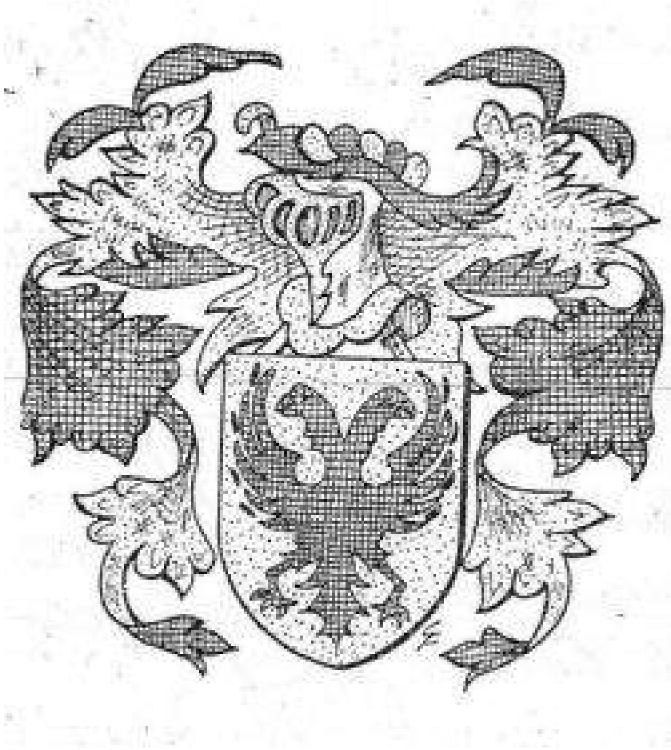
Johannes Martin Bijvoet
1892-1980



Artemisia Vulgaris

A.L.Spek
Bijvoet Center for Biomolecular Research
Utrecht University.The Netherlands

Zurich, june 21, 2012

Bijvoet, a Scientist and Teacher

- Bijvoet retired 50 years ago, in 1962, at age 70, that was 50 years after the Laue et al. diffraction experiment.
- He was a member of the pioneer generation of X-ray crystallography, both as a teacher and as a scientist,
- He was one of those giants of the field with an impressive scientific impact, certainly worth a Nobel price.
- He received many distinctions including a honorary doctorate from ETH Zurich (1970).
- He was proposed several times as a Nobel prize candidate. However that unfortunately never materialized
- Interesting in that context is the following letter, from the WEB, of Linus Pauling to Sir W. Laurence Bragg:

From a letter by L.Pauling to W.L.Bragg (Dec 15, 1959)

…

With respect to X-ray diffraction and chemistry, I have a proposal to make to you, and I should be glad to have your opinion about it. I should like to nominate Dorothy Hodgkin and J.M. Bijvoet for a Nobel Prize in chemistry, to be devided between them. The award would be for their use of X-ray diffraction in the solution of chemical problems, the determination of the structure of penicillin and cobalamine, in the case of Dorothy Hodgkin, and the determination of the correct absolute configuration of asymmetric molecules, in the case of Bijvoet. Would you support this nomination ?

...

Note: Dorothy Hodgkin received the Nobel prize in 1964

Note: Cobalamine = Vitamine B12

Bijvoet's Crystallographic Footprint

– Bijvoet was the father of most crystallographic groups in the Netherlands.
– Many of his former students became professors in the Netherlands, Belgium and elsewhere.
– He was the second President of the IUCr after Bragg.
– He was the main author of an early (1938,1948) textbook on X-ray crystallography – theory, methods and applications (translated into German and English)
– Initiated methods for (absolute) structure determination of non-centrosymmetric structures
– Showed that the Emil Fischer absolute configuration convention by chance turned out to be the correct choise out of two absolute structure options.
– The concept: Bijvoet pairs [I(H) .ne. I(-H)]

Education

- Bijvoet was born in 1892 in Amsterdam from non-academic parents.
- His father had a dye factory.
- He attended primary school from 1897-1903.
- Attended secondary school (HBS) 1903-1908 (HBS = Gymnasium minus Greek and Latin)
- Studied Greek & Latin, required at that time to enter a study at a university 1908-1910.
- Chemistry at the Univ. of Amsterdam 1910-1919
- Interrupted by military service from 1914-1918. Spare time (Holland neutral) was used to study Thermodynamics and Statistical Mechanics.

Early Scientific Career

- 1919-1928 assistent in the inorganic chemistry department of Prof. A. Smits (U of A) (photo next)
- Early inspired by the structural work of the Braggs
- His supervisor, A. Smits, was one of the disbelievers of the NaCl model (no discernable molecules).The visiting Bragg met with a lot of disbelieve of the Amsterdam chemists. In response, Bijvoet was allowed to start his own X-ray investigations in this new field.
- Early experiments ($NaClO4$ & LiH) in Utrecht at the Veterinary College (where van 't Hoff came up in 1870 with his tetrahedral carbon model) with a funding grand of the ministry of agriculture for carbon! Research.
- PhD thesis in 1923 on the structure of Li & LiH.
- Short but inspiring 'postdoc' stay in Manchester with Sir Laurence Bragg.

A.Smits J.M.Bijvoet

Lecturer and Professor

- In 1929 Bijvoet was appointed as a lecturer in the geology department to teach macroscopic crystallography, mineralogy and thermodynamics.
- The following years were probably not his happiest time with a lot of struggles with the geology department for space to be able to do experimental work.
- Research mainly involved the structure determination of dihalogenides supported by the physicists.
- In 1939 he accepted, not without nostalgia for his Amsterdam, a professorship in general and inorganic chemistry in Utrecht where he stayed until his retirement in 1962 at age 70.
- His extended knowledge was collected (1938,1948) in a, also now, very informative textbook (with co-authors)

RÖNTGENANALYSE VAN KRISTALLEN

DOOR

Prof. Dr. J. M. BIJVOET Dr. N. H. KOLKMEIJER
Van 't Hoff-Laboratorium der Rijks-Universiteit te Utrecht

Dr. C. H. MacGILLAVRY
Laboratorium voor Algemene Chemie, Universiteit van Amsterdam

2e DRUK

D. B. CENTEN'S UITGEVERS-MAATSCHAPPIJ N.V.
AMSTERDAM (C.)
1948

kristalrooster trillingen met grote golflengte in het algemeen groter amplitudo hebben dan die met kleine. In het reciproke rooster liggen punten, die lange storingsgolven representeren dichter om het ongestoorde roosterpunt. Om een reciprook roosterpunt neemt dus het gewicht af met toenemende afstand van het roosterpunt. Opmeting dier hoven, dus der kristalverstrooiing bij straalrichtingen iets afwijkend van die der optimum reflectie, geeft gegevens voor het berekenen der amplitudines dier warmtegolven in afhankelijkheid van hun voorplantingsrichting in het kristal. Dit opent de mogelijkheid elastische constanten uit diffractiemetingen te bepalen, daar immers de amplitudines der warmtegolven met de elastische constanten samenhangen.

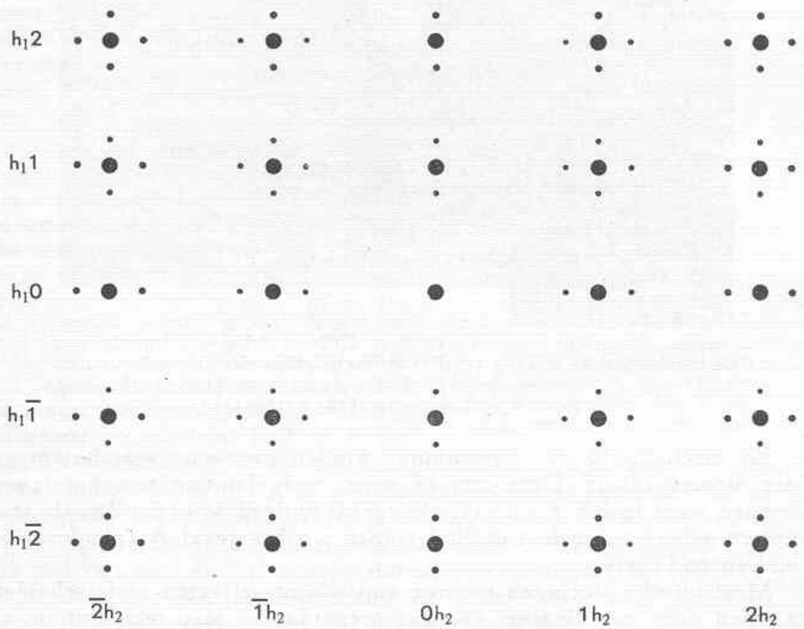
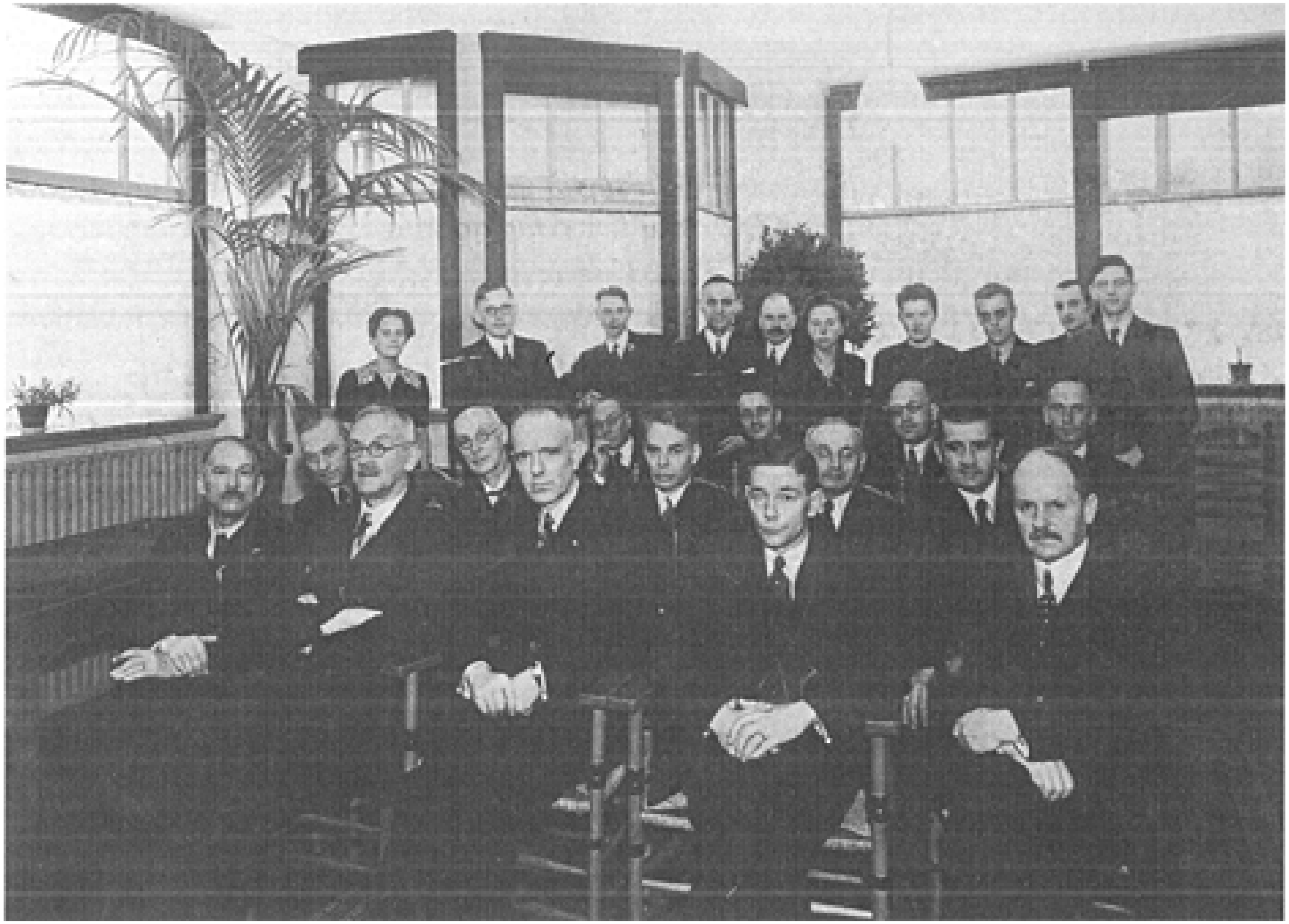


Fig. A. 25. Fourier-afbeelding van een twee-dimensionaal rooster, gestoord door twee longitudinale modulerende golven, één in de x, en één in de y-richting; het gewicht der satellieten is evenredig met h_1, resp. h_2.

Fig. 26 toont het diffractie-effect van deze door de warmtebeweging veroorzaakte „hoven". Het stilstaande kristal werd belicht met straling uit een buis met koper anode. De scherpe stippen zijn de gewone reflecties van een Laue-diagram, dus uit de witte straling geselecteerd. Deze reflecties ziet men niet extra verbreed, daar het gewicht in de hof veel geringer is dan die van het reciproke roosterpunt zelf. Loopt nu echter de uitbreidingsbol der karakteristieke straling dicht langs een reciprook roosterpunt, dus door de hof der warmtegolven, dan



Bijvoet

Kogl

Utrecht, 1943

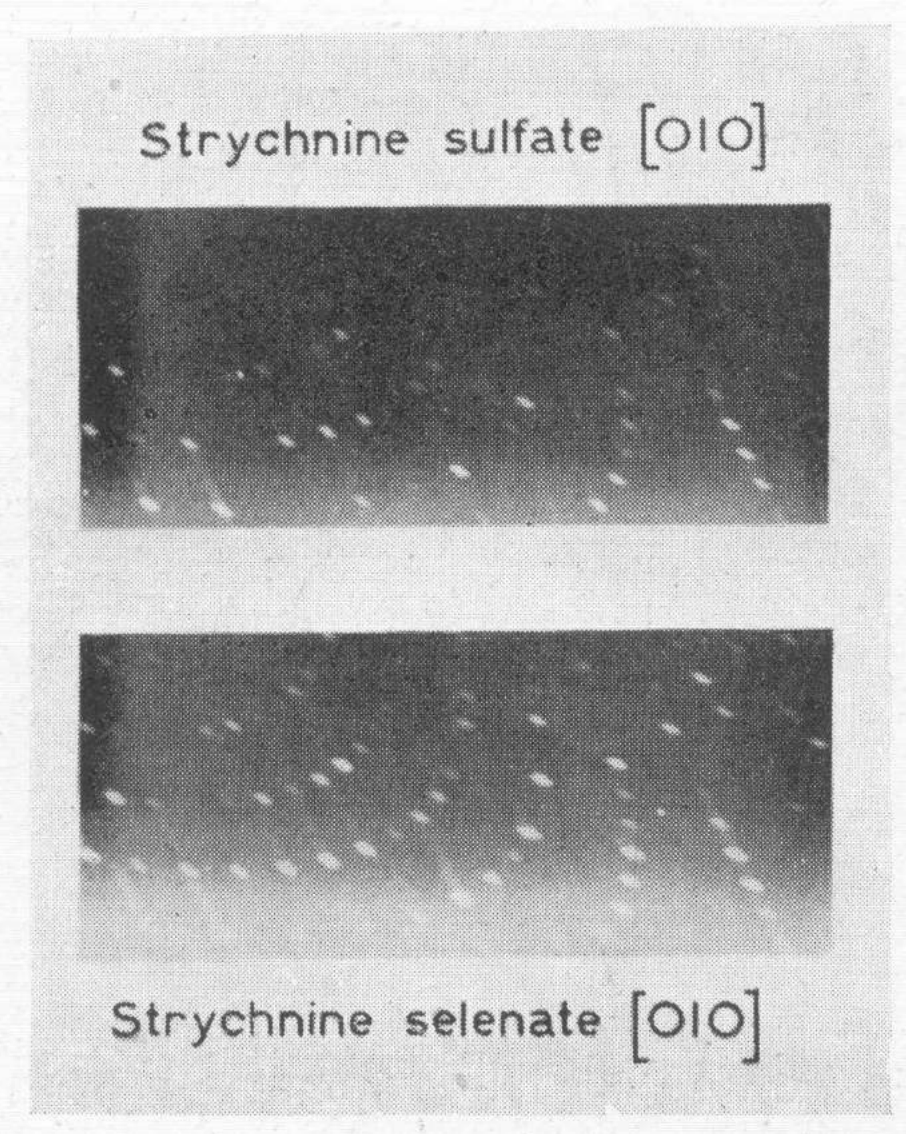
Research in Utrecht

- Research interest shifted from inorganic compounds to the development of methods to determine the structures of organic molecules and in particular of natural products, many of which were of interest to or suggested by his colleague in (bio) organic chemistry Prof Kogl (Working on the theory of cancer-abs conf.)
- Shift from trial&error to Fourier and Patterson methods to solve the Phase Problem.
- Major pioneering contributions were:
- The extension of the isomorphous replacement method to solve non-centrosymmetric structures
- Structure determination using Bijvoet pair differences
- Absolute structure determination.

Isomorphous Replacement Method

- Early use of isomorphous replacement (Centro):
  - Cork, 1927
  - Lipson & Beevers, 1935

- Extension to noncentrosymmetric structures
  - 1949 – Strychnine sulphate and selenate
  - Bijvoet, Bokhoven & Schoone, 1949
  - Formulae for single and multiple isomorphous replacement phases



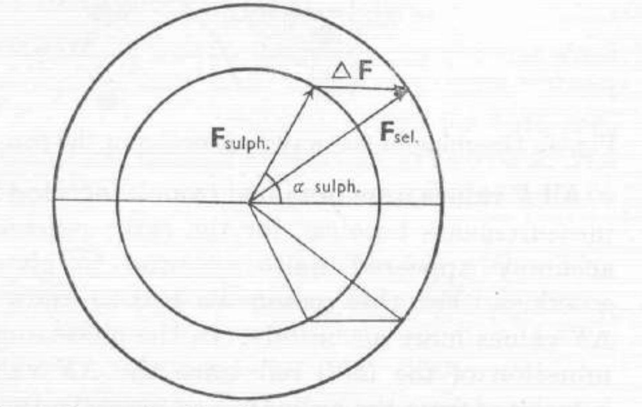
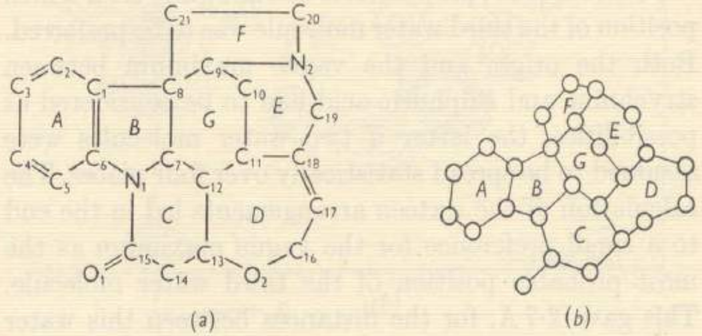


Fig. 2. Phase determination in non-centro-symmetrical case by the isomorphous substitution method.

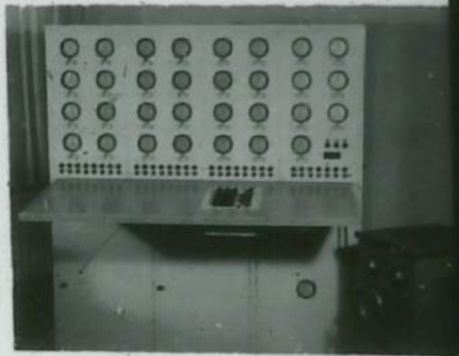


(a) (b)

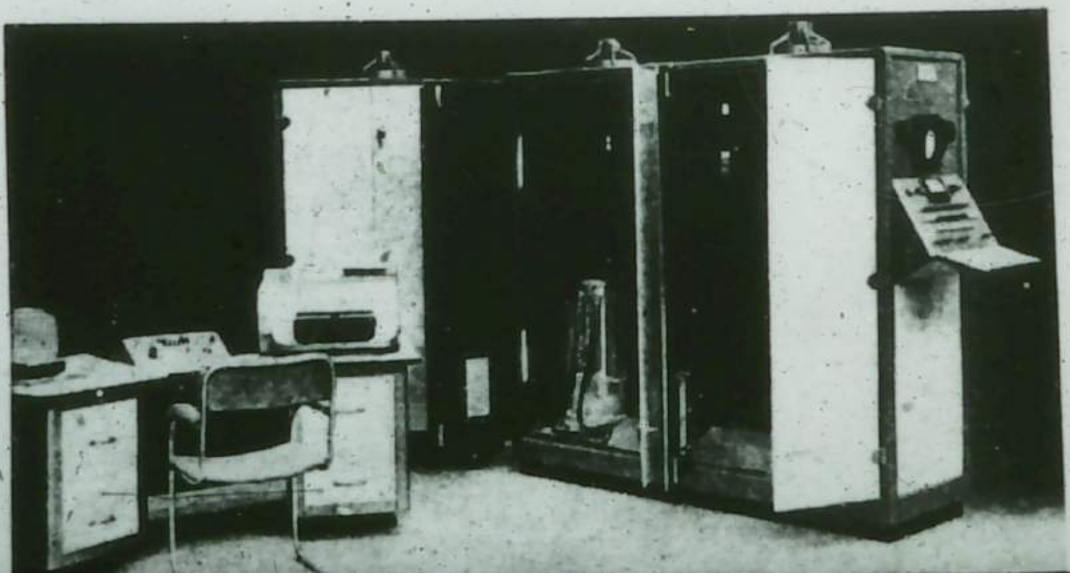
Fig. 3. Structure formulae of strychnine: (a) according to chemical custom, (b) according to a model of the molecule.

C. Bokhoven, J.C. Schoone & J.M. Bijvoet, Acta Cryst. (1951), 4, 275

Hand calculations of Fourier maps took many man-months

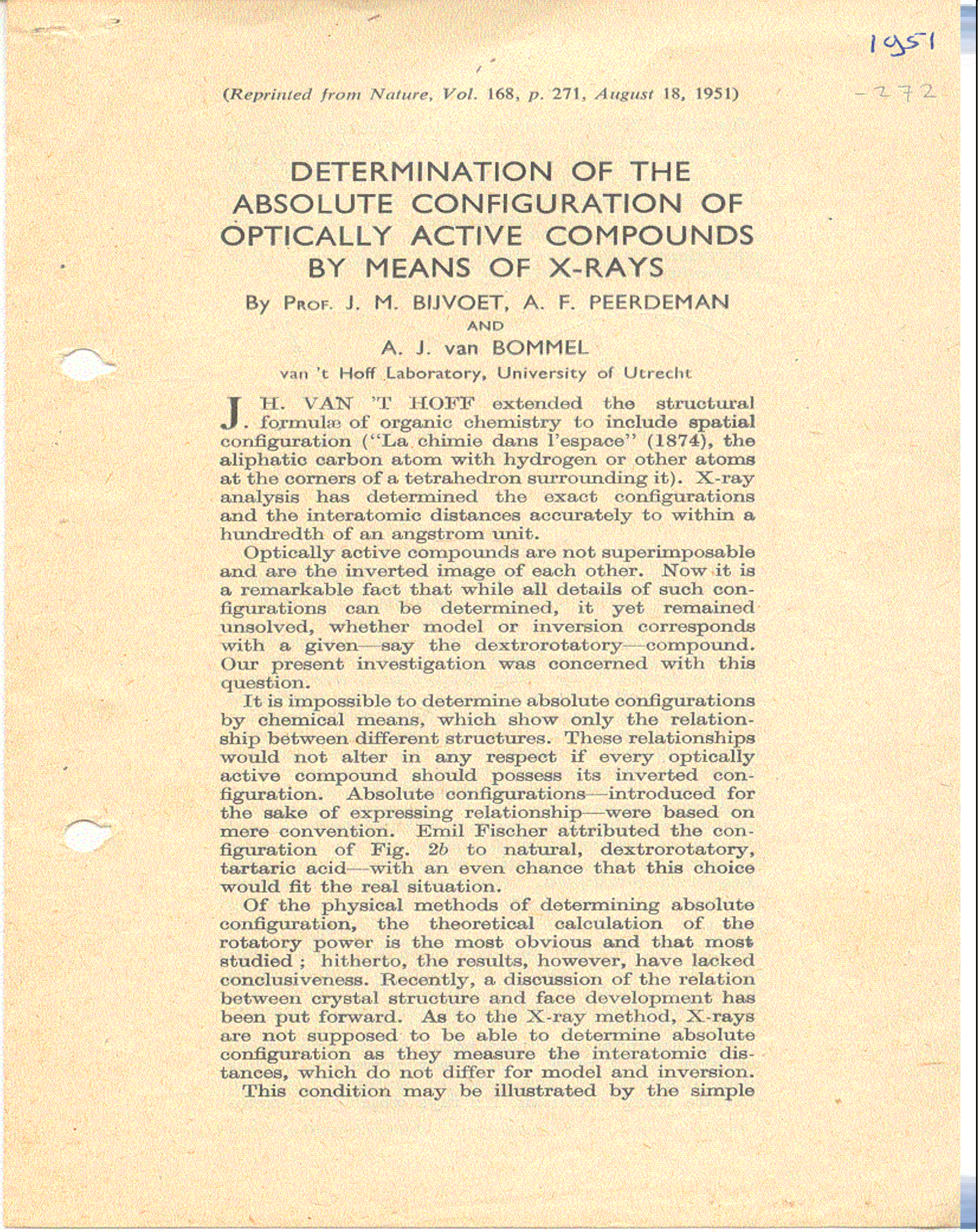


First (in-house) University Computer: Zebra



Absolute Structure Determination

- Friedels law broken: I(hkl) .ne. I(-h,-k,-l)
- Early reports and use:
  - Determination polarity of ZnS (shiny and dull (111) faces)
  - Nishikawa & Matukawa, 1928
  - Coster, Knol & Prins, 1930
- Bijvoet:
  - Generalization of 1D polarity determination to 3D chirality determination
  - 1950 – Absolute structure of Rubidium Sodium (+)Tartrate with Peerdeman and van Bommel.
  - The absolute configuration of (+) tartaric acid was that of the arbitrary Emil Fischer convention



1951

- 272

(*Reprinted from Nature, Vol.* 168, *p.* 271, *August* 18, 1951)

DETERMINATION OF THE ABSOLUTE CONFIGURATION OF OPTICALLY ACTIVE COMPOUNDS BY MEANS OF X-RAYS

By PROF. J. M. BIJVOET, A. F. PEERDEMAN
AND
A. J. van BOMMEL
van 't Hoff Laboratory, University of Utrecht

J. H. VAN 'T HOFF extended the structural formulæ of organic chemistry to include spatial configuration ("La chimie dans l'espace" (1874), the aliphatic carbon atom with hydrogen or other atoms at the corners of a tetrahedron surrounding it). X-ray analysis has determined the exact configurations and the interatomic distances accurately to within a hundredth of an angstrom unit.

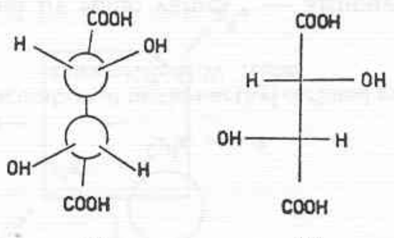
Optically active compounds are not superimposable and are the inverted image of each other. Now it is a remarkable fact that while all details of such configurations can be determined, it yet remained unsolved, whether model or inversion corresponds with a given—say the dextrorotatory—compound. Our present investigation was concerned with this question.

It is impossible to determine absolute configurations by chemical means, which show only the relationship between different structures. These relationships would not alter in any respect if every optically active compound should possess its inverted configuration. Absolute configurations—introduced for the sake of expressing relationship—were based on mere convention. Emil Fischer attributed the configuration of Fig. 2*b* to natural, dextrorotatory, tartaric acid—with an even chance that this choice would fit the real situation.

Of the physical methods of determining absolute configuration, the theoretical calculation of the rotatory power is the most obvious and that most studied; hitherto, the results, however, have lacked conclusiveness. Recently, a discussion of the relation between crystal structure and face development has been put forward. As to the X-ray method, X-rays are not supposed to be able to determine absolute configuration as they measure the interatomic distances, which do not differ for model and inversion.

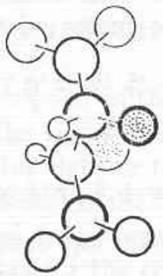
This condition may be illustrated by the simple

The First page
of the famous
1951 Article
in Nature
-
E. Fischer
with his arbitrary
convention of
absolute structure
turned out to
have made by chance
the correct choice
-



(*a*) (*b*)

Fig. 2. *a*) Model of dextrorotatory tartaric acid according to Fischer's convention.
b) Same in conventional projection.



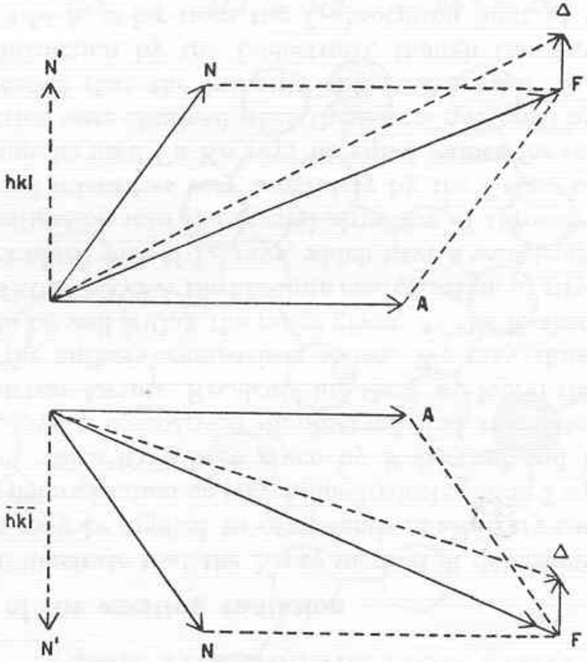


Fig. 16. Phase diagrams of reflection and counterreflection showing the decisive role of the component N′ of the normally scattered amplitude in anomalous diffraction.

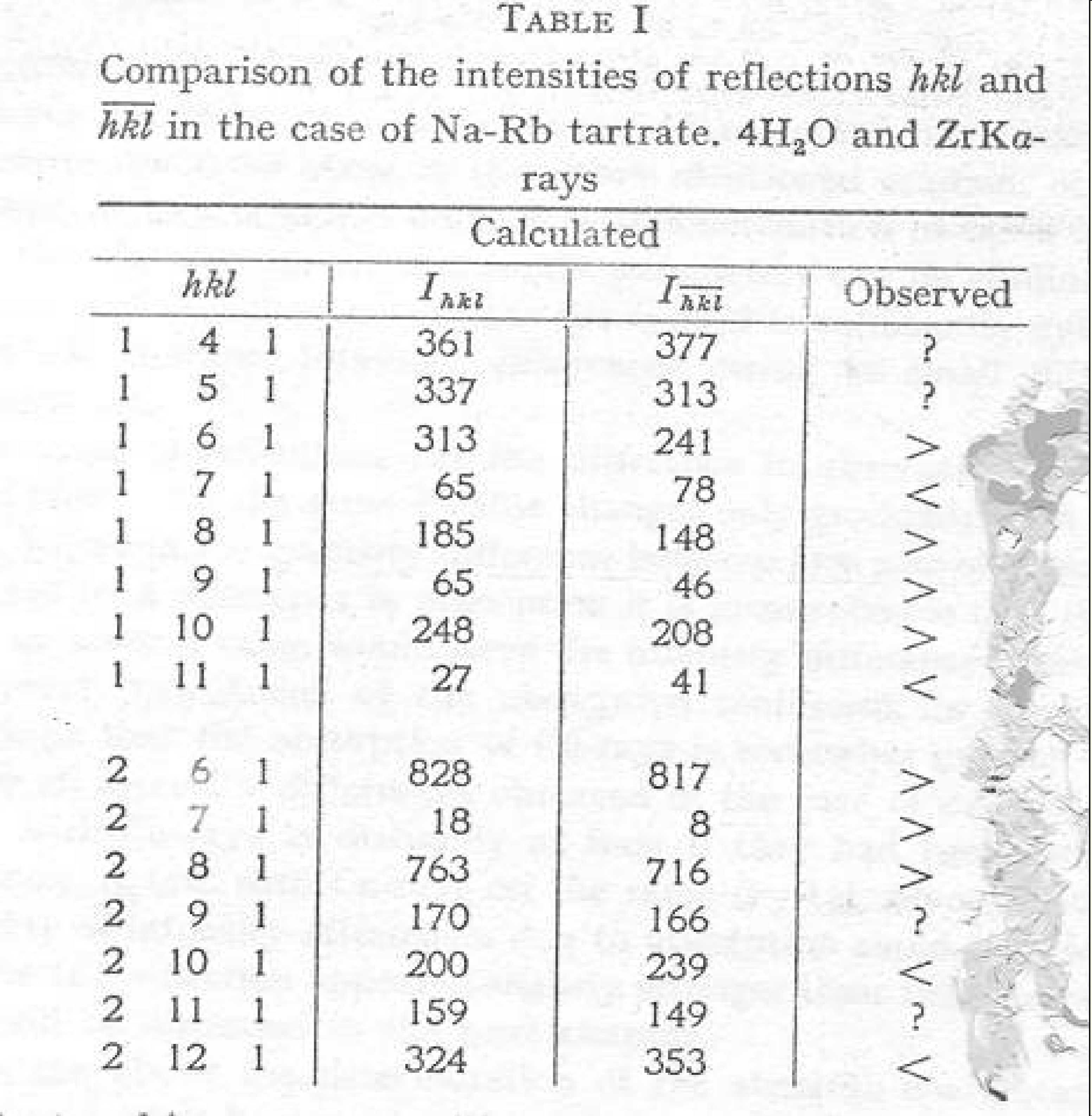


TABLE I

Comparison of the intensities of reflections hkl and $\overline{hkl}$ in the case of Na-Rb tartrate. $4H_2O$ and ZrKα-rays

hkl	Calculated		
	I_{hkl}	$I_{\overline{hkl}}$	Observed
1 4 1	361	377	?
1 5 1	337	313	?
1 6 1	313	241	>
1 7 1	65	78	<
1 8 1	185	148	>
1 9 1	65	46	>
1 10 1	248	208	>
1 11 1	27	41	<
2 6 1	828	817	>
2 7 1	18	8	>
2 8 1	763	716	>
2 9 1	170	166	?
2 10 1	200	239	<
2 11 1	159	149	?
2 12 1	324	353	<

Qualitative

Long Exposures

Unstable
X-Ray Sources

Use of Anomalous Differences in Phasing

- It was soon realized that the qualitative use anomalous differences could resolve the phase ambiguity problem of SIR
- The first application was the structure determination of glycylthyrosine HCl/HBr
- Later it was realized that quantitative use of anomalous differences could avoid the need isomorphous replacement (SAD)
  - Cytosine.HBr

(Pepinski) Pennsylvania State College 1950 (travel by ship)

Elected President of the IUCr 1951-1954

IUCr Paris, 1954 with Harker

Madrid 1956 with wife

MIT 1957 International Conference on Crystal Physics

1952: Moving from the 'van 't Hoff lab' to the 'Crystal Palace' (institute + private home)

Later Research Interests

- The absolute structure determination of tartaric acid led in Utrecht to the study of many related carboxylic acids.
- Structure determination techniques by the Direct Methods (Symbolic Addition Method (Beurskens, Kroon) and Correlation Method (de Vries)
- Editor of several volumes of Structure Reports

Lifelong interests

– Walking

– Teaching
(please ask a question)

– Thermodynamics
(most stable !!)

– Music (Mozart)
(liked to make music with
Guests and co-workers)

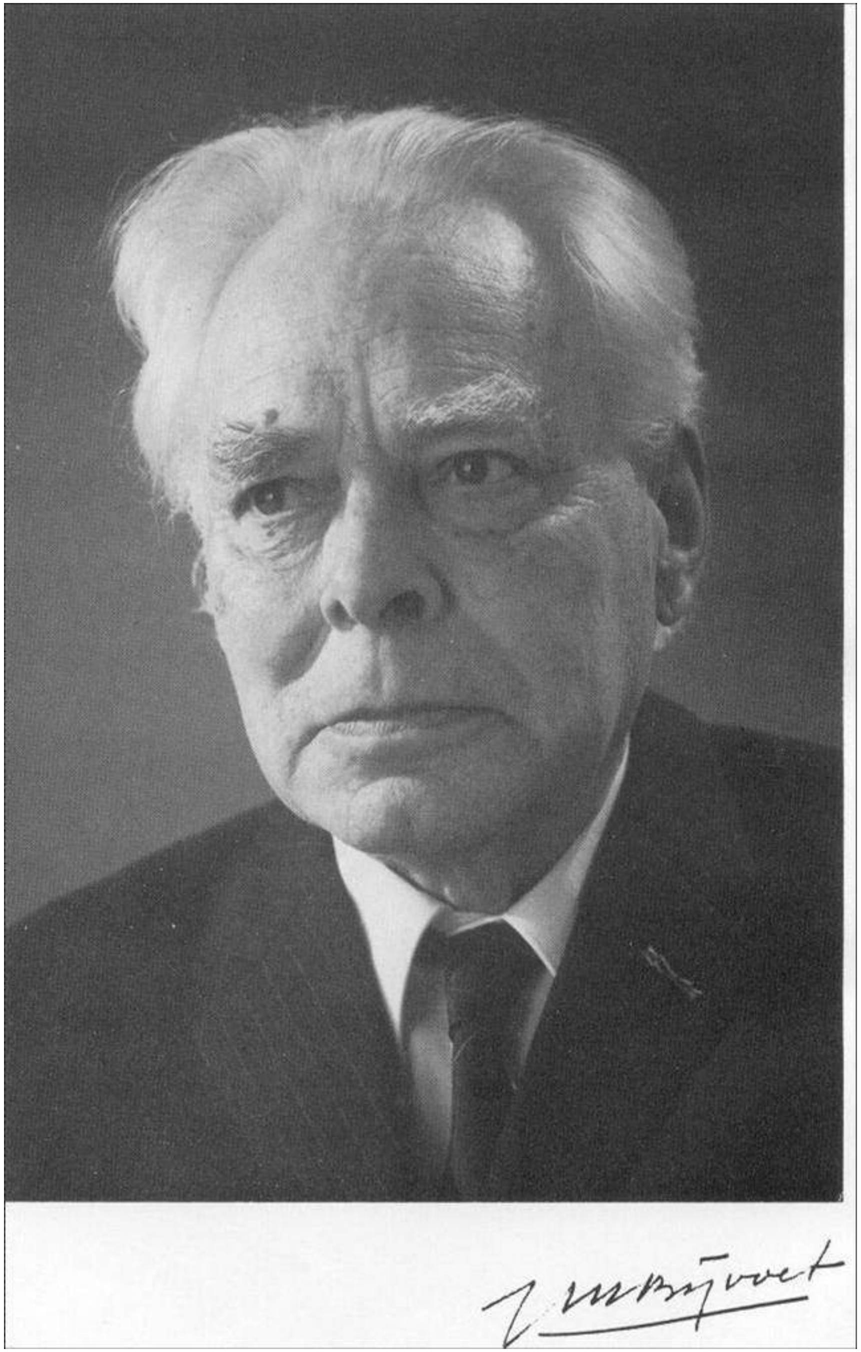
– Crystals (Collection)

– Cats
(present at examinations)

Absolute Structure to be reversed?

- Bijvoet's assignment of the absolute structure depends on the assumed positive sign of f”.
- In 1972 an experiment (based on circular dichroism) by Tanaka suggested that all assignments had to reversed
- Independent experiments involving molecular beams (He+ against CdS surface) re-confirmed Bijvoet's assignment of absolute configuration.
- Discussed during a conference in Madrid (1974)

1974 Madrid, Meeting on Anomalous Dispersion



Bijvoet 1973

– Bijvoet retired in 1962 and moved to a Saxon style farmhouse in the east of the Netherlands.
In that very year I started in chemistry
– Was succeeded by his student A.F. Peerdeman (and later J. Kroon).
– For many years there were regular visits to the lab where he had a bedroom to stay when in Utrecht with a double function as 'Student room' (housing me around 1966)
– Died in 1980

Epilogue

- The use of anomalous dispersion is now standard in protein structure determination.
- Flack extended the use of Bijvoet pairs to determine the enantiopurity of a chiral compound. This was further extended by Hooft et al. and Parsons. (FLACK x, HOOFT y, PARSONS z)
- The absolute structure determination of RbNa-tartrate has recently been re-confirmed with modern techniques.
- Research moved to protein crystallography (Piet Gros) along with a national small molecule service component.
- Crystallography is now part of the Bijvoet Centre for Biomolecular research (X-Ray, NMR, MS, BioChem)
- Bijvoet introduced crystallography into the chemistry curriculum. This is still the case in Utrecht.

Thanks !

Small Molecule and Protein Crystallography

Bijvoet Center for Biomolecular Research

Moved to 1973