COMPOUND/STRUCTURE INDEX

A

(+)-5-Acetoxygoniothalamin 39
(-)-5α-Acetoxygoniothalamin 249
(-)-5β-Acetoxygoniothalamin 231
5-Acetoxyisogoniothalamin epoxide 39
8-Acetylgoniotriol 38, 100
(-)-Anolobine 77
Annohexocin 46, 54
Annomonicin 51
Annomontacin 51, 65, 104
Annomutacin 52
Annonacin 50, 64, 103, 255, 257, 258
Annonacin A 64
Annonacin-10-one 50
(-)-Annonaine 77
Annonastatin 50, 64
Annonin 44
Annonin I 48, 64
Annonin VI 48, 64
Aristolactam 26, 28, 29
Aristolactam A II 28, 78
Aristolactam A III 28
Aristolactam B II 28, 78, 289
Aristolactam B III 28
Aristolactam C II 30
Aristolactam C III 30
Aristolactam C II diacetate 30
Aristolactam D II 30
Aristolactam β-D-glucoside 28
Aristolamide 30
Aristolinic acid methyl ester 30
Aristolochic acid 27, 29
Aristolochic acid B 27
Aristolochic acid C 27
Aristolochic acid D 27
Aristolochic acid Iva 27
Aristolochic acid II 27
Aristolochic acid D methyl ether lactam 28
Aristolodione 24
Aristored 28
Asimicin 48, 64
Asimilobine 80
Atemoyin 46, 49

B

Bullatacin 48, 64
Bullatacinone 43, 48, 64
30-OH-Bullatacinone 49
31-OH-Bullatacinone 49
32-OH-Bullatacinone 49
Bullatalicin 54, 64
Bullatalicinone 55
Bullatanocin 54
Bullatenin 53

C

Cataline 25
Cepharadione A 24
Cepharadione B 24
(2,4-*Cis*)-10*R*-annonacin-A-one 52
Cis- and *trans*-gigantetrocinone 53
(2,4-*Cis* and *trans*)-longicinone 52
(2,4-*Cis* and *trans*)-goniothalamicinone 52
Cis-lactone 35
Corunnine 22
Corydione 23
Crossoline 50
Crossolone 50

D

6a,7-Dehydro-2-hydroxy-4,5-dioxonoraporphine 24
4-Deoxygigantecin 54, 66
(+)-5-Deoxygoniopypyrone 39, 101, 172, 200
Desacetyluvaricin 48
Diepomuricanin 47, 55, 67
Dieporeticanin 55
Dieporeticanin 2 55
Dihydropontevedrine 23
5,7-Dioxoaporphine 25
4,5-Dioxodehydroasimilobine 24
Disepalin 270, 273, 275
Doryflavine 28

E

7-Epi-goniofufurone 39
Epomuricenin A 47
Epoxyrollin A 55
Epoxyrollin B 55
Erythro-7,8-dibromogoniothalamin 32
Erythro-6*R*,7*S*,8*S*-goniodiol 172, 213

G

Giganenin 53, 65
Giganin 66
Gigantecin 54, 64, 66, 103
Gigantetrocin 51, 66
Gigantetronenin 53, 66, 104
Gigantriocin 51, 66
Gigantrionenin 53, 66, 104
Glaucanisin 49
Goniocin 54, 104
Goniodiol 38, 158, 165
Goniodiol diacetate 38
(+)-Goniodiol diacetate 38, 174
Goniodiol-7-monoacetate 38
Goniodiol-8-monoacetate 38
Goniofufurone 39, 101
Goniopedaline 28, 78
(+)-Goniopypyrone 38, 101, 173, 214
(+)-(6R)-Goniothalamin 31, 34, 35, 99, 136, 144, 158, 166, 237, 248

G
(6*S*)-Goniothalamin 35
(+)-Goniothalamin epoxide 38, 144, 158, 214
Goniothalamicin 50, 64, 66, 102
(+)-Goniothalenol 38, 100, 215, 224
(+)-Goniothavensin 39
Goniotriol 38, 100
H
14-Hydroxy-25-desoxyrollinicin 48
4-Hydroxy-25-desoxyneorollinicin 48
5-Hydroxygoniothalamin 237
5α-Hydroxygoniothalamin 238, 240, 247
(+)-5β-Hydroxygoniothalamin 39, 225
5β-Hydroxygoniothalamin 224
5β-Hydroxygoniothalamin epoxide 224
5β-Hydroxyisogoniothalamin epoxide 224
I
(+)-Isoaltholactone 38, 224
Isoannonacin 50
Isoannonacin-10-one 50
Isodesacetyl uvaricin 48
(-)-Iso-5-deoxygoniopypyrone 39, 172, 197, 213
(-)-Iso-5-deoxygoniopypyrone acetate 200
(+)-Isogoniothalamin epoxide 149, 157, 158, 165
Itrabin 44, 50
J
Jetein 53
L
Laherradurine 48, 50
Lanuginosine 22
Liriodendronine 22
Liriodenine 22, 77, 296
Longicin 52
M
Membranacin 48
3-Methoxycepharadione B 24
Methyl aristolochate 30
Molvizarin 49
Montacin 51
Motrillin 48
Muricatetrocin 51
Muricatetrocin A 51
Murihexocin A 46, 54
Murihexocin B 46, 54
Murisolin 50
N
Naringenin 188
Nandazurine 22
Narumicin I 49
Narumicin II 49
Neoannonin 48
Norcepharadione B 24
O
Olefinic aldehyde 34
Otivarin 55
Ouregidione 24, 302
Oxolaureline 22
Oxonantenine 22
Oxopurpureine 22
Oxostephanine 22
P
Panalicin 49
Phenanthrene 29
Pinocembrin 180, 187
Pontevedrine 24, 25, 26
Pyranone 34
R
Reticulatacin 45, 51
Rioclarin 48, 49
Rolliniastatin 48, 64
Rollinone 48
S
Scorazanone 79
(-)-Scoulerine 80
Solamin 50, 67
Squamocin 48
Squamocin-28-one 48, 49
Squamone 50, 64
Squamostatin-A 55
6-Styryl-2-pyrone 32
Subsessiline 22
Sylvaticin 54, 64
T
Taliscanine 28, 78
Threo-7,8-dibromogoniothalamin 32
Threo-(6*R*,7*R*,8*S*)-goniodiol 166
Threo-(6*R*,7*S*,8*R*)-goniodiol 166, 172
(2,4-*Trans*)-10*R*-annonacin-A-one 52
Trans-lactone 35
Trilobacin 48
U
Uleicin A, B, C, D, E 49
Uvariamicin I 51
Uvariamicin II 51
Uvariamicin III 51
Uvariamicin IV 51
Uvaricin 44, 48, 64
V
Velutinam 28, 78

APPENDICES

Appendix 1

Appendix 1-4 are examples of probit analysis results. The following tables summarise the results of probit analysis for *Goniothalamus andersonii* (hexane extract)- *Aedes aegypti* bioassay experiment.

No.	Total No. of larvae	No. of larvae killed	Dose of extract (µg/ml)
1	30	8	25
2	20	7	40
3	40	21	50
4	20	15	60
5	20	16	70
6	30	28	80
7	20	20	150

Control: Total → 20 killed → 0

% control mortality: 0 (0/20)

No.	Killed	Total	Dose	Observed mortality	Corrected mortality
1	8	30	25	26.7	26.7
2	7	20	40	35.0	35.0
3	21	40	50	52.5	52.5
4	15	20	60	75.0	75.0
5	16	20	70	80.0	80.0
6	28	30	80	93.3	93.3
7	20	20	150	100.0	100.0

Log transformation of the dose (-1 = NO, Enter = YES)?

→ Yes

iterations → 1, 2, 3

$p(CHI^2 = 5.407527, df = 5) = 0.6318051$

The data are well represented by a line. Option 6 of Menu 2 is suggested.

No.	Dose	Mortality correlation (%)	Probit	Total treated	Killed	Killed expected	CHI^2 contribution
1	25	26.7	4.377413	30	8	5.35	1.5946
2	40	35.0	4.615124	20	7	9.22	0.9897
3	50	52.5	5.062545	40	21	24.60	1.3722
4	60	75.0	5.674189	20	15	14.59	0.0416
5	70	80.0	5.841457	20	16	16.22*	0.0162
6	80	93.3	6.501385	30	28	26.03*	1.1232
7	150	100.0	-	20	20	19.73*	0.2700

Mortality in the control: 0%
Number of iteration: 3

$CHI^2 = 5.407527$ df = 5 Probability = 0.6318051

LC	Level of confidence	Range of LC				
1 = 11.20716	0.95	5.72659	<	LC	<	16.15296
2 = 13.09437	0.95	7.14948	<	LC	<	18.23230
3 = 14.45350	0.95	8.22884	<	LC	<	19.69272
4 = 15.56822	0.95	9.14570	<	LC	<	20.87089
5 = 16.53818	0.95	9.96541	<	LC	<	21.88348
10 = 20.35218	0.95	13.36823	<	LC	<	25.77336
20 = 26.16811	0.95	19.01948	<	LC	<	31.52397
30 = 31.36771	0.95	24.41969	<	LC	<	36.60822
40 = 36.61786	0.95	30.05672	<	LC	<	41.83209
50 = 42.30637	0.95	36.16597	<	LC	<	47.79361
60 = 48.87856	0.95	42.91663	<	LC	<	55.36880
70 = 57.05958	0.95	50.55343	<	LC	<	66.11082
80 = 68.39733	0.95	59.91013	<	LC	<	83.17692
90 = 87.94304	0.95	74.21325	<	LC	<	116.84700
95 = 108.22400	0.95	87.82302	<	LC	<	155.99900
96 = 114.96680	0.95	92.16886	<	LC	<	169.82380
97 = 123.83380	0.95	97.77648	<	LC	<	188.56750
98 = 136.68690	0.95	105.71520	<	LC	<	216.81440
99 = 159.70400	0.95	119.46590	<	LC	<	270.36450

LC is lethal concentration

Regression line: Y = A + Slope x (X - M)

A = 5.2993 ± 0.1080209 5.191279 < A < 5.407321
Slope = 4.03319 ± 0.6251858 3.408005 < B < 4.658376
M = 11.70062

Variance of the LC_{50} = 8.496515E - 04
Heterogeneity = 1

LC	Level of confidence	Range of LC				
1 = 11.20716	0.95	5.72659	<	LC	<	16.15296
2 = 13.09437	0.95	7.14948	<	LC	<	18.23230
3 = 14.45350	0.95	8.22884	<	LC	<	19.69272
4 = 15.56822	0.95	9.14570	<	LC	<	20.87089
5 = 16.53818	0.95	9.96541	<	LC	<	21.88348
10 = 20.35218	0.95	13.36823	<	LC	<	25.77336
20 = 26.16811	0.95	19.01948	<	LC	<	31.52397
30 = 31.36771	0.95	24.41969	<	LC	<	36.60822
40 = 36.61786	0.95	30.05672	<	LC	<	41.83209
50 = 42.30637	0.95	36.16597	<	LC	<	47.79361
60 = 48.87856	0.95	42.91663	<	LC	<	55.36880
70 = 57.05958	0.95	50.55343	<	LC	<	66.11082
80 = 68.39733	0.95	59.91013	<	LC	<	83.17692
90 = 87.94304	0.95	74.21325	<	LC	<	116.84700
95 = 108.22400	0.95	87.82302	<	LC	<	155.99900
96 = 114.96680	0.95	92.16886	<	LC	<	169.82380
97 = 123.83380	0.95	97.77648	<	LC	<	188.56750
98 = 136.68690	0.95	105.71520	<	LC	<	216.81440
99 = 159.70400	0.95	119.46590	<	LC	<	270.36450

LC is lethal concentration

Regression line: $Y = A + \text{Slope} \times (X - M)$

A = 5.2993 ± 0.1080209 $\quad 5.191279 < A < 5.407321$

Slope = 4.03319 ± 0.6251858 $\quad 3.408005 < B < 4.658376$

M = 11.70062

Variance of the LC_{50} = 8.496515E - 04

Heterogeneity = 1

Appendix 2

The tables below summarise the results of probit analysis for *Mezzetia umbellata* (ethanol extract)- *Aedes aegypti* bioassay experiment.

No.	Total No. of larvae	No. of larvae killed	Dose of extract (µg/ml)
1	30	5	3
2	20	5	4
3	20	8	5
4	20	9	6
5	20	13	7
6	20	16	8
7	20	18	9

Control: Total → 20 killed → 0

% control mortality: 0 (0/20)

No.	Killed	Total	Dose	Observed mortality	Corrected mortality
1	5	30	3	16.7	16.7
2	5	20	4	25.0	25.0
3	8	20	5	40.0	40.0
4	9	20	6	45.0	45.0
5	13	20	7	65.0	65.0
6	16	20	8	80.0	80.0
7	18	20	9	90.0	90.0

Log transformation of the dose (-1 = NO, Enter = YES)?

→ Yes

iterations → 1 2 3

$p(CHI^2 = 2.702376, df = 5) = 0.2542444$

The data are well represented by a line. Option 6 of Menu 2 is suggested.

No.	Dose	Mortality correlation (%)	Probit	Total treated	Killed	Killed expected	CHI^2 contribution
1	3	16.7	4.032637	30	5	3.69*	0.5307
2	4	25.0	4.325811	20	5	5.43	0.0460
3	5	40.0	4.747067	20	8	8.56	0.0643
4	6	45.0	4.874619	20	9	11.33	1.1102
5	7	65.0	5.384877	20	13	13.57	0.0743
6	8	80.0	5.841457	20	16	15.28*	0.1436
7	9	90.0	6.281729	20	18	16.55*	0.7334

Mortality in the control: 0%

Number of iterations: 3

$CHI^2 = 2.7023765$ df = 5

Probability = 0.2542444

LC	Level of confidence	Range of LC				
1 = 1.63181	0.95	0.89108	<	LC	<	2.23897
2 = 1.88129	0.95	1.09784	<	LC	<	2.49792
3 = 2.05903	0.95	1.25291	<	LC	<	2.67833
4 = 2.20374	0.95	1.38359	<	LC	<	2.82313
5 = 2.32892	0.95	1.49967	<	LC	<	2.94711
10 = 2.81541	0.95	1.97482	<	LC	<	3.42039
20 = 3.54269	0.95	2.74231	<	LC	<	4.11739
30 = 4.18106	0.95	3.44903	<	LC	<	4.74164
40 = 4.81645	0.95	4.15120	<	LC	<	5.40544
50 = 5.49613	0.95	4.86115	<	LC	<	6.20091
60 = 6.27171	0.95	5.58985	<	LC	<	7.24405
70 = 7.22481	0.95	6.38345	<	LC	<	8.70372
80 = 8.52669	0.95	7.35096	<	LC	<	10.93516
90 = 10.72932	0.95	8.86439	<	LC	<	15.17510
95 = 12.97054	0.95	10.29049	<	LC	<	19.97828
96 = 13.70734	0.95	10.74287	<	LC	<	21.65337
97 = 14.67069	0.95	11.32423	<	LC	<	23.91071
98 = 16.05673	0.95	12.14276	<	LC	<	27.28665
99 = 18.51159	0.95	13.54800	<	LC	<	33.61596

LC is lethal concentration

Regression line: Y = A + Slope x (X - M)

A = 5.017203 ± 0.1123308 4.904872 < A < 5.129534
Slope = 4.411916 ± 0.730235 3.681681 < B < 5.142151
M = 10.74396

Heterogeneity = 1

Appendix 3

Below are tables showing the results of probit analysis for *Mezzetia umbellata* (methanol extract)- *Aedes aegypti* bioassay experiment.

No.	Total No. of larvae	No. of larvae killed	Dose of extract (µg/ml)
1	10	0	1
2	10	0	2
3	10	1	3
4	10	1	4
5	30	4	5
6	20	2	6
7	30	6	7
8	30	14	8
9	30	15	9
10	30	15	10
11	10	10	15

Control: Total → 10 killed → 0

% control mortality: 0 (0/10)

No.	Killed	Total	Dose	Observed mortality	Corrected mortality
1	0	10	1	0.0	0.0
2	0	10	2	0.0	0.0
3	1	10	3	10.0	10.0
4	1	10	4	10.0	10.0
5	4	30	5	13.3	13.3
6	2	20	6	10.0	10.0
7	6	30	7	20.0	20.0
8	14	30	8	46.7	46.7
9	15	30	9	50.0	50.0
10	15	30	10	50.0	50.0
11	10	10	15	100.0	100.0

Log transformation of the dose (-1 = NO, Enter = YES)?

→ Yes

iterations → 1 2 3 4

$p(CHI^2 = 11.23972, df = 8) = 0.8115152$

The data are well represented by a line. Option 6 of Menu 2 is suggested.

No.	Dose	Mortality correlation %	Probit	Total treated	Killed	Killed expected	CHI^2 contribution
1	2	0.0	-	10	0	0.02*	0.0165
2	3	10.0	3.718271	10	1	0.15*	4.7201
3	4	10.0	3.718271	10	1	0.54*	0.4123
4	5	13.3	3.889172	30	4	3.59*	0.0544
5	6	10.0	3.718271	20	2	4.08*	1.3368
6	7	20.0	4.158544	30	6	8.94	1.3379
7	8	46.7	4.916555	30	14	11.77	0.6956
8	9	50.0	5.000000	30	15	14.44	0.0417
9	10	50.0	5.000000	30	15	16.86	0.4680
10	15	100.0	-	10	10	8.25*	2.1163

Mortality in the control: 0%
Number of iterations: 4

$CHI^2 = 11.23972$ $df = 8$
Probability = 0.8115152

LC	Level of confidence	Range of LC				
1 = 2.75070	0.95	1.58946	<	LC	<	3.62592
2 = 3.16951	0.95	1.96705	<	LC	<	4.03855
3 = 3.46774	0.95	2.25109	<	LC	<	4.32601
4 = 3.71047	0.95	2.49086	<	LC	<	4.55684
5 = 3.92041	0.95	2.70408	<	LC	<	4.75469
10 = 4.73587	0.95	3.57731	<	LC	<	5.51349
20 = 5.95395	0.95	4.97313	<	LC	<	6.65970
30 = 7.02233	0.95	6.19819	<	LC	<	7.76475
40 = 8.08506	0.95	7.30042	<	LC	<	9.07060
50 = 9.22128	0.95	8.31203	<	LC	<	10.72988
60 = 10.51718	0.95	9.32816	<	LC	<	12.87734
70 = 12.10883	0.95	10.47056	<	LC	<	15.78495
80 = 14.28162	0.95	11.92690	<	LC	<	20.13697
90 = 17.95493	0.95	14.22782	<	LC	<	28.34556
95 = 21.68959	0.95	16.42858	<	LC	<	37.65857
96 = 22.91681	0.95	17.12822	<	LC	<	40.91461
97 = 24.52093	0.95	18.02766	<	LC	<	45.30927
98 = 26.82821	0.95	19.29434	<	LC	<	51.89610
99 = 30.91285	0.95	21.46881	<	LC	<	64.28776

LC is lethal concentration

Regression line : $Y = A + Slope \times (X - M)$

A = 4.653009 $\pm$ 9.844739E - 02 $\quad 4.554562 < A < 4.751457$
Slope = 4.42039 $\pm$ 0.771167 $\quad 3.657872 < B < 5.200206$
M = 10.88645

Heterogeneity = 1

Appendix 4

The following are tables showing the results of probit analysis for annonacin-

Aedes aegypti bioassay experiment.

No.	Total No. of larvae	No. of larvae killed	Dose of compound (µg/ml)
1	0	10	2
2	1	10	3
3	2	10	5
4	2	10	7
5	5	10	10
6	14	20	15
7	10	10	20
8	10	10	40

Control: Total → 10 killed → 0

% control mortality: 0 (0/10)

No.	Killed	Total	Dose	Observed mortality	Corrected mortality
1	0	10	2	0	0
2	1	10	3	10	10
3	2	10	5	20	20
4	2	10	7	20	20
5	5	10	10	50	50
6	14	20	15	70	70
7	10	10	20	100	100
8	10	10	40	100	100

Log transformation of the dose (-1 = NO, Enter = YES)?

→ Yes

iterations → 1 2 3 4

$p(CHI^2 = 3.628126, df = 5) = 0.3959034$

The data are well represented by a line. Option 6 of Menu 2 is suggested.

No.	Dose	Mortality correlation (%)	Probit	Total treated	Killed	Killed expected	CHI^2 contribution
1	2	0	-	10	0	0.09*	0.0913
2	3	10	3.718271	10	1	0.40*	0.9382
3	5	20	4.158544	10	2	1.64*	0.0946
4	7	20	4.158544	10	2	3.19*	0.6564
5	10	50	5.000000	10	5	5.28*	0.0315
6	15	70	5.524002	20	14	15.06*	0.3004
7	20	100	-	10	10	8.68*	1.5157

Mortality in the control: 0%
Number of iterations: 4

$CHI^2 = 3.528126$ df = 5
Probability = 0.3959034

LC	Level of confidence	Range of LC				
1 = 2.05001	0.95	0.73267	<	LC	<	3.29029
2 = 2.45483	0.95	0.98002	<	LC	<	3.76410
3 = 2.75224	0.95	1.17789	<	LC	<	4.10227
4 = 2.99951	0.95	1.35209	<	LC	<	4.37849
5 = 3.21696	0.95	1.51214	<	LC	<	4.61838
10 = 4.09080	0.95	2.21345	<	LC	<	5.56371
20 = 5.47290	0.95	3.47400	<	LC	<	7.04697
30 = 6.75093	0.95	4.73993	<	LC	<	8.47651
40 = 8.07592	0.95	6.07340	<	LC	<	10.09889
50 = 9.54583	0.95	7.49119	<	LC	<	12.15017
60 = 11.28327	0.95	9.02078	<	LC	<	14.97331
70 = 13.49781	0.95	10.75505	<	LC	<	19.17198
80 = 16.64983	0.95	12.94345	<	LC	<	26.14485
90 = 22.27508	0.95	16.39996	<	LC	<	41.01969
95 = 28.32577	0.95	19.75974	<	LC	<	60.03534
96 = 30.37926	0.95	20.84300	<	LC	<	67.13958
97 = 33.10864	0.95	22.24702	<	LC	<	77.06666
98 = 37.11981	0.95	24.24662	<	LC	<	92.62416
99 = 44.45012	0.95	27.73928	<	LC	<	123.88930

LC is lethal concentration

Regression line: Y = A + Slope x (X - M)

A = 5.004762 ± 0.171524 $4.833238 < A < 5.176286$
Slope = 3.482904 ± 0.6935132 $2.789391 < B < 4.176417$
M = 10.98118

Heterogeneity = 1

Appendix 5

The following tables are X-ray data for (+)-5α-hydroxygoniothalamin.

Data collection and processing parameters

Molecular formula	$C_{13}H_{12}O_3$
Molecular weight	216.2
Colour and habit	light yellow prism
Crystal size	0.20 x 0.30 x 0.50 mm^3
Crystal system	orthorhombic
Space group	$P2_12_12_1$ (No. 19)
Unit cell parameters	a = 4.838(1) Å V = 1124.9(4)Å^3
	b = 5.959(1) Z = 4
	c = 39.023(8) $F(000)$ = 456
Density (calcd)	1.28 g cm^{-3}
Radiation	graphite-monochroamtised MoKα, λ = 0.71073 Å
Standard reflections	(1, 1, 6); (0, 1, 14); (1, 1, 3)
Intensity variation	±1.1%
R_{int} (from merging of eqiv. reflections)	0.058
Absorption coefficient (mm^{-1})	0.09 mm^{-1}
Scan type and rate	ω-scan; 3.00 - 30.00 deg min^{-1}
Scan range	0.60° below $K\alpha_1$ to 0.60° above $K\alpha_2$
Background counting	stationary counts for one-fourth of scan time at each end of scan range
Collection method	$0 \le h \le 5$, $0 \le k \le 6$, $-1 \le l < 42$; $2\theta_{max} = 46°$
Unique data measured	1018
Absorption data with $\|F_o\| \ge 4\sigma(\|F_o\|)$, n	702
No. of variables, p	146
Weighting scheme	$w = [\sigma^2\|F_o\| + 0.0001\|F_o\|^2]^{-1}$
$R_F = \Sigma \|\|F_o\| - \|F_c\|\|/\Sigma\|F_o\|$	0.045
$wR = [\Sigma w(\|F_o\| - \|F_c\|)^2/\Sigma w\|F_o\|^2]^{1/2}$	0.044
$S = [\Sigma w(\|F_o\| - \|F_c\|)^2/(n - p)]^{1/2}$	1.44
Largest and mean Δ/σ	0.00, 0.00
Residual extrema in final difference map	+0.14 to -0.19 eÅ^{-3}

Atomic coordiantes (x 10^4) and equivalent isotropic temperature factors* (Å^2 x 10^4)

Atom	x	y	z	U_{eq}
O(1)	4200(7)	-2344(6)	3455(1)	50(1)
C(2)	4940(12)	-3849(10)	3213(1)	55(2)
O(2)	6741(8)	-5197(6)	3279(1)	73(2)
C(3)	3553(12)	-3706(10)	2881(1)	61(2)
C(4)	2007(12)	-1946(9)	2802(1)	54(2)
C(5)	1481(11)	-66(9)	3048(1)	47(2)
O(3)	-1199(7)	798(6)	2983(1)	62(1)
C(6)	1640(10)	-1013(8)	3414(1)	43(2)
C(7)	1670(12)	798(8)	3677(1)	49(2)
C(8)	-315(11)	1014(9)	3907(1)	52(2)
C(1')	-548(11)	2759(9)	4175(1)	51(2)
C(2')	1044(13)	4723(10)	4177(1)	66(2)
C(3')	781(14)	6298(10)	4434(1)	76(30
C(4')	-1058(14)	5991(12)	4699(1)	77(3)
C(5')	-2675(15)	4062(12)	4698(1)	84(3)
C(6')	-2416(13)	2456(10)	4442(1)	73(2)

*U_{eq} defined as one third of the trace of the orthogonalised U tensor.

Non-hydrogen bond distances (Å)

Atoms	Distance	Atoms	Distance
O(1)-C(2)	1.351(6)	O(1)-C(6)	1.480(6)
C(2)-O(2)	1.213(7)	C(2)-C(3)	1.460(8)
C(3)-C(4)	1.325(8)	C(4)-C(5)	1.497(7)
C(5)-O(3)	1.418(6)	C(5)-C(6)	1.540(6)
C(6)-C(7)	1.490(6)	C(7)-C(8)	1.320(7)
C(8)-C(1')	1.479(7)	C(1')-C(2')	1.401(8)
C(1')-C(6')	1.391(7)	C(2')-C(3')	1.380(8)
C(3')-C(4')	1.376(8)	C(4')-C(5')	1.391(10)
C(5')-C(6')	1.389(8)		

Non-hydrogen interatomic angles (°)

Atoms	Angle	Atoms	Angle
C(2)-O(1)-C(6)	120.1(4)	O(1)-C(2)-O(2)	118.7(5)
O(1)-C(2)-C(3)	117.4(5)	O(2)-C(2)-C(3)	123.9(5)
C(2)-C(3)-C(4)	120.9(5)	C(3)-C(4)-C(5)	122.5(5)
C(4)-C(5)-O(3)	108.2(4)	C(4)-C(5)-C(6)	108.2(4)
O(3)-C(5)-C(6)	110.1(4)	O(1)-C(1)-C(6)-(5)	109.8(4)
O(1)-C(6)-C(7)	107.8(4)	C(5)-C(6)-C(7)	112.0(4)
C(6)-C(7)-C(8)	122.1(5)	C(7)-C(8)-C(1')	127.2(5)
C(8)-C(1')-C(2')	123.3(5)	C(8)-C(1')-C(6')	119.2(5)
C(2')-C(1')-C(6')	117.5(5)	C(1')-C(2')-C(3')	121.4(5)
C(2')-C(3')-C(4')	121.0(6)	C(3')-C(4')-C(5')	118.1(6)
C(4')-C(5')-C(6')	121.4(6)	C(1')-C(6')-C(5')	120.5(6)

Anisotropic thermal parameters* ($Å^2 \times 10^3$)

Atom	$U_{1,1}$	$U_{2,2}$	$U_{3,3}$	$U_{1,2}$	$U_{1,3}$	$U_{2,3}$
O(1)	50(2)	50(2)	49(2)	7(2)	-5(2)	-7(2)
C(2)	44(3)	46(3)	74(4)	-10(3)	7(3)	-8(4)
O(2)	63(3)	53(2)	104(3)	18(3)	-2(3)	-4(2)
C(3)	59(4)	58(4)	67(4)	-2(4)	9(3)	-22(3)
C(4)	61(4)	61(3)	41(3)	-7(4)	7(3)	-9(3)
C(5)	47(3)	50(3)	43(3)	-1(3)	-2(3)	-5(3)
O(3)	69(3)	65(3)	52(2)	22(3)	-15(2)	-9(2)
C(6)	38(3)	51(3)	41(2)	7(3)	-2(2)	-7(3)
C(7)	54(4)	54(3)	38(2)	3(3)	-6(3)	-7(3)
C(8)	46(3)	59(4)	51(3)	3(3)	-4(3)	1(3)
C(1')	60(4)	57(4)	36(3)	15(3)	-2(3)	-6(3)
C(2')	84(5)	64(4)	51(3)	0(4)	8(3)	-11(3)
C(3')	106(6)	56(4)	66(3)	-4(4)	-3(4)	-20(3)
C(4')	92(5)	90(5)	49(3)	17(5)	-8(4)	-18(4)
C(5')	89(5)	102(5)	62(4)	8(5)	27(4)	-12(4)
C(6')	72(4)	78(4)	69(4)	6(4)	13(4)	-17(4)

*The exponent takes the form: $-2\pi^2\Sigma\Sigma\ U_{ij}h_ih_ja_i^*.a_j^*$.

Hydrogen atom coordinates ($\times 10^4$) and assigned isotropic temperature factors* ($Å^2 \times 10^3$)

Atom	x	y	z	U
H(3)	3829	-4929	2725	80
H(4)	1172	-1880	2579	80
H(5)	2870	1075	3025	80
H(30)	-1425	2104	3103	80
H(6)	76	-1971	3453	80
H(7)	3139	1881	3675	80
H(8)	-1742	-103	3895	80
H(2')	2416	4909	4002	80
H(3')	1803	7678	4424	80
H(4')	-1206	7058	4883	80
H(5')	-3963	3843	4882	80
H(6')	-3551	1134	4447	80

*The exponent takes the form: $-8\pi^2U\sin^2\theta/\lambda^2$.

Appendix 6

The following tables are X-ray data for (+)-isogoniothalamin epoxide.

Atomic coordinates and equivalent temperature factors (B in $Å^2$)

Atom	x	y	z	B($Å^2$)
O1	0.5083(5)	-0.0044(6)	0.2593(1)	3.93(8)
O2	0.5259(6)	-0.0256(6)	0.1716(1)	5.28(9)
O3	0.6990(5)	-0.1202(6)	0.3628(1)	4.93(9)
C2	0.4119(8)	-0.0185(8)	0.2106(2)	3.9(1)
C3	0.1733(8)	-0.0178(9)	0.2096(2)	4.3(1)
C4	0.0596(8)	0.023(1)	0.2521(2)	4.9(2)
C5	0.1650(7)	0.0525(8)	0.3051(2)	4.4(1)
C6	0.3778(8)	-0.0479(8)	0.3067(2)	3.3(1)
C7	0.5163(8)	-0.0014(9)	0.3535(2)	3.6(1)
C8	0.5218(9)	-0.1191(8)	0.4007(2)	3.9(1)
C9	0.5645(7)	-0.0539(8)	0.4559(2)	3.3(1)
C10	0.4147(8)	-0.0871(9)	0.4953(2)	4.0(1)
C11	0.4543(9)	-0.0317(9)	0.5470(2)	5.2(2)
C12	0.6444(9)	0.056(1)	0.5594(2)	5.3(2)
C13	0.7940(9)	0.0900(8)	0.5205(2)	5.0(2)
C14	0.7534(9)	0.0369(8)	0.4684(2)	4.4(1)
H3	0.108(8)	-0.029(7)	0.174(2)	7(1)*
H4	-0.079(6)	0.041(6)	0.251(1)	5(1)*
H5a	0.074(6)	0.002(6)	0.332(1)	4(1)*
H5b	0.191(8)	0.194(6)	0.313(2)	6(1)*
H6	0.355(6)	-0.171(5)	0.306(1)	3(1)*
H7	0.563(6)	0.132(7)	0.359(1)	5(1)*
H8	0.435(5)	-0.214(4)	0.398(1)	0.4(7)*
H10	0.286(7)	-0.156(7)	0.487(1)	4(1)*
H11	0.361(6)	-0.059(6)	0.574(1)	4(1)*
H12	0.676(7)	0.102(6)	0.596(1)	5(1)*
H13	0.911(7)	0.157(6)	0.526(1)	4(1)*
H14	0.848(5)	0.068(5)	0.444(1)	1.2(7)*

Starred atoms were refined istropically.

Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: (4/3) * [a^2*B(1,1) + b^2*B(2,2) + c^2*B(3,3) + ab(cos γ)*B(1,2) + ac(cos β)*B(1,3) + bc(cos α)*B(2,3)].

Atoms bond distances (Å)

Atoms		Distance	Atoms		Distance
O1	C2	1.355(8)	C7	C8	1.46(1)
O1	C6	1.462(8)	C7	H7	1.03(7)
O2	C2	1.198(8)	C8	C9	1.479(9)
O3	C7	1.435(9)	C8	H8	0.87(4)
O3	C8	1.438(9)	C9	C10	1.367(9)
C2	C3	1.459(9)	C9	C14	1.37(1)
C3	C4	1.30(1)	C10	C11	1.37(1)
C3	H3	0.98(6)	C10	H10	0.96(6)
C4	C5	1.49(1)	C11	C12	1.36(1)
C4	H4	0.86(6)	C11	H11	0.90(6)
C5	C6	1.50(1)	C12	C13	1.36(1)
C5	H5a	0.94(6)	C12	H12	1.00(6)
C5	H5b	1.07(7)	C13	C14	1.38(1)
C6	C7	1.48(1)	C13	H13	0.88(7)
C6	H6	0.91(6)	C14	H14	0.88(5)

Interatomic angles (°)

Atoms			Angle	Atoms			Angle
C2	O1	C6	118.1(6)	C7	C6	H6	109.0(4)
C7	O3	C8	61.1(5)	O3	C7	C6	115.6(7)
O1	C2	O2	118.6(7)	O3	C7	C8	59.6(5)
O1	C2	C3	124.6(8)	C6	C7	C8	120.8(8)
C2	C3	C4	121.4(9)	C6	C7	H7	119.0(4)
C2	C3	H3	115.0(4)	C8	C7	H7	116.0(4)
C4	C3	H3	123.0(4)	O3	C8	C7	59.4(5)
C3	C4	C5	121.8(8)	O3	C8	C9	118.7(7)
C3	C4	H4	123.0(4)	O3	C8	H8	114.0(3)
C5	C4	H4	115.0(4)	C7	C8	C9	124.2(8)
C4	C5	C6	109.2(8)	C7	C8	H8	114.0(3)
C4	C5	H5a	108.0(4)	C9	C8	H8	115.0(3)
C4	C5	H5b	111.0(4)	C8	C9	C10	119.6(7)
C6	C5	H5a	107.0(4)	C8	C9	C14	121.3(6)
C6	C5	H5b	110.0(4)	C10	C9	C14	119.1(7)
H5a	C5	H5b	110.0(6)	C9	C10	C11	120.3(8)
O1	C6	C5	110.2(7)	C9	C10	H10	119.0(4)
O1	C6	C7	106.0(6)	C11	C10	H10	121.0(3)
O1	C6	H6	106.0(4)	C10	C11	C12	120.1(8)
C5	C6	C7	113.9(8)	C10	C11	C11	121.0(4)
C5	C6	H6	111.0(4)	C12	C11	H11	119.0(4)
C11	C12	C13	120.0(8)	C14	C13	H13	116.0(4)
C11	C12	H12	122.0(4)	C9	C14	C13	120.4(8)
C13	C12	H12	118.0(4)	C9	C14	H14	121.0(4)
C12	C13	C14	120.0(9)	C13	C14	H14	118.0(4)
C12	C13	H13	123.0(4)				

Table of general displacement parameter expressions - U's [Anisotropic thermal parameters* ($Å^2 \times 10^3$)]

Name	U(1, 1)	U(2, 2)	U(3, 3)	U(1, 2)	U(1, 3)	U(2, 3)
O1	0.034(1)	0.072(3)	0.043(2)	0.003(2)	0.004(2)	0.003(2)
O2	0.078(2)	0.073(3)	0.049(2)	0.000(3)	0.022(2)	-0.004(2)
O3	0.049(2)	0.086(3)	0.052(2)	0.011(2)	0.004(2)	0.002(2)
C3	0.060(3)	0.063(4)	0.042(3)	-0.003(4)	-0.007(3)	0.004(4)
C4	0.038(3)	0.079(5)	0.071(3)	0.004(4)	-0.010(3)	0.000(4)
C5	0.034(2)	0.069(4)	0.063(3)	0.004(3)	0.013(3)	0.002(4)
C6	0.047(3)	0.040(4)	0.040(3)	-0.008(3)	0.005(2)	0.006(3)
C7	0.044(3)	0.050(4)	0.043(3)	0.002(3)	0.002(3)	0.001(3)
C8	0.043(3)	0.047(4)	0.060(3)	-0.013(3)	-0.003(3)	0.001(3)
C9	0.041(3)	0.044(4)	0.041(3)	-0.001(3)	-0.007(2)	0.003(3)
C10	0.049(3)	0.057(4)	0.047(3)	-0.015(4)	-0.004(3)	0.008(3)
C11	0.069(4)	0.081(5)	0.048(3)	-0.013(5)	0.005(3)	0.010(4)
C12	0.076(3)	0.078(5)	0.047(3)	-0.002(4)	-0.007(3)	-0.007(4)
C13	0.057(3)	0.054(5)	0.078(4)	-0.010(4)	-0.021(3)	-0.005(4)
C14	0.055(3)	0.055(4)	0.056(3)	-0.003(4)	-0.009(3)	0.010(3)

The form of the anisotropic displacement parameter is: * $\exp[-2\pi^2\{h^2a^2U(1,1) + k^2b^2U(2,2) + l^2c^2U(3,3) + 2hkabU(1,2) + 2hlacU(1,3) + 2klbcU(2,3)\}]$ where a, b and c are reciprocal lattice constants. (or-$2\pi^2\Sigma\Sigma\ U_{ij}h_ih_ja_i^*.a_j^*$.).

Values of 10*Fobs and 10*Fcalc [gsh^4]

H	K	L	Fobs	Fcalc	SigF	H	K	L	Fobs	Fcalc	SigF
0	0	2	266	275	3	0	3	2	233	243	8
0	0	4	696	751	8	0	3	4	92	95	4
0	0	6	316	328	5	0	3	5	182	181	8
0	0	8	98	98	3	0	3	7	156	154	8
0	0	10	245	249	7	0	3	8	126	124	3
0	0	12	124	122	6	0	3	9	89	90	4
0	0	14	130	127	3	0	3	10	114	111	4
0	0	16	108	109	6	0	3	14	82	80	5
0	0	18	131	135	6	0	3	15	61	61	6
0	0	20	248	242	9	0	3	18	67	66	7
0	0	26	65	75	8	0	3	20	173	178	5
0	1	1	188	191	8	0	3	21	160	163	7
0	1	2	380	335	4	0	3	22	105	105	6
0	1	3	98	97	5	0	3	23	72	72	7
0	1	4	101	104	3	0	3	24	143	142	5
0	1	5	244	244	6	0	4	0	380	378	6
0	1	6	383	379	6	0	4	1	152	146	5
0	1	7	158	161	9	0	4	2	429	430	14
0	1	8	117	118	3	0	4	4	268	261	5
0	1	9	157	156	3	0	4	6	69	64	7
0	1	'0	327	326	5	0	4	7	141	142	6
0	1	16	74	74	6	0	4	8	181	178	5
0	1	20	350	354	8	0	4	9	69	68	6
0	1	21	106	114	8	0	4	10	186	182	7
0	1	22	222	221	5	0	4	14	85	82	8
0	1	24	121	121	5	0	4	24	60	59	9
0	2	0	1833	2148	7	0	5	1	76	76	5
0	2	1	432	432	12	0	5	2	97	94	5
0	2	2	464	462	10	0	5	3	129	127	7
0	2	3	402	402	8	0	5	4	62	69	6
0	2	4	640	644	6	0	5	8	86	86	5
0	2	6	86	85	5	0	5	20	80	76	6
0	2	7	74	74	4	0	5	24	64	77	9
0	2	8	229	225	8	0	7	6	80	95	7
0	2	9	86	82	9	0	7	9	58	47	8
0	2	10	307	302	9	0	8	8	70	67	8
0	2	11	145	144	3	1	0	1	720	726	6
0	2	12	63	61	5	1	0	2	168	167	6
0	2	14	118	118	5	1	0	3	55	60	5
0	2	15	76	77	6	1	0	4	81	83	4
0	2	16	63	65	6	1	0	5	429	429	6
0	2	20	149	146	7	1	0	6	208	210	3
0	2	23	96	91	6	1	0	8	63	60	5
0	2	24	70	72	7	1	0	9	181	176	4

Values of 10*Fobs and 10*Fcalc [gsh^4] (continued)

H	K	L	Fobs	Fcalc	SigF	H	K	L	Fobs	Fcalc	SigF
1	0	10	352	349	6	1	3	2	333	330	5
1	0	11	69	66	5	1	3	3	265	269	6
1	0	12	333	321	7	1	3	4	91	92	4
1	0	13	234	229	3	1	3	6	69	69	5
1	0	15	109	104	4	1	3	8	71	68	5
1	0	18	179	178	4	1	3	9	116	117	1
1	0	22	132	134	5	1	3	10	123	121	4
1	1	0	60	56	9	1	3	11	258	257	6
1	1	1	686	705	8	1	3	12	92	88	7
1	1	2	820	838	5	1	3	14	135	133	4
1	2	3	330	329	7	1	3	20	60	59	8
1	1	4	246	247	4	1	3	21	114	117	5
1	1	5	208	209	4	1	3	22	72	85	7
1	1	8	270	269	4	1	3	23	83	76	6
1	1	9	144	142	3	1	4	0	366	363	6
1	1	10	490	478	6	1	4	1	208	206	3
1	1	11	341	338	5	1	4	2	53	52	7
1	1	13	78	75	4	1	4	3	246	244	5
1	1	14	99	95	4	1	4	4	158	156	4
1	1	16	73	71	5	1	4	5	89	84	4
1	1	20	108	112	5	1	4	6	241	239	4
1	1	21	262	269	6	1	4	7	76	74	6
1	1	23	63	60	8	1	4	8	55	54	7
1	1	24	76	70	6	1	4	10	90	90	5
1	2	0	749	749	6	1	4	11	105	102	5
1	2	1	138	433	5	1	4	14	86	90	5
1	2	2	111	110	6	1	4	20	91	86	5
1	2	3	514	519	7	1	5	0	152	153	6
1	2	4	140	139	4	1	5	1	68	69	6
1	2	5	313	314	7	1	5	6	89	86	6
1	2	6	163	164	4	1	5	11	137	136	4
1	2	7	112	112	4	1	5	12	69	67	9
1	2	9	105	101	4	1	5	14	82	80	7
1	2	10	253	244	5	1	7	4	54	39	8
1	2	11	156	155	4	1	7	11	55	65	8
1	2	12	81	77	5	1	8	2	79	60	6
1	2	13	111	111	4	2	0	0	567	563	5
1	2	14	91	89	4	2	0	2	393	393	6
1	2	15	88	86	6	2	0	3	250	252	4
1	2	18	130	129	4	2	0	4	86	87	4
1	2	20	94	91	5	2	0	5	335	340	5
1	2	22	106	109	5	2	0	6	286	283	4
1	3	0	213	212	3	2	0	7	98	99	3
1	3	1	129	124	3	2	0	8	111	108	4

Values of 10*Fobs and 10*Fcalc [gsh^4] (continued)

H	K	L	Fobs	Fcalc	SigF	H	K	L	Fobs	Fcalc	SigF
2	0	9	116	112	3	2	3	1	258	255	1
2	0	10	288	271	6	2	3	2	66	64	5
2	0	11	309	303	5	2	3	3	285	286	5
2	0	12	366	357	7	2	3	4	142	147	3
2	0	14	223	218	6	2	3	5	124	125	4
2	0	17	51	46	7	2	3	6	99	99	4
2	0	18	136	135	6	2	3	7	94	93	4
2	0	20	141	146	5	2	3	8	107	102	5
2	1	0	78	76	8	1	3	10	171	174	4
2	1	1	329	324	6	2	3	12	216	216	4
2	1	2	64	68	5	2	3	13	119	116	5
2	1	3	199	196	4	2	3	15	76	82	6
2	1	4	174	172	5	2	3	16	126	126	4
2	1	6	65	67	5	2	3	22	62	80	8
2	1	7	132	130	3	2	4	0	275	276	7
2	1	8	266	262	4	2	4	2	188	189	4
2	1	9	230	225	3	2	4	3	102	103	4
2	1	10	202	202	3	2	4	4	219	219	5
2	1	11	104	101	5	2	4	5	78	81	5
2	1	12	126	117	4	2	4	7	95	96	5
2	1	13	90	86	6	2	4	8	111	113	4
2	1	14	154	151	5	2	4	10	241	241	6
2	1	15	91	90	5	2	4	12	147	148	6
2	1	19	91	95	5	2	4	16	92	97	6
2	1	22	149	149	5	2	5	0	134	141	4
2	2	0	489	484	6	2	5	1	115	113	5
2	2	2	365	364	5	2	5	2	61	63	7
2	2	4	270	266	4	2	5	3	94	98	5
2	2	5	131	129	4	2	5	4	83	86	6
2	2	6	145	145	3	2	5	6	82	84	6
2	2	7	98	95	4	2	5	10	75	74	7
2	2	8	121	122	3	2	5	11	118	113	5
2	2	9	197	197	5	2	5	12	132	137	5
2	2	10	328	318	6	2	5	13	68	69	10
2	2	11	139	137	4	2	5	20	70	71	8
2	2	12	300	299	6	2	6	10	77	81	7
2	2	13	132	138	5	3	0	1	413	404	7
2	2	14	108	107	4	3	0	3	78	74	4
2	2	16	95	98	5	3	0	4	155	151	5
2	2	17	105	96	7	3	0	5	90	90	4
2	2	18	67	69	7	3	0	6	96	96	4
2	2	22	59	48	8	3	0	8	61	62	6
2	2	24	64	57	8	3	0	9	131	131	3
2	3	0	123	117	5	3	0	10	78	74	5

Values of 10*Fobs and 10*Fcalc [gsh^4] (continued)

H	K	L	Fobs	Fcalc	SigF	H	K	L	Fobs	Fcalc	SigF
3	0	11	128	127	4	3	3	14	133	130	5
3	0	12	89	91	5	2	3	15	78	82	6
3	0	13	81	83	5	3	3	17	94	99	6
3	0	17	97	97	5	3	3	21	98	94	6
3	0	18	124	123	4	3	4	1	180	175	4
3	1	0	323	312	7	3	4	3	94	101	7
3	1	1	77	75	4	3	4	6	65	63	8
3	1	2	107	106	4	3	4	7	52	45	7
3	1	3	169	166	3	3	4	9	127	127	5
3	1	4	273	264	4	3	4	10	126	124	5
3	1	5	110	109	3	3	4	11	106	109	5
3	1	6	96	91	4	3	4	12	98	98	5
3	1	8	138	132	4	3	4	15	95	97	6
3	1	9	104	102	4	3	4	16	60	42	7
3	1	10	83	84	5	3	4	17	65	79	8
3	1	11	78	78	5	3	4	18	60	69	9
3	1	12	89	86	5	3	4	21	54	37	8
3	1	14	101	103	5	3	5	2	79	89	9
3	1	15	115	115	4	3	5	3	69	66	7
3	1	21	103	118	6	3	5	5	81	85	6
3	1	23	76	77	6	3	5	6	125	128	5
3	2	1	339	334	6	3	5	8	71	72	7
3	2	2	66	63	5	3	5	9	101	102	6
3	2	3	144	140	4	3	5	10	63	66	8
3	2	4	80	79	7	3	5	11	103	108	7
3	2	6	183	186	3	3	5	12	66	65	7
3	2	7	87	89	4	3	6	10	97	103	6
3	2	8	72	69	5	3	6	11	66	71	8
3	2	10	86	87	5	3	7	9	76	76	7
3	2	11	119	116	4	4	0	0	156	156	4
3	2	12	123	119	4	4	0	3	76	75	5
3	2	14	94	96	6	4	0	7	129	126	4
3	2	15	127	129	6	4	0	8	221	221	3
3	2	18	140	136	8	4	0	9	100	98	5
3	3	0	107	101	4	4	0	10	230	232	4
3	3	2	132	130	4	4	0	12	109	108	7
3	3	3	76	76	5	4	0	14	149	147	4
3	3	4	178	177	6	4	0	15	91	90	6
3	3	5	138	135	6	4	0	16	97	111	6
3	3	6	87	89	6	4	0	17	89	90	6
3	3	7	91	88	5	4	1	0	62	64	6
3	3	10	71	71	7	4	1	2	72	74	5
3	3	11	179	178	5	4	1	3	96	94	4
3	3	12	69	67	5	4	1	4	99	98	4

Values of 10*Fobs and 10*Fcalc [gsh^4] (continued)

H	K	L	Fobs	Fcalc	SigF
4	1	5	165	165	4
4	1	6	68	67	6
4	1	8	116	123	6
4	1	9	104	105	5
4	1	10	156	156	4
4	1	11	191	193	4
4	1	12	142	144	4
4	1	13	91	93	6
4	1	14	106	108	5
4	1	15	161	164	6
4	1	17	85	89	6
4	2	0	100	98	4
4	2	5	61	60	7
4	2	6	135	136	4
4	2	7	82	88	5
4	2	8	152	152	5
4	2	9	87	89	6
4	2	10	207	206	4
4	2	11	105	102	7
4	2	12	124	124	5
4	2	14	101	101	5
4	3	0	62	60	7
4	3	3	74	75	6
4	3	4	62	60	7
4	3	5	108	106	5
4	3	6	77	79	6
4	3	7	56	63	8
4	3	8	132	134	4
4	3	9	159	157	4
4	3	10	109	111	5
4	3	11	124	126	5
4	3	12	102	104	6
4	3	14	92	96	6
4	3	15	74	75	6
4	4	3	59	61	7
4	4	5	78	76	6
4	4	6	82	91	7
4	4	10	136	141	5
4	4	11	86	82	8
4	4	12	67	67	7
4	4	15	60	61	8
4	5	6	59	64	7
4	5	8	59	48	7
4	5	9	91	90	6
4	5	10	81	78	6
5	0	1	96	98	5
5	0	2	118	118	4
5	0	4	71	67	6
5	0	6	111	113	5
5	0	7	141	137	4
5	0	9	200	205	4
5	0	11	142	144	5
5	0	13	88	88	6
5	0	14	83	84	6
5	0	20	58	56	8
5	1	0	129	129	5
5	1	3	121	123	5
5	1	5	86	88	6
5	1	6	108	108	7
5	1	8	79	79	6
5	1	9	74	74	7
5	1	10	68	67	9
5	1	11	132	134	5
5	1	12	75	77	8
5	1	13	66	61	7
5	1	17	69	60	7
5	1	18	64	62	8
5	2	0	65	68	8
5	2	2	77	79	6
5	2	4	99	102	5
5	2	5	63	68	7
5	2	6	83	90	6
5	2	7	95	96	6
5	2	8	66	62	8
5	2	9	131	134	6
5	2	11	130	130	5
5	2	13	73	85	7
5	3	0	60	60	8
5	3	6	109	111	5
5	3	8	57	67	8
5	3	9	57	52	8
5	3	11	60	54	8
5	4	6	56	49	8
5	4	11	94	100	7
6	0	2	111	115	5
6	0	3	84	82	6
6	0	4	77	73	6
6	1	0	68	62	7
6	1	1	138	144	5
6	1	2	50	34	7
6	1	4	86	82	6
6	1	5	62	47	7
6	1	8	59	68	8
6	2	2	96	93	6
6	3	0	94	89	7
6	4	7	54	35	8
7	0	7	68	73	9

Appendix 7

The work in this thesis has been presented and published in part in the following conferences and articles:

1. Ee G. C. L. and Chuah C. H. (1992). Styrylpyrones from *Goniothalamus andersonii* and *G. dolichocarpus* (Annonaceae) of Sarawak. In: Proceedings of The Silver Jubilee Chemical Congress '92. Kuala Lumpur, 17-19 November 1992, p. 60.
2. Ee G. C. L., Goh S. H. and Chuah C. H. (1993). Bioactive Constituents from three Malaysian *Goniothalamus* Species. In: Proceedings of The 5th Asian Chemical Congress, Kuala Lumpur, 8-11 November 1993. Abstracts, p.190.
3. Ee G. C. L. and Chuah C. H. (1994). Insecticidal Plants from Sarawak. In: Proceedings of The 4th Eurasia Conference on Chemical Sciences, Kuala Lumpur, 17-20 December 1994. Abstracts, p. 43.
4. Goh S. H., Ee G. C. L. and Chuah C. H. (1994). New Larvicides From *Goniothalamus dolichocarpus*. Malaysian Patent Application # PI 9402780, 18 October 1994.
5. Goh S. H., Ee G. C. L., Chuah C. H. and Chen Wei (1995). Styrylpyrone Derivatives from *Goniothalamus dolichocarpus*. *Australian Journal of Chemistry*, **48**: 199. (reprint on pp. 368-374).
6. Goh S. H., Ee G. C. L., Chuah C. H. and Mak T. C. W. (1995). 5β-Hydroxygoniothalamin, a styrylpyrone derivative from *Goniothalamus dolichocarpus* (Annonaceae). *Natural Product Letters*, **5**: 255. (reprint on pp. 375-379).
7. Ee G. C. L., Goh S. H. and Chuah C. H. (1995). Insecticidal Principles from some Sarawak Plants. In: Proceedings of The Malaysian Chemical Congress 1995, Kuching, Sarawak. 13-16 November, 1995. Abstracts, p. 122.
8. Goh S. H., Lee K. H., Ee G. C. L., Ong H. C., Geh S. L. and Sylvester R. (1995). A Phytochemical Study of Borneo: Sarawak Lowland Forests. *Journal of Herbs, Spices and Medicinal Plants*, **3**: 55.
9. Goh S. H. and Ee G. C. L. (1995). Insecticidal Principles From Some Malaysian Annonaceae. Poster presentation at the 35th IUPAC Congress, Istanbul, Turkey, 4-8 August, 1995. Abstracts, p. 727.
10. Ee G. C. L., Chuah C. H., Sha C. K. and Goh S. H. (1996). Disepalin a new acetogenin from *Disepalum anomalum* (Annonaceae). *Natural Product Letters.*, submitted for publication.

Aust. J. Chem., 1995, **48**, 199–205

Styrylpyrone Derivatives from *Goniothalamus dolichocarpus**

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Abstract

Styrylpyrone derivatives (+)-goniothalamin (1), (+)-goniothalamin epoxide (2) and (−)-iso-5-deoxygoniopypyrone (4b), and the acetogenin (+)-annonacin (7) were bioactive compounds isolated from the stem bark of *Goniothalamus dolichocarpus*. The stereochemical relationships for (+)-goniothalamin epoxide (2), (+)-isogoniothalamin epoxide (3) and (+)-goniodiol diacetate (6) were established by chemical transformations and single-crystal X-ray crystallography.

Introduction

Goniothalamus dolichocarpus (Annonaceae), known locally as *Lukai bukit*, is endemic in Sarawak, Malaysia. The trees grow up to about 2 m tall with up to 6 cm girth. They thrive in light shade and hilly areas of the secondary forests of Sarawak. The stem bark is burnt by the natives to repel insects, especially mosquitoes.

Several *Goniothalamus* species have provided a number of styrylpyrone derivatives of which (+)-goniothalamin (1) is usually dominant.[1–4] (+)-Goniothalamin (1), originally isolated from *Cryptocarya caloneura*[5] and *Goniothalamus andersonii*,[1] was assigned the (6*S*)-configuration based on a degradation study[5] but this was later revised to the (6*R*)-configuration on the basis of synthetic studies.[6–9] (+)-Goniothalamin epoxide (2), isogoniothalamin epoxide (3) and other hydroxy derivatives of goniothalamin[2–4,10,11] have unknown absolute configurations. Relative

* This paper is dedicated to Professor A. L. J. Beckwith.

[1] Jewers, J. R., Davis, J. B., Dougan, J., Machanda, A. H., Blunden, G., Kyi, A., and Wetchapinan, S., *Phytochemistry*, 1972, **11**, 2025.
[2] Sam, T. W., Yeu, C. S., Matsjeh, S., Gan, E. K., Razak, D., and Mohamed, A. L., *Tetrahedron Lett.*, 1987, **28**, 2541.
[3] Ahmad, F. B., Tukol, W. A., Omar, S., and Sharif, A. M., *Phytochemistry*, 1991, **30**, 2430.
[4] ElZayat, A. A. E., Ferrigni, N. R., McCloud, T. G., McKenzie, A. T., Byrn, S. R., Cassady, J. M., Chang, C. J., and McLaughlin, J. L., *Tetrahedron Lett.*, 1985. **26**, 955.
[5] Hlubucek, J. R., and Robertson, A. V., *Aust. J. Chem.*, 1967, **20**, 2199.
[6] Meyer, H. H., *Liebigs Ann. Chem.*, 1979, 484.
[7] O'Connor, B., and Just, G., *Tetrahedron Lett.*, 1986, **27**, 5201.
[8] Bennett, F., and Knight, D. W., *Tetrahedron Lett.*, 1988, **29**, 4625.
[9] Honda, T., Kametani, T., Kanai, K., Tatsuzaki, Y., and Tsubuki, M., *J. Chem. Soc., Perkin Trans. 1*, 1990, 1733.
[10] Wu, Y. C., Chang, F. R., Duh, C. Y., Wang, S. K., and Wu, T. S., *Phytochemistry*, 1992, **31**, 2851.
[11] Alkofahi, A., Ma, W. W., McKenzie, A. T., Byrn, S. R., and McLaughlin, J. L., *J. Nat. Prod.*, 1989, **52**, 1371.

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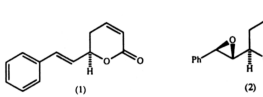
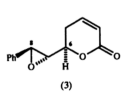
configurations and X-ray crystallographic structures however are known for (+)-5-deoxygoniopypyrone (4a), (+)-goniodiol (5) and a few other styryldihydropyrone derivatives previously isolated from the stem bark of the *Goniothalamus giganteus*.[12] (+)-Goniodiol (5), if derived from natural (+)-goniothalamin with a (6*R*)-configuration, will have a configuration of 6*R*,7*S*,8*R* while (4a) would take the configuration 6*R*,7*S*,8*S*.

Since natural (+)-goniothalamin (1) isolated from several *Goniothalamus* species[1-4] has the (6*R*)-configuration based on several synthetic studies, it should now be possible to assign the absolute configurations of several other related styryldihydropyrone derivatives which are minor natural products. This paper describes the isolation of larvicidal compounds from *G. dolichocarpus*, and examines the stereochemical relationships of (+)-goniothalamin epoxide (2), (+)-goniodiol (5) and (−)-iso-5-deoxygoniopypyrone (4b) in natural and semisynthetic samples.

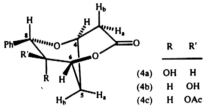


(1)

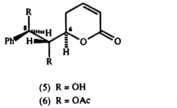
(2)



(3)



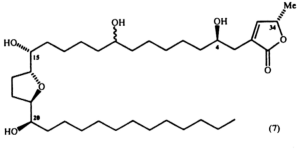
	R	R'
(4a)	OH	H
(4b)	H	OH
(4c)	H	OAc



(5) R = OH
(6) R = OAc

Results and Discussion

The ethyl acetate extract of the stem bark of *Goniothalamus dolichocarpus* showed significant toxicity to the *Aedes aegypti* mosquito larvae. Bioactivity-directed isolation provided the following bioactive compounds: (+)-goniothalamin (1), (−)-iso-5-deoxygoniopypyrone (4b), (+)-goniothalamin epoxide (2) and (+)-goniodiol (5). The ethanol extract provided the bioactive tetrahydroxy monotetrahydrofuranoid acetogenin (+)-annonacin (7).



(7)

[12] Fang, X. P., Anderson, J. E., Cheng, C. J., McLaughlin, J. L., and Fanwick, P. E., *J. Nat. Prod.*, 1991, **54**, 1034.

The structures of isolated products were elucidated by mass spectroscopy and two-dimensional n.m.r. spectrometry. The major natural product was (+)-goniothalamin (1), the *m*-chloroperoxybenzoic acid epoxidation of which provides (+)-goniothalamin epoxide (2) and (+)-isogoniothalamin epoxide (3) in the ratio of 1·8:1 respectively. The relative configuration for (+)-isogoniothalamin epoxide (3) is supported by a single-crystal X-ray structure analysis (Fig. 1), and, since the absolute configuration of (+)-goniothalamin is 6*R*, the epoxide (3) is therefore 6*R*,7*S*,8*S*. By inference (+)-goniothalamin epoxide (2) (the diastereoisomer from the expoxidation) is assigned the 6*R*,7*R*,8*R* configuration. Neither of the epoxides (2) and (3) showed high toxicity against the larvae of *Aedes aegypti* requiring a concentration of up to and more than 100 ppm (see Table 1).

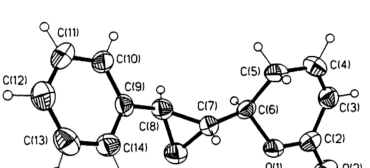


Fig. 1. A perspective view of (3).

Table 1. Larvicidal (*Aedes aegypti*) activity of compounds (1)–(3), (4b), (6) and (7)

Compound	(1)	(2)	(3)	(4b)	(6)	(7)
LC_{50} (μg/ml)	15	50–100	150–200	15–20	50–100	9·5

The mass spectrum of (4b) gave a prominent peak at m/z 234 (M). The presence of the hydroxy group was indicated by the ion m/z 216 ($M - H_2O$), and a broad absorption band at 3541 cm^{-1} in the infrared spectrum. The presence of the carbonyl group was confirmed by the presence of a band at 1736 cm^{-1} in the infrared spectrum and a resonance at δ 168·3. Compound (4b) is a new natural product as suggested by the n.m.r. spectra (^1H–^1H COSY, ^{13}C–^1H HETCOR and n.O.e. difference) of the acetylated compound (4c); the structure assigned is consistent with a stereoisomer of the known (+)-5-deoxygoniopypyrone (4a) previously isolated from *G. giganteous*.[12] N.O.e. difference spectra show n.O.e. enhancement between the phenyl protons and H 7 and H 8, these effects suggesting that H 7 and the phenyl group are in close proximity. For an assumed preferential average conformation of the phenyl group in a quasi-equatorial position H 7 and H 8 will assume a *transoid* geometry. A coupling constant of 10·4 Hz between H 7 and H 8 is in agreement of an almost antiparallel geometry of the two hydrogens. Similarly a 10·0 Hz doublet for H 8 was also observed in the ^1H n.m.r. spectrum of (4b); in contrast, a singlet is reported[12] for H 8 in compound (4a) due to an almost orthogonal H 7–H 8 orientation. In the new compound (4b) n.O.e. enhancements were observed between $H 5_b$ and H 7, and between $H 3_b$ and H 8. Since the compound is a stereoisomer of the previously isolated

(+)-5-deoxygoniopypyrone (4a) it is assigned as (−)-iso-5-deoxygoniopypyrone (4b) with a 6*R*,7*R*,8*R* configuration.

Isogoniothalamin epoxide (3) on acid hydrolysis provided (+)-(6*R*,7*S*,8*R*)-goniodiol (5), which has been previously isolated, and characterized by X-ray crystallography.[12] It is rationalized that this diol undergoes an internal Michael addition to provide the presently isolated (−)-iso-5-deoxygoniopypyrone (4b).[13] While it is noted that (4b) is formed from a precursor derived from *trans* dihydroxylation of goniothalamin, the previously reported[12] (4a) requires a precursor derived from a formal *cis* hydroxylation. It is therefore noted that there can be considerable stereochemical diversity in styryldihydropyrone derivatives, and it is possible that the stereochemical assignments to structures for some reported styrylpyrone derivatives[2–4,10] are in need of revision.

The molecular weight of (7) was determined to be 596 by e.i. mass spectrometry. The e.i. mass spectrum of the trimethylsilyl derivative of (7), obtained from reacting (7) with 'bis(trimethylsilyl)trifluoroacetamide', gave an M of 884, which indicates a tetrakis(trimethylsilyl) derivative and suggests that (7) has four hydroxy groups. Also, the c.i. mass spectrum gave fragments confirming that (7) has four hydroxy groups, at C4, C10, C15 and C20. The ^{1}H n.m.r. spectrum indicated an unsaturated lactone ring having a methyl group at C34: (δ 1·44, d, J 6·8 Hz), and a CH_2 at C3 (δ 2·38, dd, $J_{3a,3b}$ 15·1, $J_{3a,4}$ 7·8 Hz, and 2·51, dd, $J_{3b,3a}$ 15·1, $J_{3b,4}$ 3·9 Hz). The ^{1}H n.m.r. spectrum also indicated a terminal methyl group, δ 0·85, t, $J_{32,31}$ 6·6 Hz, at C32. The optical rotation together with the spectral data indicate that the compound is likely to be (+)-annonacin (7) also isolated previously from *Annona densicoma*[14] and *Goniothalamus giganteus*.[15]

Experimental

General

^{1}H and ^{13}C n.m.r. spectra were recorded on a Jeol JNM-GSX 270 Fourier-transform spectrometer by using $CDCl_3$ as solvent. Mass spectra were measured on VG Prospec, VG 7070 and VG ZAB-2SEQ spectrometers. Melting points are uncorrected. Optical rotations were determined on a Jasco DIP 370 digital polarimeter.

Plant Material

The stem bark of *G. dolichocarpus* was collected from Sarawak, East Malaysia. Identification (voucher specimen No. 105) was carried out at the Herbarium, Forest Department Headquarters, Kuching, Sarawak, where voucher specimens were deposited.

Bioassays

Bioassay tests on *Aedes aegypti* larvae were carried out typically at 5-200 ppm concentration of compounds in 1% EtOH/H_2O. The cytotoxicity tests were performed according to standard protocols from the World Health Organization.[16]

[13] Zhou, W. S., and Yang, Z. C., *Tetrahedron Lett.*, 1993, **34**, 7075.
[14] McCloud, T. G., Smith, D. L., Chang, C. J., and Cassady, J. M., *Experientia*, 1987, **43**, 947.
[15] Alkofahi, A., Rupprecht, J. K., Smith, D. L., Chang, C. J., and McLaughlin, J. L., *Experientia*, 1988, **44**, 83.
[16] World Health Organization—Instructions for Determining the Susceptibility or Resistance of Mosquito Larvae to Insecticides (WHO/VBC/81.807).

Extraction and Isolation

The dried ground bark (1 kg) of *Goniothalamus dolichocarpus* was extracted with ethyl acetate for more than 48 h. Goniothalamin (1) (4 g) was recrystallized from the residue of the crude extract (44 g). The mother liquor was then separated by column chromatography (Merck Kieselgel 60) to give (−)-iso-5-deoxygoniopypyrone (4b) (250 mg), (+)-goniothalamin epoxide (2) (200 mg) and (+)-goniodiol (5) (10 mg). (−)-Iso-5-deoxygoniopypyrone (4b) was acetylated with Ac_2O/pyridine at room temperature for 24 h and the mixture purified by SiO_2 preparative layer chromatography.

Another sample (1·16 kg) of the bark of the *G. dolichocarpus* was extracted with ethanol, and after concentration the extract was partitioned between $CHCl_3$ and water. The $CHCl_3$-soluble fraction was further partitioned between hexane and MeOH/H_2O (9:1). The methanol-soluble fraction (29 g) was then separated by SiO_2 column chromatography and preparative layer chromatography to give the tetrahydroxy monotetrahydrofuranoid acetogenin (+)-annonacin (7) (80 mg).

(+)-Goniothalamin (1), m.p. 83–84°C (lit.[1] 85°C), $[\alpha]_D^{20}$ +193·2° (*c*, 1·0 in $CHCl_3$) (lit.[1] +178·5°), ^{13}C n.m.r., ^1H n.m.r., and mass spectroscopic values are in agreement with reported data.[2,1]

(−)-Iso-5-deoxygoniopypyrone acetate (4c), $[\alpha]_D^{20}$ −170·47° (*c*, 1·0 in $CHCl_3$), m.p. 140–142°C. ^1H n.m.r. (270 MHz, $CDCl_3$) δ 4·82, dd, $J_{7,8}$ 10·4, $J_{7,6}$ 2·0 Hz, H 7; 4·68, d, $J_{8,7}$ 10·4 Hz, H 8; 5·02, ddd, $J_{6,7}$ 2·0, $J_{6,5a}$ 4·4, $J_{6,5b}$ 3·9 Hz, H 6; 2·33, dddd, $J_{5b,5a}$ 14·2, $J_{5b,6}$ 3·9, $J_{5b,3a}$ 2, $J_{5b,4}$ 2 Hz, H 5_b; 2·20, ddd, $J_{5a,5b}$ 14·2, $J_{5a,6}$ 4·4, $J_{5a,4}$ 2·0 Hz, H 5_a; 2·95, d, $J_{3b,3a}$ 19·5 Hz, H 3_b; 3·06, ddd, $J_{3a,3b}$ 19·5, $J_{3a,4}$ 2, $J_{3a,5b}$ 2 Hz, H 3_a; 4·52, ddd, $J_{4,3a}$ 2, $J_{4,5b}$ 2, $J_{4,5a}$ 2 Hz, H 4; 1·94, s, OAc; 7·34, m, Ph. ^{13}C n.m.r. (67·8 MHz, $CDCl_3$) δ 20·4 (OAc), 29·4 (C 5), 36·2 (C 3), 65·9 (C 4), 71·0 (C 8), 72·8 (C 7), 73·8 (C 6), 127·0 (C 2′, C 6′), 128·6 (C 3′, C 5′), 128·3 (C 4′), 136·9 (C 1′), 168·3 (C=O), 169·4 (C=O, OAc). E.i. mass spectrum m/z 233 (52%, M − CH_3CO), 216 (34, M − CH_3COOH), 172 (88), 127 (32), 107 (61), 91 (37), 77 (38), 69 (19), 43 (100).

(−)-Iso-5-deoxygoniopypyrone (4b). ^1H n.m.r. (270 MHz, $CDCl_3$) δ 4·79, br s, H 6; 4·39, d, $J_{8,7}$ 10·0 Hz, H 8; 4·34, m, H 4; 3·71, br s, 7-OH; 3·41, br d, $J_{7,8}$ 10·0 Hz, H 7; 2·88, d, $J_{3b,3a}$ 19·1 Hz, H 3b; 2·78; dd, $J_{3a,3b}$ 19·1, $J_{3a,4}$ 4·8 Hz, H 3a; 2·10, br s, H 5a and H 5b; 7·33, m, Ph. E.i..mass spectrum m/z 234 (29%, M), 216 (2, M − H_2O), 177 (8), 144 (9), 128 (24), 107 (100), 91 (19), 79 (20), 77 (19). High-resolution e.i. mass spectrum m/z 234·0898 ($C_{13}H_{14}O_4$ requires 234·0892).

(+)-Annonacin (7), m.p. 54–56°C (lit.[14] 57°C), $[\alpha]_D^{20}$ +2·4° (*c*, 1·0 in $CHCl_3$) (lit.[14] +1·4°). ^{13}C n.m.r., ^1H n.m.r. and mass spectroscopic values are in agreement with reported data.[14]

Goniothalamin Epoxides

Goniothalamin (1) (50 mg, 0·34 mmol) in 10 ml of CH_2Cl_2 was epoxidized with *m*-chloroperoxybenzoic acid (72 mg, 0·42 mmol) over 24 h at room temperature. After washing the ether extract with $NaHCO_3$ and drying with K_2CO_3, a crude product (47 mg, 80%), consisting of a mixture of approximately 1·8:1·0 goniothalamin epoxide (2) and isogoniothalamin epoxide (3) was obtained. Goniothalamin epoxide (2) (m.p. 89°C, lit.[2] 90–94°C) was fractionally crystallized as plates from CH_2Cl_2/cyclohexane mixtures. Similarly, isogoniothalamin epoxide (3) (m.p. 108–110°C, lit.[2] 111–114°C) was fractionally crystallized as needles.

(+)-Goniothalamin epoxide (2), m.p. 89°C (lit.[2] 90–94°C), $[\alpha]_D^{20}$ +128·4° (*c*, 1·0 in $CHCl_3$) (lit.[2] +100·7°). ^1H n.m.r., ^{13}C n.m.r., and mass spectroscopic values are in agreement with reported data.[2]

Isogoniothalamin epoxide (3) crystals were subjected to a single-crystal X-ray crystallographic structure analysis for stereochemical determination. The crystal was colourless needle, 0·1 by 0·18 by 0·2 mm, and the intensities were measured with Mo Kα radiation (λ 0·71073 Å). The space group is $P\,2_1;2_1;2_1$, M_r 216·24, *a* 6·1158(4), *b* 7·3408(4), *c* 24·91(2) Å, R_F 0·029, *Z* 4, $F(000)$ 456, D_c 1·284 g cm^{-3}. The scan type was ω–2θ. 1139 unique data is measured; 449 observed data with $I > 3\sigma(I)$ were used for the structure analysis. The number of reflections measured 4342; number of independent reflections 1139; number of observed reflections

449 [$>3\sigma(I)$]; R 0·029; R_w ($w = [\sigma(F)^2]^{-1}$) 0·034; (shift/e.s.d.)$_{max}$ 0·01; $\Delta\rho_{max}$ 0·124 e/Å^3. Hydrogen atoms were generated geometrically and refined isotropically. The lengths of the molecules are packed running parallel to the c-axis. The structure was solved by the direct method MULTAN (Fig. 1 and Tables 2–4).*

Table 2. Atomic coordinates, and equivalent temperature factors (B in Å^2)

Atom	x	y	z	B [A]	Atom	x	y	z	B [B]
O(1)	0·5083(5)	−0·0044(6)	0·2593(1)	3·93(8)	H(3)	0·108(8)	−0·029(7)	0·174(2)	7(1)
O(2)	0·5259(6)	−0·0256(6)	0·1716(1)	5·28(9)	H(4)	−0·079(6)	0·041(6)	0·251(1)	5(1)
O(3)	0·6990(5)	−0·1202(6)	0·3628(1)	4·93(9)	H(5a)	0·074(6)	0·002(6)	0·332(1)	4(1)
C(2)	0·4119(8)	−0·0185(8)	0·2106(2)	3·9(1)	H(5b)	0·191(8)	0·194(6)	0·313(2)	6(1)
C(3)	0·1733(8)	−0·0178(9)	0·2096(2)	4·3(1)	H(6)	0·355(6)	−0·171(5)	0·306(1)	3(1)
C(4)	0·0596(8)	0·023(1)	0·2521(2)	4·9(2)	H(7)	0·563(6)	0·132(7)	0·359(1)	5(1)
C(5)	0·1650(7)	0·0525(8)	0·3051(2)	4·4(1)	H(8)	0·435(5)	−0·214(4)	0·398(1)	0·4(7)
C(6)	0·3778(8)	−0·0479(8)	0·3067(2)	3·3(1)	H(10)	0·286(7)	−0·156(7)	0·487(1)	4(1)
C(7)	0·5163(8)	−0·0014(9)	0·3535(2)	3·6(1)	H(11)	0·361(6)	−0·059(6)	0·574(1)	4(1)
C(8)	0·5218(9)	−0·1191(8)	0·4007(2)	3·9(1)	H(12)	0·676(7)	0·102(6)	0·596(1)	5(1)
C(9)	0·5645(7)	−0·0539(8)	0·4559(2)	3·3(1)	H(13)	0·911(7)	0·157(6)	0·526(1)	4(1)
C(10)	0·4147(8)	−0·0871(9)	0·4953(2)	4·0(1)	H(14)	0·848(5)	0·068(5)	0·444(1)	1·2(7)
C(11)	0·4543(9)	−0·0317(9)	0·5470(2)	5·2(2)					
C(12)	0·6444(9)	0·056(1)	0·5594(2)	5·3(2)					
C(13)	0·7940(9)	0·0900(8)	0·5205(2)	5·0(2)					
C(14)	0·7534(9)	0·0369(8)	0·4684(2)	4·4(1)					

[A] Atoms were refined anisotropically. The isotropic equivalent displacement parameter is defined as: $(4/3)[a^2B(1,1)+b^2B(2,2)+c^2B(3,3)+ab(\cos\gamma)B(1,2)+ac(\cos\beta)B(1,3)+bc(\cos\alpha)B(2,3)]$.
[B] Atoms were refined isotropically.

Table 3. Non-hydrogen bond distances (Å)

Atoms	Distance	Atoms	Distance	Atoms	Distance
O(1)–C(2)	1·355(8)	C(3)–C(4)	1·30(1)	C(9)–C(10)	1·367(9)
O(1)–C(6)	1·462(8)	C(4)–C(5)	1·49(1)	C(9)–C(14)	1·37(1)
O(2)–C(2)	1·198(8)	C(5)–C(6)	1·50(1)	C(10)–C(11)	1·37(1)
O(3)–C(7)	1·435(9)	C(6)–C(7)	1·48(1)	C(11)–C(12)	1·36(1)
O(3)–C(8)	1·438(9)	C(7)–C(8)	1·46(1)	C(12)–C(13)	1·36(1)
C(2)–C(3)	1·459(9)	C(8)–C(9)	1·479(9)	C(13)–C(14)	1·38(1)

Table 4. Non-hydrogen interatomic angles (degrees)

Atoms	Angle	Atoms	Angle
C(2)–O(1)–C(6)	118·1(6)	O(3)–C(7)–C(6)	115·6(7)
C(7)–O(3)–C(8)	61·1(5)	O(3)–C(7)–C(8)	59·6(5)
O(1)–C(2)–O(2)	118·6(7)	C(6)–C(7)–C(8)	120·8(8)
O(1)–C(2)–C(3)	116·7(8)	O(3)–C(8)–C(7)	59·4(5)
O(2)–C(2)–C(3)	124·6(8)	O(3)–C(8)–C(9)	118·7(7)
C(2)–C(3)–C(4)	121·4(9)	C(7)–C(8)–C(9)	124·2(8)
C(3)–C(4)–C(5)	121·8(8)	C(8)–C(9)–C(10)	119·6(7)
C(4)–C(5)–C(6)	109·2(8)	C(8)–C(9)–C(14)	121·3(6)
O(1)–C(6)–C(5)	110·2(7)	C(10)–C(9)–C(14)	119·1(7)
O(1)–C(6)–C(7)	106·0(6)	C(9)–C(10)–C(11)	120·3(8)
C(5)–C(6)–C(7)	113·9(8)	C(10)–C(11)–C(12)	120·1(8)
C(11)–C(12)–C(13)	120·0(8)	C(9)–C(14)–C(13)	120·4(8)
C(12)–C(13)–C(14)	120·0(9)		

* Material deposited consists of anisotropic displacement parameters, full molecular geometries, and lists of structure factors (copies are available from the Australian Journal of Chemistry, P.O. Box 89, East Melbourne, Vic. 3002).

Goniodiol Diacetate (6)

Isogoniothalamin epoxide (3) (82·5 mg) in 8 ml of ether was stirred with 1 M perchloric acid (2 ml) at room temperature for 1 h. After drying with K_2CO_3 and removal of ether, 79 mg (85% yield) of (+)-goniodiol (5) was obtained. The diol (78 mg) was acetylated with Ac_2O/pyridine to give 101 mg (94% yield) of the diacetate (6) (m.p. 140°C, lit.[12] 141–143°C). (+)-Goniodiol diacetate (6), m.p. 140°C (lit.[12] 141–143°C), $[\alpha]_D^{25}$ +51·6° (*c*, 1·0 in $CHCl_3$). ^{13}C n.m.r. (67·8 MHz, $CDCl_3$) δ 20·3 (OAc), 21·0 (OAc), 26·1 (C5), 72·3 (C8), 73·5 (C7), 74·6 (C6), 121·4 (C3), 127·4 (C2′, C6′), 128·4 (C3′, C5′), 128·7 (C4′), 136·5 (C1′), 144·2 (C4′), 162·9 (C2′), 169·0 (OAc), 169·8 (OAc), 26·1 (C4). ^1H n.m.r. values are in agreement with reported data.[12] E.i. mass spectrum *m/z* 258 (12%, M − CH_3COOH), 233 (38, M − $2CH_3CO$+1), 216 (43), 172 (48), 152 (55), 149 (17), 128 (22), 127 (46), 120 (31), 110 (55), 107 (65), 105 (57), 97 (23), 91 (46), 89 (10), 82 (55), 79 (32), 77 (45), 43 (100).

Acknowledgments

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5β-HYDROXYGONIOTHALAMIN, A STYRYLPYRONE DERIVATIVE FROM *GONIOTHALAMUS DOLICHOCARPUS* (ANNONACEAE)

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Abstract : A new styrylpyrone derivative (+)-5β-hydroxygoniothalamin (1) was isolated from the stem bark of *Goniothalamus dolichocarpus*. The structure and stereochemistry of (1) and its diastereoisomer (+)-5α-hydroxygoniothalamin (2) were established by NMR spectra, X-ray crystallography and partial synthesis.

Key words : *Goniothalamus dolichocarpus*, styrylpyrones, 5-hydroxygoniothalamin.

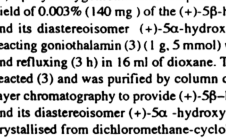
INTRODUCTION

Goniothalamus, a genus of shrubs and trees of the Annonaceae is found in Southeastern Asia and throughout Malaysia. A number of *Goniothalamus* species have been used for timber and medicinal purposes[1]. *Goniothalamus dolichocarpus* (Annonaceae) is endemic in Sarawak, Malaysia. The timber is aromatic. The trees grow up to about two metres tall with up to a six centimetre girth. They thrive in light shade and hilly areas of the secondary forests of Sarawak. The stem bark is burnt by the natives to repel insects especially mosquitoes. Several styrylpyrone derivatives have been isolated from *Goniothalamus* species[2-5]. Of these, goniothalamin (3) is usually prominent. We report here the isolation and characterization of a new goniothalamin derivative (+)-5β-hydroxygoniothalamin (1) and its preparation together with its diastereoisomer (+)-5α-hydroxygoniothalamin (2).

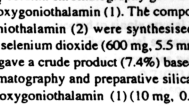
RESULTS AND DISCUSSION

The styrylpyrone (+)-5β-hydroxygoniothalamin (1) was isolated from the stem bark of *Goniothalamus dolichocarpus* as a yellow oil[6]. Column chromatography of 44 g of the crude ethyl acetate extract of the stem bark of *Goniothalamus dolichocarpus* through silica gel 60 (80-100 mesh) with solvent mixtures of increasing polarity

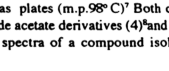
(hexane, hexane-chloroform, chloroform and chloroform- methanol) gave the crude (+)-5β-hydroxygoniothalamin. Repeated SiO_2-column chromatography gave a total yield of 0.003% (140 mg) of the (+)-5β-hydroxygoniothalamin (1). The compound and its diastereoisomer (+)-5α-hydroxygoniothalamin (2) were synthesised by reacting goniothalamin (3) (1 g, 5 mmol) with selenium dioxide (600 mg, 5.5 mmol) and refluxing (3 h) in 16 ml of dioxane. This gave a crude product (7.4%) based on reacted (3) and was purified by column chromatography and preparative silica gel layer chromatography to provide (+)-5β–hydroxygoniothalamin (1) (10 mg, 0.6%) and its diastereoisomer (+)-5α -hydroxygoniothalamin (2) (116 mg, 6.8 %). (2) crystallised from dichloromethane-cyclohexane as plates (m.p.98° C)[7] Both compounds were acetylated (Ac_2O/pyridine) to provide acetate derivatives (4)[8]and (5)[9], the former having identical ^1H and ^{13}C NMR spectra of a compound isolated previously[2] from *Goniothalamus uvaroides*.



(1) R=OH, R'=H
(2) R=H, R'=OH
(3) R=R'=H
(4) R=OAc, R'=H
(5) R=H, R'=OAc



(6)



(7)

^1H-^1H COSY, ^1H-^{13}C HETCOR and NOE difference spectra were used to obtain the following structural assignments :-

(a) A coupling constant of 2.9 Hz between H-5 and H-6 of (1) indicates a dihedral angle of approximately 50°. Moreover, the acetate derivative (4) also shows a similar $J_{5,6}$ coupling of 2.9 Hz.

(b) A coupling constant of 8 Hz between H-5 and H-6 in the diastereomeric alcohol (2) indicates the two protons are approximately of diaxial orientation. Similarly a relatively large value of 6 Hz was observed for the acetate derivative (5).

(c) There is also an NOE difference enhancement between H-7 and H-5 in (2) but not in (1). NOE interactions were also observed between H-7 and H-5 in the acetate derivative (5). H-5 and H-7 thus assumes the diaxial geometry. With the absolute configuration of (+)-6*R*-goniothalamin known[10], the absolute configurations of natural (+)-5β-hydroxygoniothalamin (1) and its acetate (4) can be assigned 5*S*, 6*S* while the semisynthetic (2) and (5) is 5*R*, 6*S*.

(d) There is observed a long-range coupling (J=2.0 Hz) between H-3 and H-5 in 5α-

hydroxy compound (2). This small coupling (J=1.0 Hz) was also observed in the acetate derivative (5).

(e) (+)-5α-Hydroxygoniothalamin (2) crystals were subjected to single crystal X-ray crystallography for stereochemical determination. The crystal system is orthorhombic, crystal size, 0.20 x 0.30 x 0.50 mm^3 and the intensities were measured with MoKα graphite-monochromatized radiation (λ=0.71073A). The space group is $P2_12_12_1$ (No.19), M_r 216.2, a=4.838(1)A, b=5.959(1), c=39.023(8), V=1124.9(4)A^3, Z=4, F(000)=456, R_f=0.045, D_c=1.28 gcm^{-3}. The scan type was ω–scan; 3.00-30.00 deg min^{-1}. 1018 unique data was measured, observed data with $|F_o| >= 4\sigma (|F_o|)$, n 702. $wR=[\Sigma w (|F_o| - |F_c|)^2 / \Sigma w |F_o|^2]^{1/2}$ 0.044 (Fig 1). Raw intensities were collected on a Siemens P4/PC four-circle diffractometer at room temperature (291°K). The crystal structure was solved by direct phase determination . All non-hydrogen atoms were subjected to anisotropic refinement . The hydrogen atom of the hydroxy group was located on a difference Fourier map, and the other hydrogen atoms were generated geometrically (C-H bonds fixed at 0.96 A) and allowed to ride on their respective parent C atoms; they were assigned the same isotropic temperature factors (U=0.08 A^2) and included in the structure-factor calculations. Computations were performed using the SHELTXL PC program package[11, 12] on a PC 486 computer. Analytic expressions of atomic scattering factors were employed, and anomalous dispersion corrections were incorporated[13].

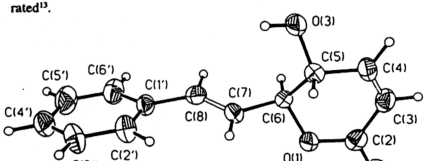


Figure 1. A perspective view of (2)

(f) The configuration of (2) is hence 5*R*, 6*S*. An intermolecular hydrogen bond is formed between O(3) and O(2a) (a=-1+x,1+y,z)with O(3)...O(2a)=2.833 A, H(30)...O(2a)=1.962 A, C(5)-O(3)...O(2a)=123.7°, C(2a)-O(2a)...O(3)=136.4°, and O(3)-H(3O)...O(2a)=158.6° (detailed X-ray data is available on request).

The finding of (1) as a simple hydroxylated derivative of the more abundant goniothalamin (3) makes it likely that a possible intermediate 5β-hydroxygoniotha-

lamin epoxide (6) can arise to provide (after hydroxyl attack on the epoxide) known natural products such as isoaltholactone (7) and goniopypyrone[14,15] reported previously from some *Goniothalamus* species.

REFERENCES AND NOTES

1. I.H. Burkill (1966) *A Dictionary of the Economic Products of the Malay Peninsula*, Vol. 1, Ministry of Agriculture and Cooperatives, Kuala Lumpur, Malaysia. p 1097.

2. F.B. Ahmad, W.A. Tukol, S. Omar and A.T. Sharif (1991) 5-Acetylgoniothalamin, a styryl dihydropyrone from *Goniothalamus uvaroides*. *Phytochemistry* **30**, 2430-2431.

3. J.R. Jewers, J.B. Davis , J. Doughan, A.H. Machanda, G. Blunden, A. Kyi and S. Wetchapinan, (1972) Goniothalamin and its distribution in four *Goniothalamus* species. *Phytochemistry* **11**, 2025.

4. T.W. Sam, C.S. Yeu, S. Matsjeh, E.K. Gan, D. Razak and A.L. Mohamad, (1988). Goniothalamin epoxide: an embryotoxic compound from *Goniothalamus macrophyllus* (Annonaceae). *Tetrahedron Lett.* **28**, 2542-2544.

5. A.A.E. Elzayat, N.R. Ferrigni, T.G. McCloud, A.T. Mckenzie, S.R. Byrn, J.M. Cassady, C.J. Chang and J.L. McLaughlin (1985) Goniothalenol: a novel, bioactive, tetrahydrofurano-2-pyrone from *Goniothalamus giganteus* (Annonaceae). *J. Nat. Prod.* **26**, 955-956.

6. (+)-5β-Hydroxygoniothalamin (1) $[\alpha]_D^{20}$= +79° (c, 0.2, $CHCl_3$), ^1H NMR (270 MHz, $CDCl_3$) δ: 6.81, br d, $J_{7,8}$ 16.1 Hz, H-8; 6.31, dd, $J_{6,7}$ 6.4 Hz, $J_{7,8}$ 16.1 Hz, H-7; 5.03, ddd, $J_{6,5}$ 2.9 Hz, $J_{6,7}$ 6.4 Hz, $J_{6,8}$ 1.5 Hz, H-6; 4.25, m, H-5; 2.10, br s, 5-OH; 6.97, dd, $J_{4,5}$ 5.4 Hz, $J_{3,4}$ 9.8 Hz, H-4; 6.12, d, $J_{3,4}$ 9.8 Hz ,H-3; 7.30, m, Ph. ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 63.1 (C-OH), 80.9 (C-6), 121.5 (C-3), 123.0 (C-8), 126.8 (C-2', C-6'), 128.6 (C-4'), 128.7 (C-3', C-5'), 135.3 (C-7), 135.6 (C-1'), 144.4 (C-4), 163.0 (C-2). EIMS: m/z (%) M⁺216(6.8), 198 (71.6), 170 (35.4), 155 (21.9), 141 (50.5), 128 (21.3), 115 (100), 105 (20.9). HREIMS: 216.0787 for $C_{13}H_{12}O_3$ (calcd 216.0786).

7. (+)-5α-Hydroxygoniothalamin (2) m.p. 98°C $[\alpha]_D^{20}$=+18° (c, 0.3, $CHCl_3$) ^1H NMR (270 MHz, $CDCl_3$) δ:5.97, dd, $J_{4,3}$ 9.8 Hz, $J_{3,5}$ 2.0 Hz, H-3; 6.83, dd, $J_{4,3}$ 9.8 Hz, $J_{4,5}$ 2.0 Hz, H-4; 4.36, m, H-5; 2.35, d, J 4.4 Hz, 5-OH; 4.80, ddd, $J_{5,6}$ 8.0 Hz, $J_{7,6}$ 7.3 Hz, $J_{6,8}$ 1.5 Hz, H-6; 6.17, dd, $J_{7,6}$ 7.3 Hz, $J_{7,8}$ 15.6 Hz, H-7; 6.74, br d, $J_{7,8}$ 15.6 Hz, H-8; 7.29, m, Ph. ^{13}C NMR (67.8 MHz, $CDCl_3$) δ:66 (C-OH),

83.3 (C-6), 120.8 (C-3), 123.0 (C-8), 126.8 (C-2', C-6'), 128.7 (C-4'), 128.8 (C-3', C-5'), 135.3 (C-7), 135.8 (C-1'), 148.0 (C-4), 162.6 (C-2). EIMS : m/z (%) M^+ 216 (9.8), 198 (62.0), 170 (43.0), 155 (43.2), 154 (40.2), 141 (59.1), 128 (48.2), 115(10.0), 105(50.4). HREIMS: 216.0785 for $C_{13}H_{12}O_3$(calcd 216.0786).

8. (-)-5β-Acetoxygoniothalamin (4)$[\alpha]_D^{20}$=-372° (c, 0.2, $CHCl_3$), (Lit[2] -325°) ^1H NMR, ^{13}C NMR and MS values are in agreement with reported data.[2]

9. (-)-5α-Acetoxygoniothalamin (5) m.p. 88°C $[\alpha]_D^{20}$=-150° (c, 0.2, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ: 6.05, dd, $J_{3,4}$ 10.0 Hz, $J_{3,5}$ 1.0 Hz, H-3; 6.75, dd, $J_{4,3}$ 10.0 Hz, $J_{4,5}$ 3.0 Hz, H-4; 5.39, ddd, $J_{5,3}$ 1.0 Hz, $J_{4,5}$ 3.0 Hz, $J_{5,6}$ 6.0 Hz, H-5; 2.05, s, OAc; 5.05, ddd, $J_{5,6}$ 6.0Hz, $J_{6,7}$ 6.4 Hz, $J_{6,8}$ 1.0 Hz, H-6; 6.11, dd, $J_{6,7}$ 6.4 Hz, $J_{7,8}$ 16.0 Hz, H-7; 6.67, dd, $J_{7,8}$ 16.0 Hz, $J_{6,8}$ 1.0 Hz, H-8; 7.28, m, Ph. ^{13}C NMR (67.8 MHz, $CDCl_3$) δ: 20.8 (CH_3), 66.2 (C-5), 80.6 (C-6), 122.5 (C-3), 123.6 (C-8), 126.8 (C-2',C-6'), 128.6 (C-4'), 128.7 (C- 3', C-5'), 135.3 (C-7), 135.4 (C-1'), 142.1 (C-4), 161.7 (C-2), 169.9 (CH_3). EIMS : m/z (%) 198 (77), 133 (33), 126 (31), 115 (13), 84 (100), 77 (14), 44 (79).

10. J.R. Hlubucek and A.V. Robertson (1967) (+)-(5S)-δ-Lactone of 5-hydroxy-7-phenylhepta-2, 6-Dienoic Acid, a natural product from *Cryptocarya caloneura* (Scheff.) Kostermans. *Aust. J. Chem.*. **20**, 2199-2206.

11. G. M. Sheldrick (1985) In *Crystallographic Computing 3: Data collection, Structure Determination, Proteins, and Databases*, G. M. Sheldrick, C. Kruger and R. Goddard, eds., Oxford University Press, New York. pp. 175-189.

12. G. M. Sheldrick, (1990) SHELXTL PC Manual, Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin,U.S.A.

13. International Tables for X-ray Crystallography (1974) Vol. IV, Kynoch Press, Birmingham. pp 55, 99, 149. (Now distributed by Kluwer Academic Publishers, Dordrecht).

14. S.M. Colegate, L. Din, A. Latiff, K.M. Salleh, M.W. Shamsudin, B.W. Skelton, K.I. Tadano, A.H. White and Z. Zakaria, (1990) (+)-Isoaltholactone: A furanopyrone isolated from *Goniothalamus species*. *Phytochemistry* **29**, 1701-1704.

15. X.P. Fang, J.E. Anderson, C.J. Cheng and J.L. McLaughlin (1991) Two new styrylactones, 9-deoxygoniopypyrone and 7-epi-goniofufurone, from *Goniothalamus giganteus*. *J. Nat. Prod.* **54**, 1034-1043.