DIRDIF - Fragment Searching to easily solve structures which direct methods won't

Robert Gould, Structural Biochemistry ICMB
University of Edinburgh

(But really Paul Beurskens et al, University of Nijmegen)

DIRDIF - The Real Thing

- P.T. Beurskens, G. Beurskens, R de Gelder, S. Garcia-Granda, R. Gould & J.M.M Smits, Crystallography Laboratory, the University of Nijmegen.
- Windows realisation by Louis Ferrugia, The University of Glasgow
- Examples from Simon Parsons, The University of Edinburgh

DIRDIF - the general idea

Strengthen Direct Methods by making use of known structural features

Heavy atoms - PATTY
Known molcular structure - ORIENT
Known molecular orientation - TRACOR
Known position - DIFTAN

PATTY Example: $Rh(C_5H_5)\{B(C_4H_5N_2S)_3\}Cl$

P-1 ; *V* = 2618 Å ^{3} ; *Z* = 4 ; data poor

Related compound: $Cd(Br)\{C_4H_5N_2S)_3\}$

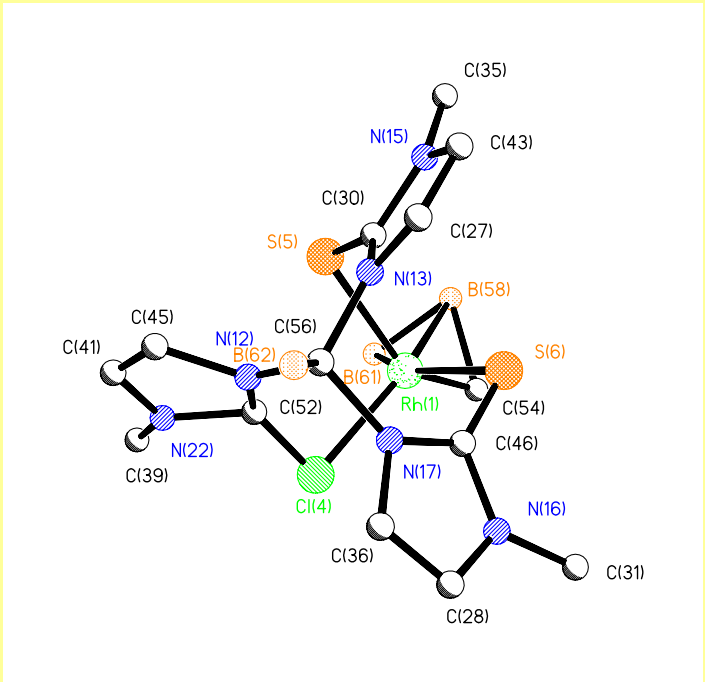
P-1 ; *V* = 1337 Å ^{3} ; *Z* = 2 ; data very good

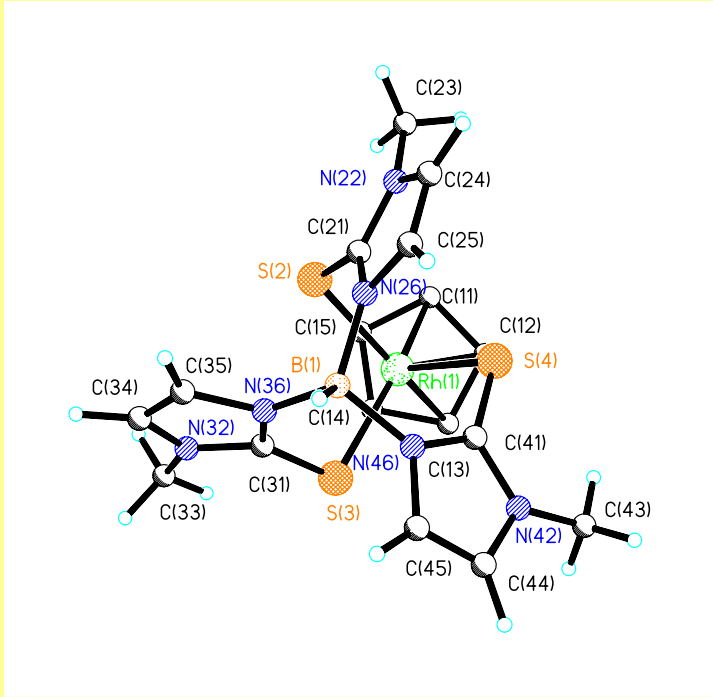
(but not, of course, known about until later!)

Patterson for $Rh(C_5H_5)\{B(C_4H_5N_2S)_3\}$

1	6000.	0.0000	0.0000	0.0000	0.00
2	2762.	0.0402	-0.1273	-0.4576	8.73
3	1774.	0.2821	0.3041	-0.1894	6.61
4	1134.	-0.3419	-0.4948	0.1759	8.46
5	1084.	0.2122	0.3148	-0.0738	4.98
6	1074.	0.0587	0.1962	0.0148	2.47
7	1036.	-0.2006	0.0525	-0.0485	2.46
8	1035.	0.4790	0.2530	-0.1397	7.18
9	1015.	-0.0707	0.0107	0.1178	2.48
10	920.	0.2423	0.4265	0.2664	6.98

$Rh(C_5H_5)\{B(C_4H_5N_2S)_3\}$





DIRDIF solution **Refined structure**

S18DEN : Patterson

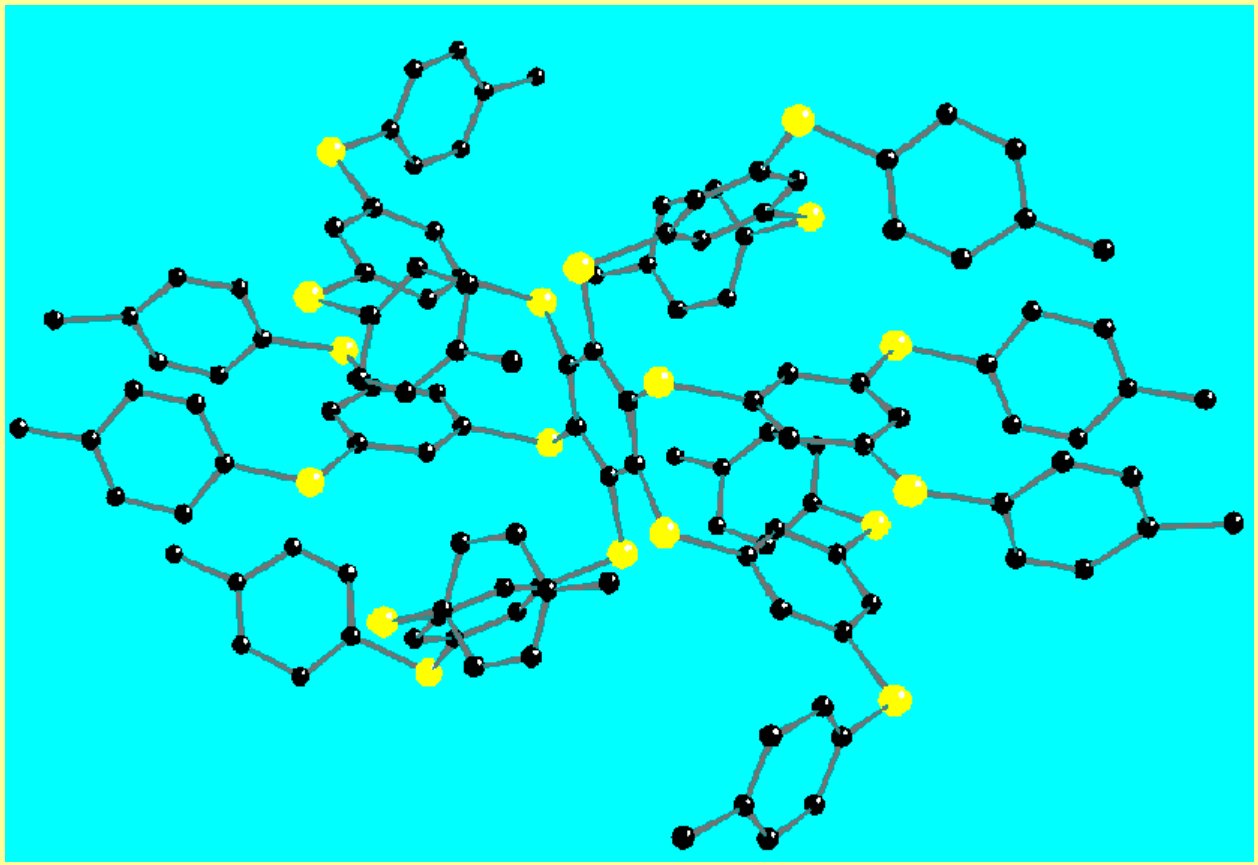
$C_{126}H_{108}S_{18}$; $P2_1/c$: V = 3800Å^3 : Z = 2

Peak	height	x	y	z	length
1	6000.	0.0000	0.0000	0.0000	0.00
2	461.	0.0000	0.2053	0.5000	8.92
3	416.	0.0000	0.1524	0.5000	8.57
4	390.	0.0000	0.3350	0.5000	10.13
5	367.	0.1657	0.1813	0.2520	5.44
6	367.	0.0000	0.0373	0.5000	8.14
7	363.	-0.1338	0.0346	0.2463	5.52
8	348.	0.0584	0.0000	0.0681	1.32
9	343.	0.2914	0.0000	0.0219	5.71
10	338.	0.0320	0.5000	0.1696	9.44

S18DEN: Patterson solution and final refinement

- S1 0.000 0.000 0.002
- S2 0.002 -0.003 0.003
- S3 0.000 0.000 0.010
- S4 -0.001 -0.001 0.000
- S5 -0.002 0.001 0.004
- S6 0.000 0.000 0.000
- S7 -0.001 0.005 0.000
- S8 0.002 -0.005 0.008
- S9 (not found in Patterson)

S18DEN - DIRDIF SOLUTION



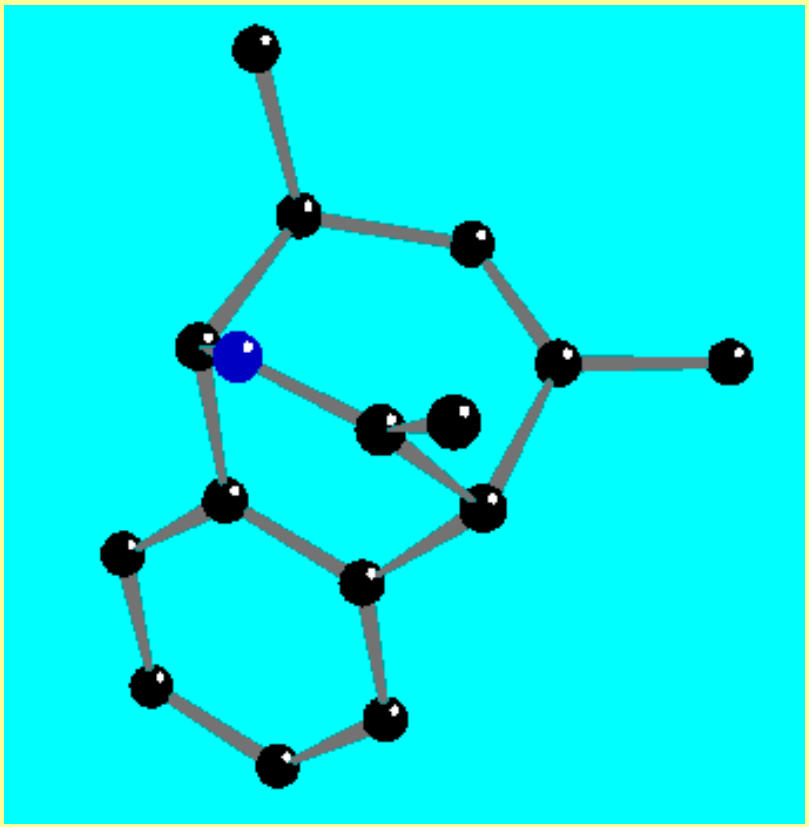
Orient Test: CHNM13

a	b	c	α	β	γ
8.280	12.915	41.666	90	90.00	90

$C_{30}H_{23}N$: Z = 8

124 atoms in asymmetric unit - strong hint of twinning!

ORIENT - the general principle



- Calculate sharpened Patterson from data
- Calculate vector map from fragment
- Rotate calculated map to achieve best overlap with Patterson.
- Here $C_{15}N$

CHNM13 Patterson

Peak	height	x	y	z	length
1	1397.	0.0000	0.0532	0.5000	20.84
2	1241.	0.2103	0.0000	-0.4999	20.90
3	1006.	0.0332	0.0000	0.0269	1.15
4	865.	0.0009	0.0869	0.0140	1.26
5	636.	0.0000	0.1872	0.0000	2.42
6	464.	0.0030	0.4896	0.2497	12.18
7	457.	0.4502	0.2590	-0.0001	5.01
8	389.	-0.2460	0.4897	0.2496	12.34
9	374.	0.2252	0.4884	0.2506	12.34
10	350.	0.1415	0.0894	0.0390	2.31

ORIENT - Matching the Vectors

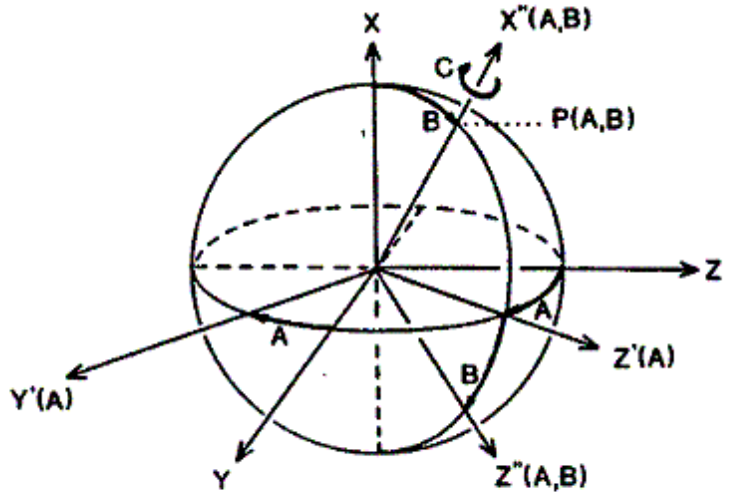


Figure 1. Definition of Eulerian angles

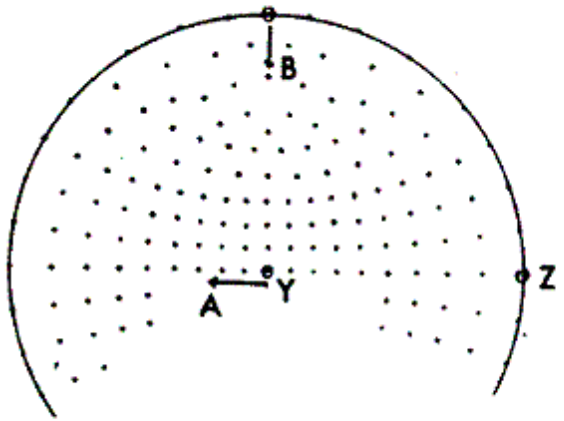


Figure 2. The coarse (A,B) grid plotted on a Wulff net, i.e., a stereographic projection of points P(A,B)

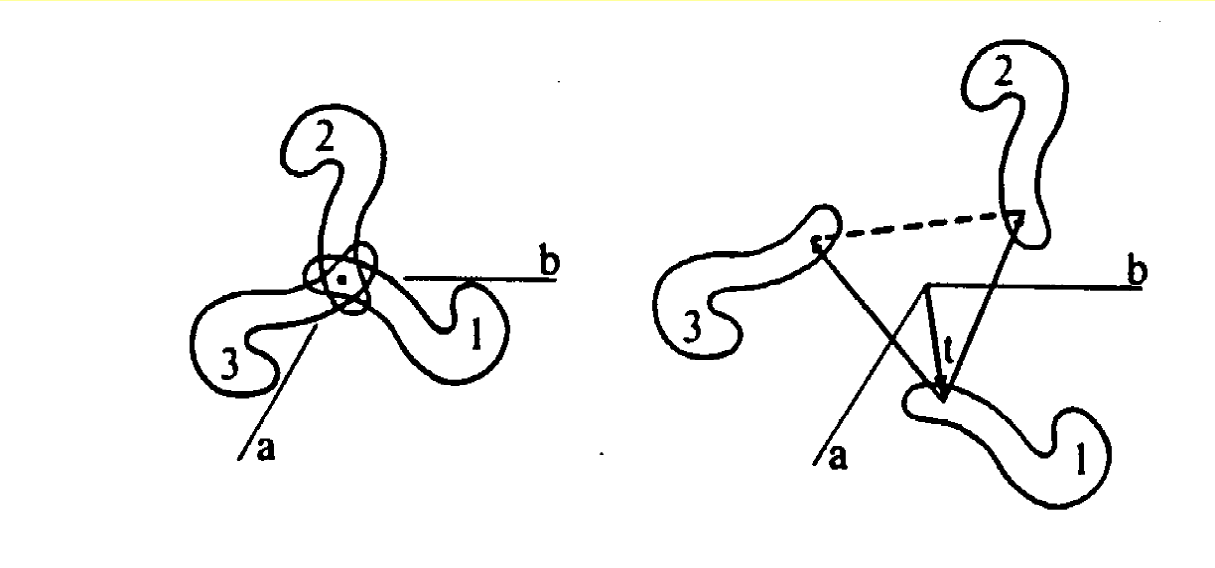
ORIENT RESULTS

Set	A	B	C	ISIG
1	216.40	69.40	199.80	392
2	184.40	32.40	176.40	346
3	170.80	33.60	174.20	328
4	90.70	40.20	16.80	309
5	346.40	71.40	87.60	288
6	145.20	61.40	27.60	282

(with Z' = 2, at least two correct orientations are present)

TRACOR - general principle

- Calculate shift of oriented fragment relative to symmetry elements



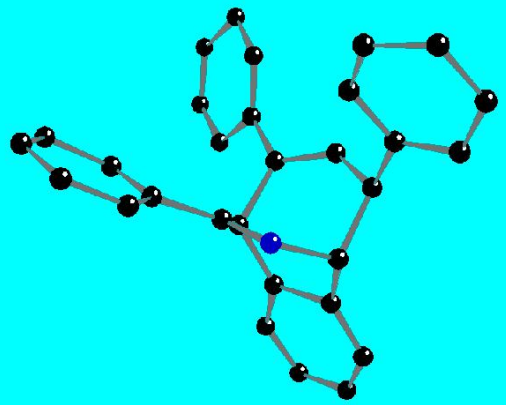
TRACOR Results

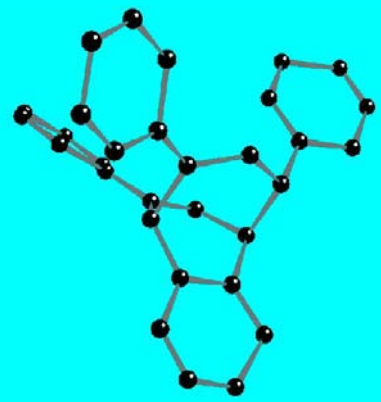
Class 2: origin not fixed in *b*-direction
Fourier is calculated in *ac*-plane:
***a* = 8.280, *c* = 41.666 Å, β = 90.00°**
No close contacts

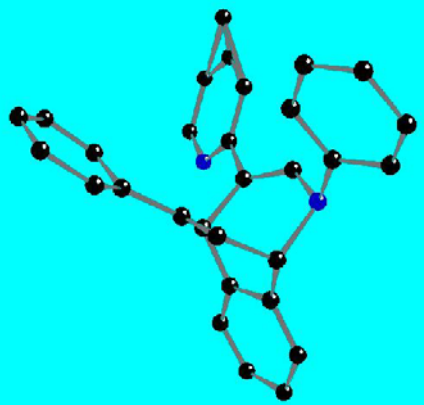
Possible shift vectors:

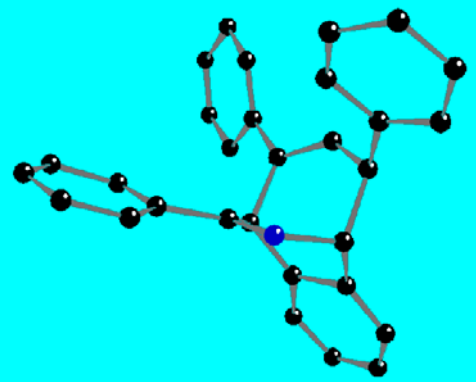
	FOM	t_x	t_y	t_z
1	912.	0.14858	0.00000	0.00627

CHNM13 – Results for 4 molecules









CHNM13 – The end of the story

- Refinement converged unconvincingly
- Twinned refinement with [100] as twin axis gave 60:40 composition for twins.
- Solution is probably due to the ability to the Fourier expansion to delete the weaker component on geometrical grounds.