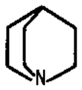
# PROFILE OF PROFESSOR H. C. BROWN

This special issue of *Heterocycles* is dedicated to one of the most prolific and influential organic chemists of all time, Professor Herbert Charles Brown of Purdue University, on the occasion of his seventieth birthday. By winning the Nobel Prize for Chemistry in 1979, H. C. Brown became one of less than thirty Nobel Prize winners in the field of organic chemistry and only the second American organic chemist (the first being R. B. Woodward) to receive this most coveted award.

Some of the most significant contributions by H. C. Brown may perhaps be found outside the area of heterocyclic chemistry, and the majority of his over 800 publications do not pertain to heterocyclic chemistry. Nonetheless, a quick glance through his nearly 100-page-long list of publications reveals that well over 100 papers do deal with various aspects of heterocyclic chemistry. Moreover, these contributions have had far reaching influence on many subsequent investigations by others in this and other related areas. The dedication of this special issue of *Heterocycles* is therefore a fitting tribute to Professor Brown.

Although a detailed presentation of Brown's heterocyclic chemistry is not intended here, it might be of interest briefly to touch on the highlights.

As is well recognized, one of Brown's major contributions of fundamental significance deals with steric effects in organic chemistry. In a series of his early publications, Brown made elegant use of quinuclidine (1) and pyridine derivatives, e.g., 2,6-di-*t*-butylpyridine (2), to develop the so-called F-, B-, I-strain theory.



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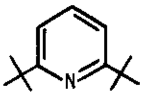

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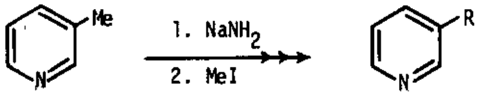
Most importantly, his contribution in this area was instrumental in helping organic chemists recognize the significance of steric effects in organic chemistry at the time the electronic theory of Ingold and Hughes was used to rationalize most, if not all, organic chemical phenomena. A vivid discussion of this subject is presented by Brown himself in Chapters V-VIII of his semiautobiographical book entitled "Boranes in Organic Chemistry." It is interesting to note that, while pursuing physical organic problems, Brown also managed to develop new and significant synthetic procedures. For example, at the time metallation of 3-picoline (3) was considered impossible, he successfully achieved it and prepared a series of 3-alkylpyridines (4).



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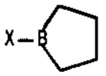
4 (R = Et, *i*-Pr, *t*-Bu)

Another major contribution by H. C. Brown to the field of heterocyclic chemistry is his more recent study of cyclic hydroboration as well as of the structure, reactions, and synthetic applications of heterocyclic organoboranes. Although a large number of boron-containing heterocycles had been synthesized before Brown started his investigation of boraheterocycles, he is a pioneer of the field in the truest sense. His study in this area has been reviewed briefly in an earlier issue of *Heterocycles* and more comprehensively in *Tetrahedron* in 1978.

Brown has not only prepared a number of boraheterocycles for the first time, but also developed practical satisfactory procedures for preparing boraheterocycles which are synthetically useful, such as 5 - 10.



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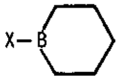

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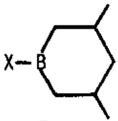

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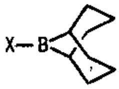

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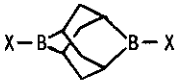

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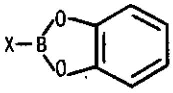

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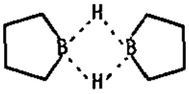
X = H, Cl, carbon group, alkoxy, etc.

As in all other studies, Brown's approach to his investigation of boraheterocycles has been unusually systematic and logical. Of course, any scientific study should be carried out in a logical manner, but, in reality, the literature is sprinkled with erroneous or premature conclusions based on untenable assumptions and intuitive feelings. Brown has been almost religious in resisting unsound conclusions.

A case in point is his study of the cyclic hydroboration of the simplest diene, 1,3-butadiene. Prior to his systematic investigation, several workers had published a number of papers on the subject, and this particular area of boron chemistry appeared to have been adequately investigated. Noting a few inconsistent results reported by others, however, he embarked on his own systematic investigation, which has revealed several errors and oversimplifications as well as numerous new facets of this fascinating reaction. For example, it had been noted that the hydroboration of butadiene with borane in the 1:1 ratio produces a chemically inert material to which the bisborolane (11) structure was assigned. To Brown, however, the assigned structure, i.e., 11, and the fact that the 1:1 compound does not react with either olefins or water at room temperature, were mutually incompatible. To him, "chemistry just has to make sense." He therefore proposed the other possible bridged dimer structure (12) as the one that can nicely account for the observed results and has since firmly established that the Brown structure 12 is indeed the correct one.



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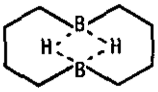

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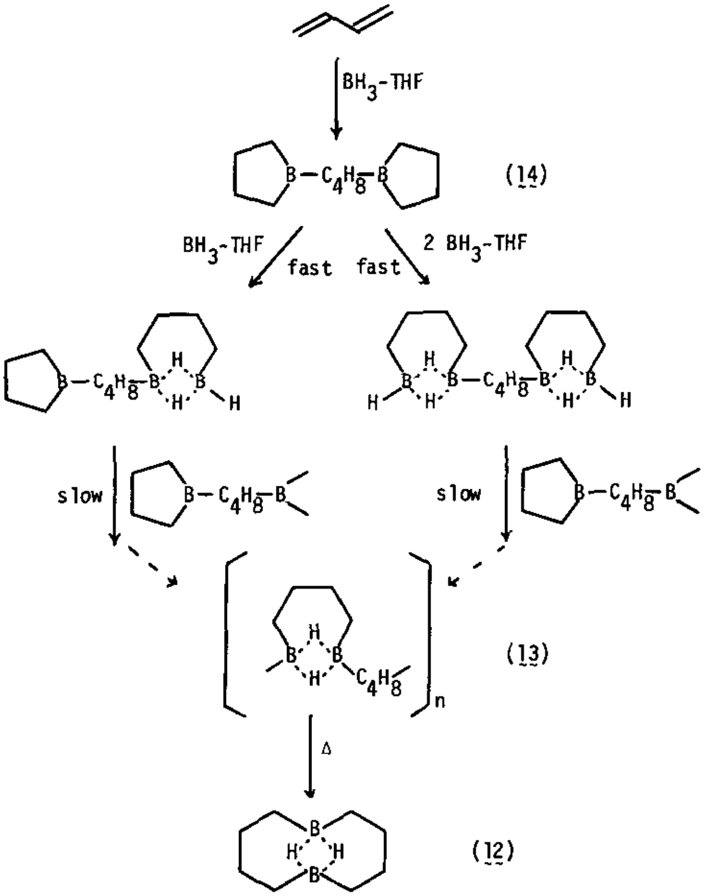
Furthermore, he noted that the initially formed 1:1 product is quite reactive and polymeric in nature. He has subsequently unraveled the mechanistic path for this highly intriguing reaction, as shown in Scheme I.

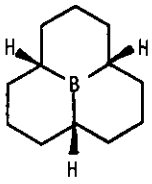
Scheme I



*The polymer 13 cyclizes to form 12 on heating. Nowhere in the entire scheme does one find 11*, as claimed in the literature, even though it may have been formed as a transitory precursor to 14. The structures of the well-defined products in Scheme I have since been confirmed by other workers. Essentially all puzzles have disappeared, and the entire chemistry now makes sense. With his "patented" tenacity, Brown, in fact, pursued this problem for almost a decade, albeit intermittently.

The chemistry described above may not be an example of some of his more important contributions in this area; however, it is a superb example, illustrating Brown's logical and scientifically uncompromising mind, his tenacity, and his skill to solve chemical "jigsaw puzzles." As he himself admits, it is with this sort of approach that he "accidentally" discovered some of his most significant contributions, such as hydroboration.

The hydroboration of 1,5,9-cyclododecatriene was reported to give 15 as the kinetic product and 16 as the thermodynamic product. In light of the relative stability of isomeric perhydrophenalenes, the above assignments again did not make sense. Indeed, Brown has shown conclusively that the original assignments should be reversed.



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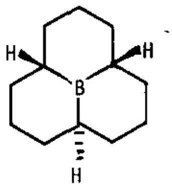

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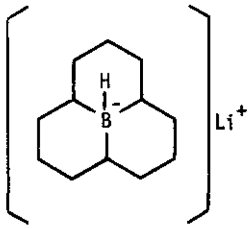

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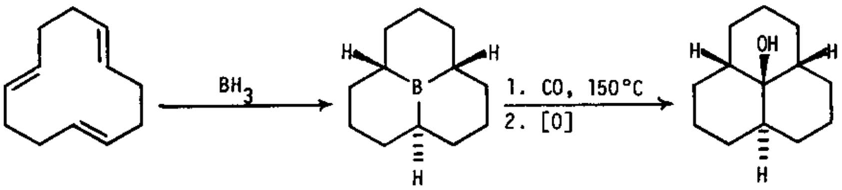
It should be emphasized here, however, that, although making accurate structural assignments is an important element, rarely is it the ultimate goal of his research. Throughout his career *Brown has been deeply committed to making his chemistry* useful and practical to other chemists and beneficial to mankind. For example, his scientific curiosity prompted him to prepare 17 as a highly selective reducing agent. From that point on, however, his pragmatic approach took over and led to his discovery and development of a series of very promising trialkylborohydrides, such as Super Hydride. Similarly, in a highly imaginative manner, 15 and 16 were subjected to the action of carbon monoxide, which led to the development of the "stitching-with-boron and riveting-with-carbon" procedure.

From a pragmatic viewpoint, 9-borabicyclo[3.3.1]nonane (9-BBN) (8a) is probably the most important and extensively studied boraheterocycle that Brown has developed to date. Here again, its synthesis by an obscure method was known, but it was Brown who came up with its most convenient, logical, and even obvious synthesis.



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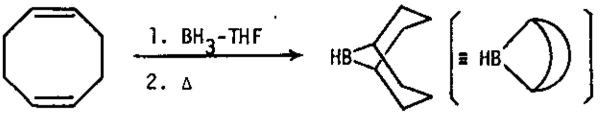

Far more important, however, is a series of his subsequent studies of the reactions of 9-BBN, primarily directed toward the development of synthetically useful procedures.

It is true that nearly all of his boraheterocycles are simple molecules. Individually, their synthesis, structural elucidation, reactions, or synthetic applications may not represent an epoch-making accomplishment, but it is the entire collection of carefully chosen and planned, meticulously executed, and judiciously applied pieces of work that gives an undeniably distinguishing feature to his contributions in this and other areas. The trademark of Brown's chemistry is simplicity and significance. His research might well be compared to successful exploration and a subsequent cultivation of a new and fertile continent hospitable to millions of people. It contrasts itself to research comparable to conquering high and remote mountains – interesting and perhaps inspiring, but of questionable significance to the majority of people.

Today, H. C. Brown no longer belongs to just Purdue University or to its Chemistry Department. As a Nobel Laureate he now belongs to the entire world. A large number of lecture engagements, no doubt, severely interferes with his research activity. Rather surprisingly, however, neither this nor his recent "retirement" has successfully slowed this truly rare individual. In 1980, the year in which he delivered over 50 lectures as a Nobel Laureate, he still managed to publish some 30 papers. He half jokingly attributes this to pressure from his wife, Sarah. According to her, "I did not give up chemistry myself to have you (HCB) become a Nobel playboy." Perhaps, even a man of extraordinary self-discipline can benefit from occasional wifely reminders.

As far as I can tell, both Professor and Mrs. Brown are in excellent health. I sincerely wish them both many more years of happy and fruitful life.

Eiichi Negishi

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