Research and Development of Chemistry in Canada

General Organic and Physical-Organic Chemistry

Committee 4

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1. Introduction

There are more organic chemists than chemists of any other kind. The unique character and importance of organic chemistry stems from the astonishing number of compounds that can be formed by the element carbon. It was realized in the mid-nineteenth century that structural formulae could account for the chemical properties of the thousand or so organic compounds then known. This was followed by a rapid flowering of the field and in the past one hundred years more than a million different organic compounds have been prepared and their structures determined. In this time the organic chemical industry grew at an enormous rate as more and more new compounds became available which could be converted to products of commercial value.

Until relatively recently basic research in organic chemistry meant work in the areas of synthesis and structure elucidation. In the past thirty years a third area of study has grown to maturity, that of physical-organic chemistry, which seeks to provide an understanding of the precise way in which organic molecules react and the forces that control the rates and routes of organic processes. This vigorous area of study interacts with the traditional areas of synthesis and structure elucidation to the benefit of all three. Physical-organic chemistry provides insights into molecular behaviour and aids the chemist planning, for example, the synthesis of a natural product. Conversely, many compounds found in Nature have structures with fixed and unique spatial arrangements and the reaction of these molecules are of great interest to anyone concerned with determining detailed reaction paths.

A second development which has profoundly affected organic chemistry is the rapid rise since World War II of instrumental analysis. Ultraviolet spectroscopy, infrared spectroscopy, mass spectrometry, nuclear magnetic resonance spectroscopy, gas chromatography, and X-ray crystallography have revolutionized the field and indeed the last of these, in those cases where

it can be applied, has taken the task of structure elucidation out of the hands of the organic chemist altogether. This is not so with the other instrumental techniques. A practicing organic chemist today, whether he be attempting the synthesis of a natural product or determining the mechanism of an organic reaction, must be thoroughly familiar with these tools. There are virtually no areas of organic chemistry where significant research can be conducted today without the aid of instrumental techniques.

In Canada research in organic chemistry was conducted in a very few laboratories until relatively recent times. In the year 1936 the total number of publications which appeared in the organic chemical literature from Canadian sources was 20. Of these 13 were from the laboratory of Professor Hibbert at McGill in the field of carbohydrate and lignin chemistry and five, dealing with alkaloids were the work of Dr. R. H. Manske at the National Research Council. The situation 30 years later was vastly different. In 1966 the number of publications was twelve times as great and the laboratories in which the research was conducted were distributed across the country. Furthermore the almost total emphasis on the chemistry of natural products has changed and the balance between the various branches of organic chemistry has improved.

II. Scope of the Study

The following topics were assigned to the field of General Organic and Physical-Organic Chemistry studied by Committee 4.

> The formation, reactions and properties of
> fundamental types of organic compounds such
> as alkanes, alcohols, ketones, amines, etc.;
> alicyclics, aromatics, heterocyclics, carbohydrates;
> reaction mechanisms, transient intermediates,
> equilibria, solvation etc. in organic chemistry.

It should be noted at the outset that the division of organic chemistry into General Organic and Physical Organic (Committee 4) and Pharmaceuticals

and Natural Products (Committee 6) is a highly artificial one indeed. As elucidation of the structure of natural products takes less and less time and effort (chiefly because of the advent of X-ray crystallography) increasing emphasis is placed on the synthesis of such compounds. The synthetic organic chemist whether he be attempting to prepare a steroid or a small-ring hydrocarbon requires the same instrumental tools, the same bench techniques and the same understanding of reaction mechanisms. Many individual research groups cover a spectrum of activities, some of which would be in the domain of one committee and some in that of the other.

Carbohydrate chemistry has been somewhat arbitrarily included in the field of General Organic and Physical-Organic Chemistry. Although carbohydrates are clearly products of Nature there is much less interaction between chemists working with carbohydrates and say, steroids, than one finds between those working with, say, steroids and alkaloids. Given the arbitrary division of organic chemistry between Committees 4 and 6 inclusion of carbohydrate chemistry in the former is probably as satisfactory as including it in the latter.

III. Survey of Publications in Organic Chemistry

Research in organic chemistry is essentially basic research and, as such, should appear ultimately in published form. The published research in organic chemistry from Canadian sources was compared with those from British and American sources for the year 1966. All research contributions from these three countries were covered in the survey provided they appeared in the following journals (or in their organic sections): Canadian Journal of Chemistry, Journal of the American Chemical Society, Journal of the Chemical Society, London, Sections B and C, Tetrahedron, Carbohydrate Research, and Journal of Organic Chemistry.

The Canadian Journal of Chemistry was surveyed from January, 1965 to June, 1967 a period of 2 1/2 years and the figures were normalized by multiplying by a factor of 0.4 to make them as comparable as possible to those obtained from the other journals. Publications from the three countries were categorized according to source - (a) university, (b) government or other institutional laboratory, or (c) industry - and according to field of study - (a) general organic and physical-organic, (b) carbohydrates, or (c) natural products and pharmaceuticals. Although carbohydrates are included in this study under general organic chemistry they were considered separately in the literature survey.

Two kinds of comparison between Canadian, British and American research in organic chemistry can be made on the basis of the results of the survey; first, the relative emphasis that each country places upon the three areas of organic chemistry (at least as this is reflected in published work) and, second, the pattern that has developed with regard to the location of such work, i.e. the proportion done in universities, government and similar laboratories, or industrial laboratories. The total number of publications from the three countries turned out to be not greatly different on a per capita basis.

Although about two-thirds of all chemical research done in Canada is published elsewhere (Committee 20 report) the situation with regard to organic chemistry is quite different. We have found that 72% of the papers that Canadian laboratories contribute to the major journals publishing organic research that were listed earlier in this section appeared in the Canadian Journal of Chemistry. Making allowance for journals that were not surveyed we estimate that roughly two-thirds of all Canadian research in organic chemistry is published in the Canadian Journal of Chemistry. It has clearly become the favored journal for the publication of organic research in this

country. This journal is now also used very extensively by foreign authors as a medium for publication.

IV. Areas of Specialization

The results of the publications survey reveal some differences in the distribution of research interests in the three countries examined, Canada, the United Kingdom, and the United States.

The percentages of papers that were assigned to the areas of general organic and physical-organic in the three countries were: Canada 62%, U.K. 63%, U.S.A. 77%. As one might expect this is the major area of research interest in organic chemistry in all three countries, the more specialized areas of carbohydrate, natural product and pharmaceutical chemistries making a much smaller contribution to the total output. It is clear, however, that in this country the emphasis on general organic and physical-organic chemistry is proportionately less than in the United States. This is partly due, no doubt, to the early influence of McGill University where, up until the 1950's the bulk of Canadian Ph.D.'s in organic chemistry were produced. The strong school that Professor Hibbert developed at McGill was devoted to the study of carbohydrate and lignin chemistry and this influence is still felt to some extent. In the journals surveyed papers on carbohydrates make up 12.2% of the total of organic papers from Canada, 10.4% of those from the United Kingdom and only 4.6% of those from the United States.

The feeling has been expressed to us that carbohydrate chemistry had perhaps in the past been overemphasized in this country and that this field had become somewhat removed from the mainstream of organic research. We feel there is some truth in this view although the situation has begun to change in recent years. Furthermore it is clear that a number of Canadians have worked in this area with great distinction.

Papers in natural product and pharmaceutical chemistry make up 26% of the output of organic papers from Canadian sources, 27% of those from British sources and 19% of those from American sources. Although our relative involvement appears to be greater than the Americans' in these areas a related field of growing importance seems to be underdeveloped in Canada - the region of organic chemistry which impinges on biochemistry and biophysical chemistry.

One is struck on examining the above data by the closeness of the Canadian and British figures with regard to relative effort in the several areas of organic chemistry and how these differ substantially from the American pattern. It is difficult to decide whether the former should be attributed to chance or to immigration; we assume that it has not been a question of policy. The next section, which deals with sources of research work, shows that distinctly different patterns have developed in all three countries and these are clearly the result of political and economic decisions.

V. Research in University, Government and Industrial Laboratories

Universities contribute the bulk of the published work in organic chemistry in all three countries, Canada, The United Kingdom and the United States. The universities in the U.K. contribute the highest proportion, 85%, those in Canada 71% and those in the U.S. 67%. As will become clear from the subsequent discussion the U.K. figure is the highest because of the importance of government laboratory research in Canada and industrial research in the United States.

Government laboratories and other non-industrial research institutes contribute 5% of the publications in the U.K., 10% in the U.S., and 21% in Canada. A considerable number of these publications come from non-government research institutes in the U.S. but very few from such laboratories in Canada (almost 3/4 come from N.R.C. itself). Government laboratories in Canada thus contribute more than four times the proportion of research in organic

Statistical data on R. and D. operating expenditures were available from the C.I.C. general survey. Pertinent data is reproduced in Table 4.4.1. In the government questionnaires, Area 061 was entitled "Pharmaceuticals and Natural Products". In the industry and university questionnaires, however, this title was shortened to "Pharmaceuticals, etc." Natural products were not mentioned explicitly, but could be inferred from the fact that a sub-heading, "Pharmaceuticals" was included. Consequently, all natural product R. and D. may not have been assigned to 061. Table 4.4.1 illustrates how rapidly the amount spent on R. and D. increases as the definition of the field covered is widened. Much of the money spent on fundamental organic research will contribute to the sums given in the first row of Table 4.4.1, i.e. under the heading of General Organic and Physical Organic Chemistry. It is clear that very much larger amounts are being spent in the areas of applied organic research and development.

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TABLE 4.4.1

INTRAMURAL CHEMISTRY[1] R. and D. OPERATING

EXPENDITURES by PERFORMER and C.I.C. AREAS

(1966 or 1966-'67)

(Tables 11, 26 and 39 - Section 18)

(in thousands of dollars)

Performer / C.I.C. Areas	Gov't	Industry[2]	Universities (Institutes)	Totals
Gen. and Phys. Organic	1,283	2,594	2,919	6,796
Other "Organic"[3]	4,048	37,843	1,309	43,200
Biochemistry	2,711	1,787	6,129	10,627
Agric. and Food	2,478	4,746	893	8,117
Total	10,520	46,970	11,250	68,740
Total Chemistry[1]	24,424	90,803	20,837	136,064

1. Including chemical engineering and other related disciplines.

2. Including provincial research councils and foundations.

3. Including Fuels, Pharmaceuticals and Natural Products, Polymers, Pulp and Paper and Textiles.

chemistry that government laboratories in the U.K. do and two and one-half to three times the proportion that those in the U.S. do. The reasons for this state of affairs are well known. Until recently most Canadian universities were essentially undergraduate colleges with little involvement in graduate work. The industrial picture was even more bleak. The only way for a research climate with appropriate standards to be established within the country was for the government to establish its own laboratories. The history of N.R.C. is well known and its striking achievements in many fields of science is evidence of the success of this policy. With the changing times, in particular with the development of very strong science departments in many Canadian universities (and the hoped-for emergence of industrial research), the need for such direct government involvement has clearly decreased.

Industrial laboratories contributed 22.4% of all organic papers from U.S. sources in 1966. The corresponding figure for the U.K. is 9.3% and for Canada, 7.8%. The latter figure is very low compared to that of the U.S. but is little different from that for the U.K. where the level of industrial research has been a subject of concern for some time.

Although the output of organic research from Canadian industrial laboratories is low it is considerably better than it was a few years ago. Indeed, many organic chemists in universities and government laboratories have been surprised to learn that the level is as high as it is. This underlines the need for much greater interaction between organic chemistry in Canadian industry and those in the other two sectors. This will be dealt with again later in the report.

The Universities Despite the rapidly growing number of graduate schools in Canada we believe that the number of Ph.D.'s produced in organic chemistry does not yet meet the real needs of a technically advanced country.

Indeed, support of scientific research as a national policy can be justified on grounds that its conduct is an essential part of the education of young scientists as easily as on the grounds that it contributes to the accretion of knowledge.

The cost of the instruments for organic research is rising rapidly and it is folly to expect first class graduate education from those laboratories that lack access to such facilities. Those universities that can supply these instruments will find that they also need to provide the technicians to service them. An assistant professor spending much of his time tinkering with an n.m.r. spectrometer wastes the potential of both the man and the machine. The cost of such waste can be very high indeed. We believe that the situation with regard to technical help is much better in Canadian than in American universities although it is less satisfactory than in European universities.

Because of the high cost of research facilities it is not reasonable to expect that graduate work at the Ph.D. level be carried on at all universities in the country even in a major field such as organic chemistry. Even some of the larger institutions with active graduate programs could benefit from the kind of centralized instrumentation laboratory referred to later in the report.

Government Research Laboratories The vital contribution made by N.R.C. in establishing a first-class centre of research in this country has been referred to earlier. A number of other federal government laboratories also do research in organic chemistry. We think it fair to say that these laboratories have not matched the excellence of N.R.C. despite the presence of some able persons within them. There are various reasons for this, a different hiring system, less dynamic leadership, and a confusion between pure and applied research demands.

The provincial government laboratories and research institutes make a very small contribution to research in organic chemistry. Their role, with a few exceptions, has been confined to applied problems of regional interest.

Industry The advantages to a large chemical company of having a fundamental

research group are well known. Its members can often give invaluable advice to their colleagues in applied research and development and they help to provide a stimulating atmosphere in the laboratories. Furthermore, those recruited to do fundamental research often become, in time, deeply interested in applied problems and this provides a source of highly skilled manpower for the company's wider requirements. Virtually all of those who submitted a brief to this committee commented upon the low level of research being done in the Canadian chemical industry. A few companies such as Dow Chemical of Canada have fundamental research groups which have done important basic research in organic chemistry. The relative paucity of such work is attributed by most Canadian chemists to extensive foreign ownership and this is undoubtedly a factor of major importance. It should be pointed out, however, that in at least two instances (Ayerst and Dunlop), the North American centers of research of foreign-owned companies are located in Canada.

The generous research incentives made available to industry by the federal government undoubtedly are having an effect although most persons we consulted felt that industry was not taking sufficient advantage of them.

The need for much greater interaction between chemists working in industry and those in universities and government laboratories was referred to earlier in the report. Those chemists working in industry may be interested to know that most university chemists who wrote to us deplored the lack of interaction and many offered suggestions to remedy it. The most frequent suggestions, made by both those in universities and industry, were

(a) that university scientists be invited to visit industrial laboratories and present seminars in their research specialities,

(b) that more industrial consulting work be undertaken by chemists in universities, (this might be done on a low-fee, short-term basis),

(c) that informal conferences, similar to the Gordon conferences and probably initiated by the C.I.C., be undertaken to improve liaison between industry, university and government scientists.

For any of the above suggestions to be really effective the number of chemists doing research in industry must be increased considerably.

Joint research projects between university and industry have also been suggested but any such arrangement should not violate the accepted principle that, except in extraordinary circumstances, university enquiry be free and open and the results immediately publishable.

The most frequent complaint made by research directors in industry about the universities was to the effect that graduate students become deeply involved in what seem to be obscure and esoteric research topics and then are either reluctant or unable to tackle the problems of industry. At the same time most industry spokesmen stress that a graduate student should not be trained for a particular kind of industrial job but should learn to do research. This, of course, is what Ph.D. work is all about. One learns how research is done by tackling an unsolved problem, preferably with the advice of an interested senior colleague. Furthermore, the research problem for a Ph.D. student in organic chemistry, as in any branch of science, must be at the expanding frontier of knowledge in the field. The complaint about university research, then, would seem to derive to some extent from the attitude of young Ph.D.'s toward industrial work rather than from deficiencies in their education. A change in this attitude will probably come about when research, both pure and applied, plays a larger role in Canadian industry and when university and industrial chemists draw closer together. These two developments, indeed, are interrelated.

Standards of Research Research that appears in most chemical journals (certainly all those surveyed in Section III) must meet standards set by knowledgeable and competent editors and referees. Judging the degree of distinction of such work is more difficult, however, and in the long run comes down to gauging the general reputation that the authors establish in the international world of science. In the opinion of most of those who wrote to us all of the large universities in Canada have organic groups in

which excellent work is being done. Of the somewhat smaller institutions the University of New Brunswick, the University of Western Ontario, and McMaster University were singled out for particular praise.

Invitations to address international meetings or to present seminars, authorship of monographs, citations in books or reviews, etc., all give some idea of the impact that a scientist has had upon his field. On these scores Canadian organic chemists have done well although it must be admitted that the number in the very first rank is smaller than it might be. We clearly have assembled an able group of organic (and other) chemists in this country; it is important that this momentum be maintained and that the best be given the massive research support that will enable them to bring the highest distinctions to themselves and the country.

VI. Support for Research

Outside support for research in the universities and in the chemical industry comes largely from the federal government. In the case of universities this takes the form of grants to individuals or groups and grants for major pieces of equipment. The next two sections deal with these aspects of support with reference to research in organic chemistry.

Instrumentation The dramatic effect instrumental analysis has had upon organic chemistry was referred to in the introduction to this report. No less dramatic has been the increasing cost of providing facilities and it is clear that many organizations will not be able to meet these costs themselves. These would benefit from the establishment of centralized laboratories equipped to do high-resolution n.m.r. spectroscopy using super-conducting magnets, high-resolution spectrometry, X-ray crystallography, Raman spectroscopy, elemental microanalyses, rotatory dispersion and circular dichroism. Most of the chemistry departments in large universities and other major laboratories will

need to be provided with many of these facilities themselves, together with efficient computer facilities, but many of the smaller organizations will find the costs too high, particularly since the trend toward increasingly sophisticated instrumentation shows no signs of abating. If these laboratories are to do significant work in organic chemistry they must have access to such services when the needs arise.

Such centralized service laboratories might be set up under either public or private auspices. In the latter case government support of one kind or another might be required although a private company in Montreal has recently begun the sort of service we envisage in the field of mass spectrometry. We believe that an examination of the feasibility of creating such facilities should be made.

Research Grants The principal source of research funds for organic chemistry in this country is N.R.C. Together with most chemists we feel that the level of support is rather modest but, with the exception noted below, we approve of the way in which these funds are dispersed. Essentially, N.R.C. bases its support on the scientific reputation of the principal investigator rather than on the apparent merits of a detailed research proposal. The difficulties in planning in advance the course of basic research is well known and the latter system of awarding research funds encourages the practice of various forms of grantsmanship. The present N.R.C. system minimizes paperwork and makes applying for an annual grant a relatively painless process. Most of us have heard the lamentations of our American colleagues about the time-consuming paperwork they are required to do when applying for grants and while administering them. If the level of research support is lower in this country than in the United States so is the level of paperwork.

An aspect of the present grant system that causes us some concern is that

it tends to overlook promise and responds rather slowly to demonstrated performance. This results in the level of support of many able young scientists being low; these persons would be more productive if this level were raised substantially. It is clear, however, that if this were done the constant reassessment of performance that is so essential to a grant system such as N.R.C.'s would require that the level of support be cut back in some cases after a few years.

The low level of support of university research in organic chemistry by Canadian foundations and the Canadian chemical industry is a matter of concern to the committee. At the moment there are few foundations able to offer such support but we feel that the chemical industry could do much more than it does. Unrestricted grants made by chemical companies to university chemistry departments or to individual research workers would play an important role in encouraging research and in promoting liaison between scientists in industry and the universities.

VII. Summary and Recommendations

Organic chemistry is well developed in Canada and the work done, particularly in the universities and at N.R.C., is of a high standard. The amount of organic research done in the Canadian chemical industry is low although some improvement has occurred recently. A considerably larger proportion of organic research is done in government laboratories in Canada than in government laboratories in the United Kingdom or the United States.

The distribution of organic research activity according to subject area is similar to that of the United Kingdom but rather different from that of the United States; there is less emphasis on natural products and, particularly, carbohydrates in the United States than in this country.

Recent advances in instrumentation have had a profound effect on research in organic chemistry and this trend is expected to continue.

We recommend that liaison between organic chemists in industry and those in universities be improved by means of seminars, consulting work, and informal conferences.

We recommend that the chemical industry be encouraged to take greater advantage of N.R.C.'s research assistance program and the federal government's research incentives and that subsidiaries of foreign companies be encouraged to do more research and development work in Canada.

We recommend that support of university research continue to be based mainly on the scientific reputation of the principal investigator rather than on a project proposal basis but that greater efforts be made to recognize and reward both exceptional performance and exceptional promise.

We recommend that the feasibility of setting up instrumentation centres throughout the country be investigated.