **1976**, *38*, 96-99.

8. $CHCl_3$ was passed through a column of silical gel to remove ethanol, and dried over 4 Å molecular sieves. A P1331 solvent suppression experiment was performed on a WH Bruker 400 MHz NMR spectrometer. See Sanders, J. K. M.; Hunter, B. K. *Modern NMR Spectroscopy*; Oxford University Press: Oxford, 1993; p. 251.

9. Unlike circumplex **3**⊙pyrazine, **3**⊙$CDCl_3$ and tetrol **1b** undergo fast exchange on the ^1H NMR timescale at 298 K in $CDCl_3$.

10. To calculate the K_s's for all circumplexes, including **3**⊙$CDCl_3$, one must determine [**1b**], [**3**⊙$CDCl_3$], [**3**⊙G] and [G], since [$CDCl_3$] is known (12.5 M). The fraction complex (see note 6), $f_{3\odot G}$, = $I_c / (I_c + I_f)$ = 2[**3**⊙G] / {2[**3**⊙G] + (2[**3**⊙$CDCl_3$] + [**1b**])}; [**3**⊙G] = ([**1b**]$_o$) x ($f_{3\odot G}$) x (0.5). [**1b**] = ([**1b**]$_o$) x (1 – $f_{3\odot G}$) x ($\delta_{obs} - \delta_c$) / ($\delta_o - \delta_c$), where δ_{obs} is the observed chemical shift of H_p, δ_o is the chemical shift of H_p for tetrol **1b**, and δ_c is the chemical shift of H_p for circumplex **3**⊙$CDCl_3$. Analogously, [**3**⊙$CDCl_3$] = (0.5) x ([**1b**]$_o$) x (1 – $f_{3\odot G}$) x [1 – ($\delta_{obs} - \delta_c$) / ($\delta_o - \delta_c$)]. The δ_c (6.438 ppm) for circumplex **3**⊙$CDCl_3$ was calculated by plotting δ_{obs} vs 1 / [**1b**]$_o^{1/2}$ according to: Connors, K. A. *Binding Constants*; John Wiley & Sons: New York, 1987; pp 202-205. The concentration range for tetrol **1b** was 0.07-3.72 mM; r^2 for the plot was 0.995. The δ_o and δ_c were found to vary slightly in the presence of different guests and were adjusted accordingly: The δ_o for tetrol **1b** shifted downfield by 0.034 ppm in the presence of 329 mM C_6D_6 and changed by less than 0.005 ppm when the other five guests were present in the concentrations used to determine the K_s's. The chemical shift for H_p for five of the circumplexes **3**⊙guest were measured in the presence of the sixth guest at the concentration of that guest used in the determination of the K_s's. These δ's changed by less than 0.003 ppm for all guests, except C_6D_6, which caused a downfield shift of 0.033 ppm. This shift was extrapolated to the δ_c for **3**⊙$CDCl_3$,

which was adjusted. Finally, the concentration of free guest can be determined from: $[\mathrm{G}] = [\mathrm{G}]_o -$ [**3**⊙G].

11. Control experiments in which the amount of water or DBU were varied did not account for the lower K_S's at lower $[\mathbf{1b}]_o$. The K_S for **3**⊙$CDCl_3$ varied from 530 to 1800 M^{-2} at $[\mathbf{1b}]_o$ of 0.4 mM to 3.9 mM, respectively.
12. Circumplex **3**⊙DMSO (dimethylsulfoxide) was shown to form in DMSO as solvent by obtaining a ^1H NMR spectrum of tetrol **1b** and DBU in a 1:1 mixture of DMSO and DMSO-d_6, and suppressing the solvent peak at 2.49 ppm, which revealed complexed DMSO at -1.2 ppm at 298 K.
13. (a) Branda, N.; Wyler, R.; Rebek, Jr., J. *Science* **1994**, *263*, 1267-1268. (b) Branda, N.; Grotsfeld, R. M.; Valdéz, C.; Rebek, Jr., J. *J. Am. Chem. Soc.* **1995**, *117*, 85-88.
14. Other assemblies that may be considered circumplexes are: (a) A diphenyl glycoluril "tennis ball", ref. 13. (b) Shinkai's calixarene capsules, Koh, K.; Araki, K.; Shinkai, S. *Tetrahedron Lett.* **1994**, *35*, 8255-8258. (c) Sanders' cyclocholate sandwiches, Bonar-Law; R. P.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1994**, *117*, 259-271. (d) Aoyama's resorcinol tetramer sandwiches, Kikuchi, Y.; Tanaka, Y.; Sutarto, S.; Kobayashi, K.; Toi, H.; Aoyama, Y. *J. Am. Chem. Soc.* **1992**, *114*, 10302-10306. Various cyclodextrin inclusion compounds can also be considered circumplexes: (e) Yoshida, Z.; Takekuma, H.; Takekuma, S.; Matsubara, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1597-1599. (f) Harada, A.; Li, J.; Kamachi, M. *Nature* **1994**, *370*, 126-128. (g) Zhang, B.; Breslow, R. *J. Am. Chem. Soc.* **1993**, *115*, 9353-9354. (h) Inoue, Y.; Liu, Y.; Tong, L.-H.; Shen, B.-J.; Jin, D.-S. *J. Am. Chem. Soc.* **1993**, *115*, 10637-10644. (i) Dick, D. L.; Rao, T. V. S.; Sukumaran, D.; Lawrence, D. S. *J. Am. Chem. Soc.* **1992**, *114*, 2664-2669. (j) Eftink, M. R.; Andy, M. L.; Bystrom, K.; Perlmutter, H. D.; Kristol, D. S. *J. Am. Chem. Soc.* **1989**, *111*, 6765-6772.

Scheme 1. Synthesis of carceplex **2**⊙guest and formation of circumplex **3**(•)guest.

Figure 1. ^{1}H NMR spectrum of tetrol **1b** (3.7 mM), DBU (7.8 mM) and pyrazine (1.9 mM) in $CDCl_3$ at 25 °C. Peaks labeled "f" are signals for the "free" species; peaks labeled "c" are signals for circumplex **3**(•)pyrazine. Assignments are: δ (ppm) 8.6, free pyrazine; 7.24, $CHCl_3$; 6.6, H_p of **3**(•)pyrazine; 6.5, H_p of (**3**(•)$CDCl_3$ + tetrol **1b**); 6.1, H_{out} of (**3**(•)$CDCl_3$ + tetrol **1b**); 6.0, H_{out} of **3**(•)pyrazine; 4.9, methine; 4.5, H_{in} of (**3**(•)$CDCl_3$ + tetrol **1b**); 4.3, encapsulated pyrazine; 4.0, H_{in} of **3**(•)pyrazine. The methyls are at 1.7 ppm (not shown).

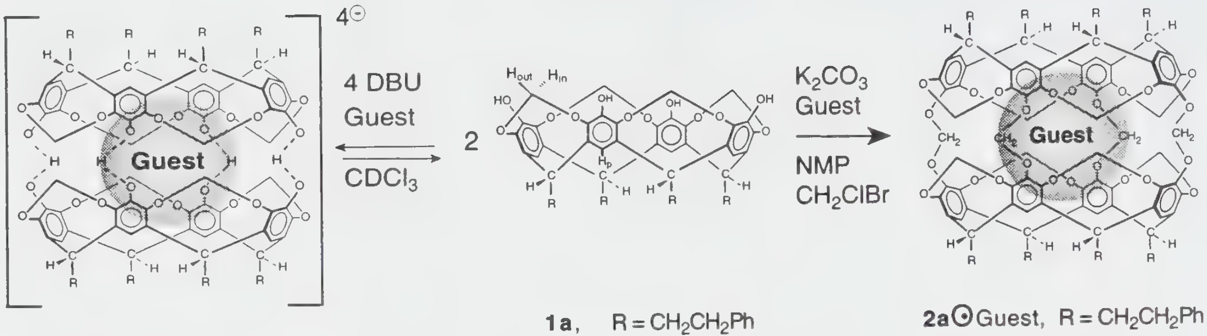
Table 1. Apparent Stability Constants and Free Energies of Binding for Circumplexes **3**⊙Guest at 298 K in $CDCl_3$

Guest	K_s (x $10^{-3}M^{-2}$)[a]	K_{rel}	- ΔG° (kcal/mol)	Template ratio (TR)[b]	ln (K_{rel})	ln (TR)
pyrazine	69 000	86 000	10.6	860	11.4	6.8
dioxane	4 400	5 400	9.1	180	8.6	5.2
DMSO	860	1 100	8.1	19	7.0	2.9
pyridine	640	790	7.9	14	6.7	2.6
acetone	63	78	6.5	2	4.4	0.6
benzene	70	87	6.6	1	4.5	0
$CDCl_3$	0.81	1	4.0			

[a] $[\mathbf{1b}]_o$ = 1.8 mM; [G] used such that [**3**⊙G] + [**3**⊙$CDCl_3$] = 0.81-0.83 mM;[10] [$CDCl_3$] = 12.5 M and was assumed to remain constant.

[b] TR determined at 25 °C using tetrol **1b**.[2]

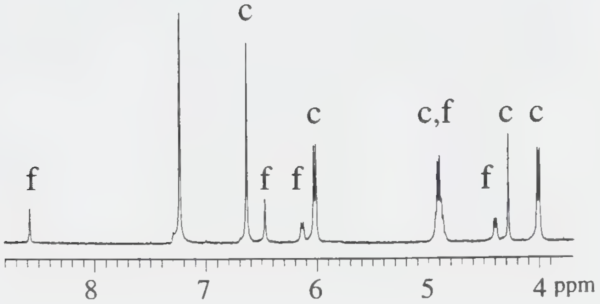
Allen J. Bard
Department of Chemistry and Biochemistry
University of Texas
Austin, Texas 78712



3⊙Guest, R = CH_3

1a, R = CH_2CH_2Ph
1b, R = CH_3

2a⊙Guest, R = CH_2CH_2Ph
2b⊙Guest, R = CH_3


f
c
f
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c
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c
8
7
6
5
4 ppm

ALFRED BADER FINE ARTS

DR. ALFRED BADER

ESTABLISHED 1961

June 22, 1995

Professor John Sherman
Department of Chemistry
University of British Columbia
2036 Main Mall
Vancouver, BC V6T 1Z1
Canada

Dear Professor Sherman:

Thank you for your letter of June 6th to Dr. Bader. Dr. Bader is traveling in England and the Continent. He will respond to your letter upon his return to Milwaukee at the end of July.

Best wishes,

Cheryl Weiss
Office Manager

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

A Chemist Helping Chemists

September 19, 1995

Professor Larry Weiler
Department of Chemistry
University of British Columbia
2036 Main Mall
Vancouver, B.C. V6T 1Z1
Canada

Dear Professor Weiler:

Thank you for writing to Mr. Wyman regarding the possibility of the Killam Foundation helping the Isabel and Alfred Bader Foundation.

In the meantime, I have heard from Mr. George Cooper of McInnes Cooper & Robertson with a great many details about the Killam Foundation.

As you know, we would like to help young chemists in Canada and in the Czech Republic, but each of these presents special problems.

The problem in Canada is the uncertainty of what will happen in Quebec. The problem in the Czech Republic is quite different and perhaps easier to solve: At the moment, income of a Czech charitable foundation is still taxable, but that is likely to change.

In any case, we are discussing our thinking with our sons, David and Daniel Bader, who will be trustees of the Foundation after our deaths. But both Isabel and I are in good health and hope to be able to work on the details leisurely.

And of course, we will study the details of the Killam Foundation, which Mr. Cooper has sent us, very carefully.

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

Yours sincerely,

AB/cw

xc: Mr. W. Robert Wyman
Mr. George Cooper

THE UNIVERSITY OF BRITISH COLUMBIA

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Tel: (604) 822-3266
Fax: (604) 822-2847

August 30, 1995

Mr. W.R. Wyman
2406 Bellevue Avenue
West Vancouver, BC
V7V 1E1

Dear Bob,

Earlier this summer I had lunch with Dr. Alfred Bader. Alfred is a very successful chemist who started a speciality chemical company in the mid 50's which has grown to become the largest such company in the world. Recently Alfred has turned his attention to philanthropy. He has been exceedingly generous with many researchers and universities, particularly his alma mater - Queen's. You may recall the article in McLean's magazine about the donation of a English castle to Queen's. That was Alfred and his wife Isabelle. In addition they have donated a very significant art collection to Queen's.

Alfred is interested in establishing a national, or international, award for Canadian chemists or scientists, and he is looking for an appropriate vehicle to manage such an award. We discussed the Killam Foundation. I suggested that I would write to you as one of the trustees of the Killam Foundation and ask you to contact Alfred to see if there might be a possibility of the Killam Foundation administering such an award. I belive this could be a significant Canadian award.

Alfred can be contacted at:

Dr. Alfred Bader
Suite 622
924 East Juneau Avenue
Milwaukee, WI 53202
U.S.A.
Telephone: 414-277-0730
FAX: 414-277-0709

If I can be of any further assistance, please call me at 822-2864. Thank you and best wishes.

Yours truly

Larry Weiler

Larry Weiler
Professor

cc. A. Bader ✓