Obituary In Memoriam André S. Dreiding

June 22, 1919 - December 24, 2013

In Memoriam André S. Dreiding

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Abstract: In his talk at the 49th Bürgenstock Conference on Stereochemistry the author paid tribute to André S. Dreiding, the founder of this event.

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André S. Dreiding June 22, 1919 – December 24, 2013

André S. Dreiding, one of the founding fathers of the Bürgenstock Conference, passed away last year at the age of 94. The organizers of this year's event decided to dedicate a presentation to this eminent Swiss scientist, including his role in the foundation of the Bürgenstock Conference.

As it happens I am one of the few remaining academics who knew André and his friends quite well and therefore I have been invited to recall some anecdotes of the last 60 years.

André S. Dreiding was born in Switzerland into a family of east-European descent. His father Boris Dreiding was a Rumanian pharmacist who left his country for Switzerland in 1914 with one precious asset in his pocket: a recipe to make a foot cream. In 1919 he started a perfume business at Bahnhofstrasse in Zurich that, even after more than 90 years, is still family-owned and is run by one of his granddaughters.

As you can see from André's birthday he was about 20 when events that would lead to the Second World War began to unfold. So it was decided that the US would be safer and he moved to Columbia University for his undergraduate education in chemistry. After a brief period at Roche in New Jersey he decided to study for a PhD with Prof. W. E. Bachmann at Ann Arbor Michigan. Probably André's choice for Bachmann wasn't just the chemistry project proposed for his PhD but also the fact that Bachmann had close ties to Switzerland. Bachmann's family came from Switzerland and he had worked in Prof. Karrer's laboratory for one year working on the structure elucidation of lycopene.

André's thesis was concerned with the structure elucidation and synthesis of steroids and related decaline analogues that drew his interest to stereochemistry, absolute configuration and the conformation of molecules.^[1]

After completion of his thesis in 1947 and a brief postdoc he became Assistant Professor at Wayne State University in 1949. In 1954 he returned to Switzerland, joining the Department of Chemistry of the University of Zurich where he became Professor of Chemistry and stayed there until his retirement in 1987.

When Dreiding arrived in Zurich the Cahn-Ingold-Prelog (CIP) system had been already invented defining static stereochemistry. However, he was convinced of the need to visualize dynamic stereochemistry and the structure of molecules in space in order to understand the regiochemistry of reactions and provide insight in how molecules might be synthesized. This led to the invention of his molecular models, which was published in 1959.[2] This paper (Fig. 1) describes all the details to

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145. Einfache Molekularmodelle von Andre S. Dreiding Herrn Prof. Dr. PAUL KARRER zum 70. Geburtstag gewidmet

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Das Verständnis der chemischen und physikalischen Eigenschaften organischer Verbindungen ist in letzter Zeit durch sorgfältige Analysen der stereochemischen Faktoren stark gefördert worden?). Auf Grund von konventionellen Formeln ist es oft nicht möglich, sich ein Bild der räumlichen Verhältnisse in der Molekel, insbesondere der internen Rotationen, zu machen. Der Chemiker greift dann zum Molekularmodell, welches somit ein wichtiges Werkzeug der organischen Chemie geworden ist. Es soll hier ein neues Molckularmodell beschrieben werden, bei dessen Konstruk-

tion die Erzielung folgender Eigenschaften wegleitend war:

- Genauigkeit der Kernabstände und Valenzwinkel, womöglich innerhalb der Grenzen der ex-perimentellen Unsicherheit.
 Freie Drehbarkeit der Einfachbindungen ohne Abnützung oder Auseinanderfallen der Ver-
- bindungsstücke. Leichte Übersicht über die geometrischen Verhältnisse in verschiedenen Konformationen. Annähernd punktförmige Atomkerne, so dass Kernabstände nicht gebundener Atome leicht
- Annahernd punktförmige Atomkerde, so dass Kernassande nicht gebundener Atome incht gemessen werden können.
 Das Aufbauen und Auseinandernehmen soll mit wenigen und einfachen Handgriffen geschehen.
 Stabilität der aufgebauten Strukturen.
 Handliche Grösse.
 Einfachheit der Konstruktion.

Konstruktionsweise. Als Baumaterial für die Modelle dienen ausschliesslich Röhrchen und darin hineinpassende Stäbchen aus rostfreiem Stahl. Von der Molekel werden nur die zentralen Achsen der o-Bindungen gezeigt, und zwar übernehmen die Stäbchen bzw. Röhrchen diese Rolle. Die Atomkerne befinden sich immer am Ende oder am Treffpunkt von Stäbchen bzw. Röhrchen. Der Kern des einwertigen Atoms liegt am Ende, derjenige eines multivalenten Atoms am Treffpunkt einer der Valenz entsprechenden Anzahl von Stäbchen bzw. Röhrchen. Auf diese Weise sind die Kerne so klein, dass ihre Abstände gemessen werden können. Wie bei manchen anderen Modellen wird auf eine räumliche Darstellung der Elektronenwolken der Über-sichtlichkeit wegen verzichtet. Dadurch wird zwar die Raum-erfüllende Natur der Atome nicht wiedergegeben; dies ist jedoch kein grosser Nachteil, weil erstens die Elektronenwolken weich und ihre Grenzen undefiniert sind, und zweitens sterische Kräfte auch anziehender Natur sein können.

Bei allen bisher beschriebenen Modellen werden die Atome durch individuelle Einheiten dargestellt*) und mittels Bindeglieder zusammengesetzt. Eine besonders einfache Konstruktion des Kohlenstoffs wurde vor einiger Zeit von H. BRET-

Fig. 1. Copy of the publication reporting the construction of molecular models.^[2]

produce tetrahedral C-atoms and functional groups from simple metal tubes and fitting rods so that rotation about single bonds is possible. Somewhat like LEGO, these parts can be assembled to form large molecules that display the correct atomic distances, dihedral angles and corresponding flexibility.

The original value of this invention can be judged best if one recalls the situation of chemical analysis/structure elucidation in the late 50s and early 60s. As most of you in the audience were not born or still in Kindergarten it may be useful to remember how difficult it was to arrive at a conclusion on the absolute stereochemistry of a rather complex molecule. At this time the available techniques to characterize a compound were rather limited as compared with today's sophisticated methods.

Spectroscopy was limited to UV and IR and elemental analysis, melting points, and optical rotation were the most important molecular constants. Most laboratories had no MS- or NMR-machine available before 1960 and if they did they would have been equipped with a rather unstable 60 MHz iron magnet. Even in the late 60s the first 100 MHz machines looked like Captain Nemo's console and required two experts to handle it (Fig. 2).

Hence structure elucidation was mainly done by chemical transformation into compounds of known constitution and configuration.



Fig. 2. A 100 MHz NMR machine in the late 60s.

As alkaloid research was a rather popular area at this time in Zurich I cite one example concerning the absolute configuration of strychnine (Fig. 3).^[3]

Strychnine was hydrogenated over Pd and dihydrostrychnine degraded to strychindole. The latter was then synthesized from

 α, α' -diethyl-succinic acid of which the absolute configuration was known. This sequence confirmed the absolute configuration of C20 of dihydrostrychnine. Since the relative configuration of strychnine was known from total synthesis^[4] the absolute configuration of strychnine was finally defined. Surprisingly to the experimentalists the hydrogenation of strychnine gave only a single product. However, if they would have used the 'Dreiding models' they would have immediately understood and even predicted the result. This is because the heterogenous catalyst can only deliver hydrogen from the *si*-face of the double bond – the other face is shielded by the five-membered ring containing the nitrogen (Fig. 4).



Fig. 3. Determination of the absolute configuration of strychnine.^[3]



Fig. 4. A 'Dreiding model' of strychnine – the red arrow shows $\rm H_{2}$ addition to the C20 double bond.

The success of his molecular models – produced by Büchi AG – and the increasing awareness of the community concerning stereochemical problems led Dreiding to initiate the first Bürgenstock Conference on Stereochemistry in 1965. He believed that stereochemistry was an ideal platform embracing all disciplines of chemistry and he convinced the European Commission and industry to offer financial support and his colleagues from ETH-Zurich, namely Arigoni, Dunitz, Eschenmoser, and Prelog, to participate in the intellectual endeavour. And against all odds this conference has been a success ever since.

During his time in Zurich Dreiding's own research became more and more focused on the synthesis of stereochemically challenging molecules such as the triaziridines^[5] to investigate pyramidal inversion at nitrogen and the preparation of complex sesquiterpenes through α -alkynone cyclizations (Fig. 5). The latter method was developed by Dreiding's student Martin Karpf as a very efficient thermal reaction involving the formation of a carbene that inserts into the nearest C–H bond – as an example the synthetic strategy leading to capnellene is shown.^[6]



Fig. 5. Triaziridines and capnellene – two selected synthetic targets of the Dreiding group.

Besides his synthetic activities Dreiding always loved calculations and in this context his group developed, for example, algorithms to define symmetry groups of mobile molecules.^[7]

I became close to Dreiding by accident – literally – because Hans Schmid, who supported me, died unexpectedly during the course of my habilitation. Subsequently André offered me an



Fig. 6. Norma and André at a birthday party.

attachment to his group without any duties other than organizing seminars for his people. Hence I could continue my own research but could also expand my knowledge as a 'supporting actor' of his group.

As André loved social activities spiced with chemistry I came to know many of his friends and contemporaries and also his wife Norma (Fig. 6), who had been with him for many years tying him down to earth from his three-dimensional phantasies.

Besides chemistry André loved his family, a good wine, his Cuban cigars and Italian cars. I believe everybody who knew him will remember him as a joyful, generous person and I hope everyone here is grateful to profit from his Bürgenstock legacy.

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