Total Synthesis of Styryl-lactones and Related Compounds

by Mr. TSUI Hon-Chung, B.Sc.(Hons.)
(徐漢忠)

A thesis submitted to
the Chemistry Division, Graduate School,
the Chinese University of Hong Kong
in partial fulfilment of the requirements
for the degree of
Master of Philosophy

(1993)

Thesis Committee :

Dr. H. N. C. Wong (Chairperson)
Dr. T. K. M. Shing
Dr. H. F. Chow
Professor J. K. Sutherland (External Examiner)

Abstract

Syntheses of a number of styryl-lactones with various structural complexities are accomplished from the inexpensive and commercially available D-*glycero*-D-*gulo*-heptono-γ-lactone **32**. This work first focused on the absolute configuration proof for the goniofufurone from D-*glycero*-D-*gulo*-heptono-γ-lactone **32** using sequential Wittig and Michael reactions as the key steps. The absolute stereochemistry of the (+)-goniofufurone is established as **21b**. Synthesis of (+)-goniofufurone **21b** is also accomplished from D-*glycero*-D-*gulo*-heptono-γ-lactone **32** using the same Wittig and Michael strategy. Work on the total syntheses of (+)-altholactone **14**, (+)-goniotriol **16**, (+)-7-acetylgoniotriol **20**, (+)-goniopypyrone **22**, (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27** has also been completed from D-*glycero*-D-*gulo*-heptono-γ-lactone **32**. This work also provides a method for the syntheses of the enantiomers of the above styryl-lactones from D-*glycero*-D-*gulo*-heptono-γ-lactone **32** for biological evaluation. Suggestions about the possible biosynthetic pathway of the styryl-lactones are also given in this work. The pyrone intermediates **16** and **52** are proposed to be the key intermediates for their biosynthesis. Rearrangement of the (+)-goniotriol **16** to the (+)-goniofufurone **21b** under basic conditions also suggests that the butenolides **49** and **62** may be the key intermediates for the five-membered lactone analogs.

Acknowledgements

I would like to express my sincere thanks to my supervisor, Dr. Tony K. M. Shing, for his invaluable advice, guidance and encouragement in the past two years. Thanks are given to Dr. Zhou Zhao-Hui who worked as my partner in this project. Special thanks are due to Messrs Law Yiu-Hung and Kwong Kwok-Wai for their assistance in recording either NMR or MS spectra. Thanks are also given to my collaborators and graduate students in the chemistry department for providing both a pleasant working and playing environment. Finally, I am grateful to the Hong Kong RGC for financial support for the past two years.

May, 1993

Mr. TSUI Hon-Chung

Chemistry Department

The Chinese University of

Hong Kong

Biography

The author graduated with a second class upper honours in the chemistry department at the Chinese University of Hong Kong in 1990 and then became a full-time teaching assistant in the chemistry department at the same university. In 1991, he received a studentship for reading a Master of Philosophy in organic chemistry under the supervision of Dr. Tony K. M. Shing.

Contents

Abbreviations

Ac	acetyl
aq.	aqueous
AIBN	2,2'-azobis(2-methylpropanenitrile)
9-BBN	9-borabicyclo[3.3.1]nonane
Bn	benzyl
Bz	benzoyl
CI	chemical ionization
MCPBA	*m*-chloroperbenzoic acid
℃	degree Celsius
d	day(s)
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N,N'*-dicyclohexylcarbodiimide
DIBAL-H	diisobutylaluminum hydride
DMAP	4,4'-dimethylaminopyridine
DMF	*N,N'*-dimethylformamide
DMSO	dimethylsulfoxide
EI	electron ionization
Et	ethyl
h	hour(s)
i.r.	infrared
Me	methyl
m/z	mass per unit charge
m.p.	melting point
min	minute(s)
Ms	methanesulfonyl
MS	mass spectra
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance

PCC	pyridinium chlorochromate
Ph	phenyl
r.t.	room temperature
t.l.c.	thin layer chromatography
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl

1. Introduction

The shrubs and trees of the genus *Goniothalamus*, which grow in Asia, have been used for timber, as fibre sources, and for ornamental purposes for many years.[1] Their chemotherapeutic usefulness was also recognized early in the past. For examples, the extracts of the seeds of *Goniothalamus amuyon* (Blanco) Merr. (Annonaceae) in the coastal regions of Taiwan have been used for the treatment of edema and rheumatism.[2] The leaves of *Goniothalamus sesquipedalis* Wall (Annonaceae) growing abundantly in the hilly regions of Manipur, when dried and powdered, have been used by local women during labor pain and the burning leaves have been used as mosquito repellant.[3] *Goniothalamus macrophyllus* (Bl.) Hook fil. & Thomas (Annonaceae) was used as an abortifacient in rural areas of North Malaysia.[4]

Recent bioactivity-directed studies by several research groups on the constituents of these plants led to the discovery, isolation and characterization of a number of novel styryl-lactones which were also tested to possess significant cytotoxicities against several human tumors.[2,14,15,17,19,28]

In the following sections, a brief review on the isolation and characterization of styryl-lactones is presented. Then some efforts made by our group and by others towards the total synthesis and the confirmation of the absolute configurations for some of these natural compounds are discussed. Finally, biosynthetic pathways for these styryl-lactones are hypothesized.

1.1 Styryl-lactones from *Piper* genus

The chemistry of naturally occurring styryl-lactones with the basic C_6–C_3–C_4 skeleton could be traced back to the isolation of kawain **1** from the *Piper* genus.[5] Continuous investigation of the *Piper* genus led to the discovery of other styryl-

lactones, including the 5-acetoxy-6-methoxykawain **2**, piperolide **3**, methylenedioxypiperolide **4**, (+)-(7*S*,8*S*)-epoxypiperolide **5**, (–)-*erythro*-7,8-dihydro-7,8-dihydroxylpiperolide **6** and (5*E*)-piperolide **7** from *Piper sanctum*. (+)-(5*S*,6*S*)-4,5-Dimethyl-6-(3',4'-methylenedioxystyryl)-2-pyrone **8** together with **2** were also obtained from *Piper fadyenolii*. The structures of the above styryl-lactones are illustrated in Figure 1.

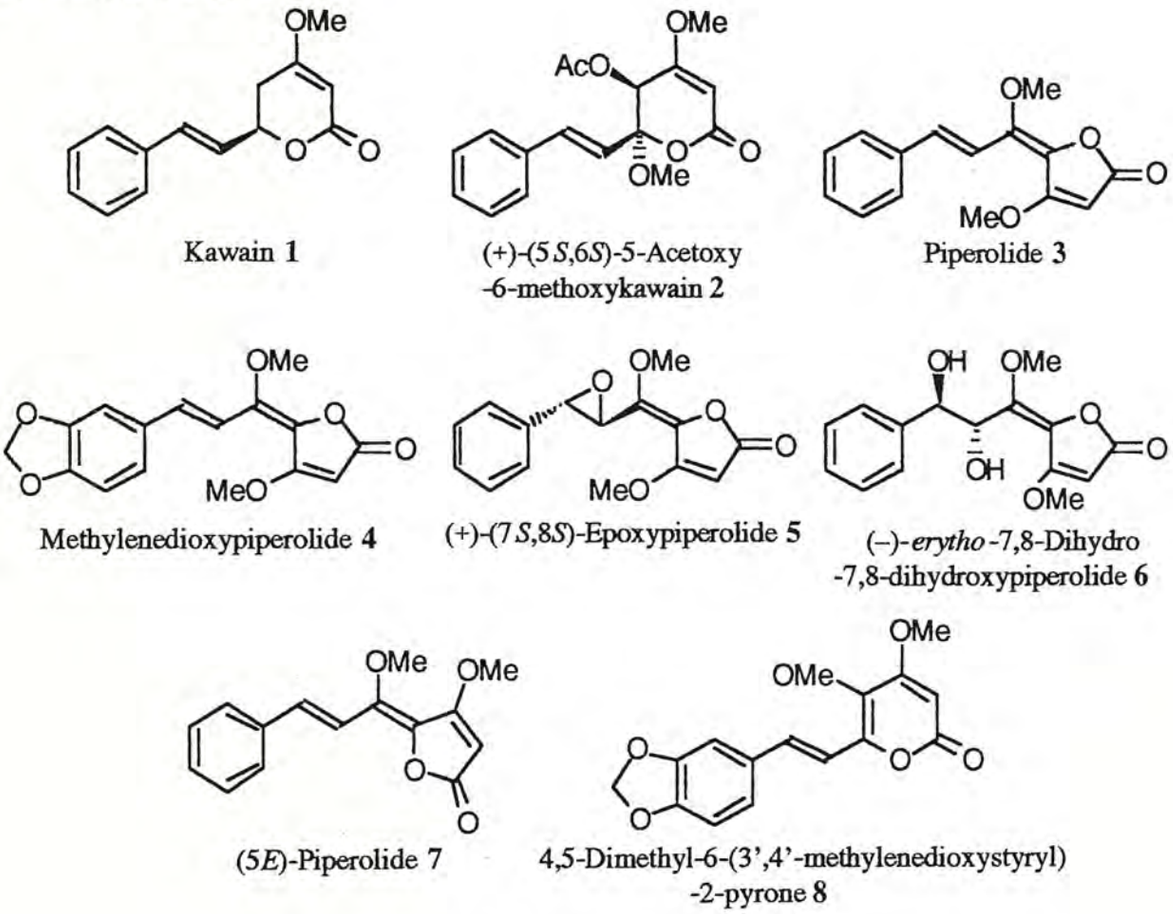


Figure 1. Styryl-lactones from the *Piper* genus

1.2 Styryl-lactones from *Goniothalamus* genus

In 1967, a δ-lactone of 5-hydroxy-7-phenylhepta-2,6-dienoic acid **11** was isolated from *Cryptocarya Caloneura* (Scheff.) by Hlubucek *et al.*[6] The structure was established by spectroscopic analysis and chemical transformations. The stereochemistry of the only chiral centre at C-5 was deduced by chemical transformation of **11** to malic acid ethyl xanthate. Comparing the optical rotatory dispersion of the derived xanthate with that of authentic L-(–)-malic acid ethyl xanthate

revealed that C-5 in **11** should have the (*S*)-absolute stereochemistry.

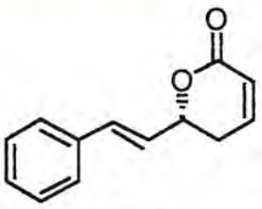
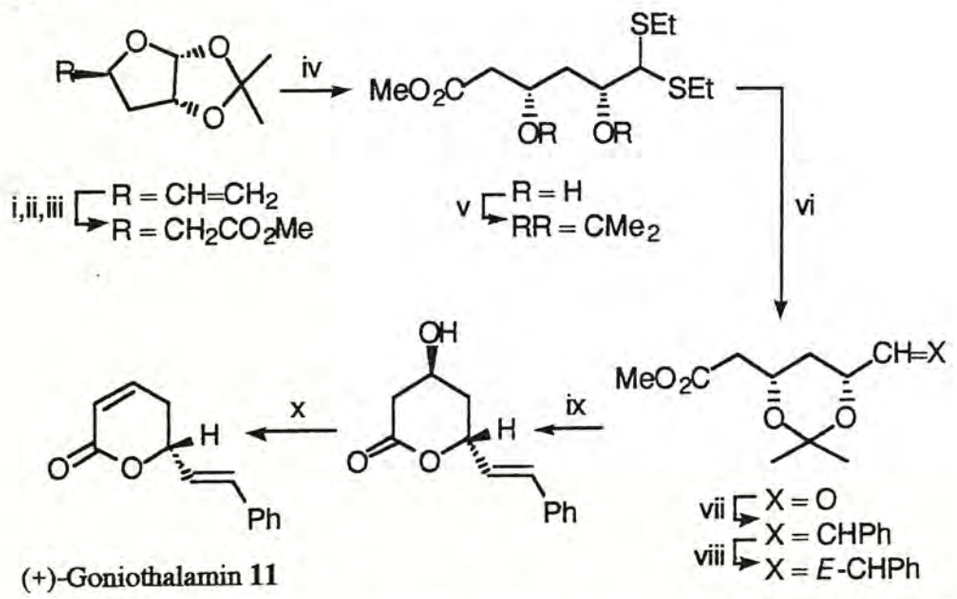


Figure 2. (+)-Goniothalamin **11**
5-hydroxyl-7-phenylhepta-2,6-dienoic acid)

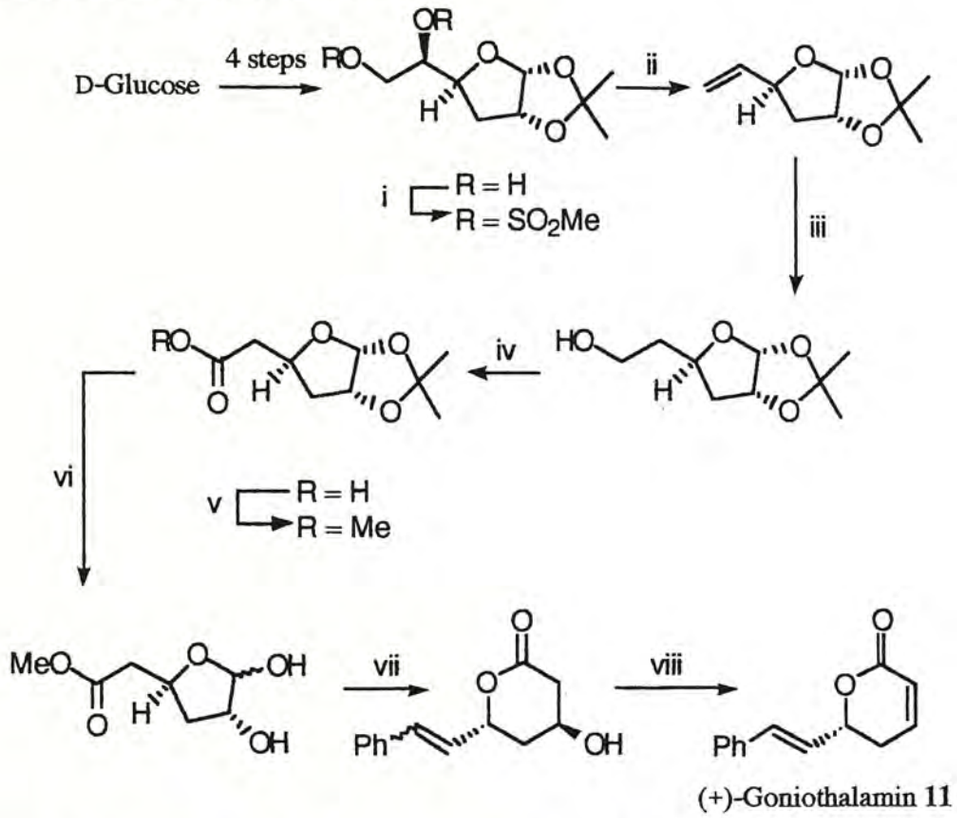
A δ-lactone with the same structure as **11**, which was named (+)-goniothalamin, was isolated from *Goniothalamus andersonii*, *Goniothalamus macrophyllus* Miq., *Goniothalamus malayanus* Hook. f. et Thomas. and *Goniothalamus velutinus* in 1972 by Jewers *et al.*[1] The structure of **11** was established by comparing the spectroscopic data with those of the lactone obtained by Hlubucek *et al.* from *Cryptocarya Caloneura* (Scheff.).[6]

In 1986, Just *et al.* proved that the absolute stereochemistry at C-5 of (+)-goniothalamin **11** was actually (*R*) as shown in Figure 2, in contrast to the (*S*) assignment by Hlubucek *et al.*, *via* an unambiguous total synthesis as shown in Scheme 1.[7]



Scheme 1 *Reagents* : i, 9-BBN, THF (99%); ii, Jones oxidation; iii, Methylation (73%); iv, $ZnCl_2$, EtSH, EtOAc (83%); v, acetone, 2,2-dimethoxypropane, *p*-TSA (83%); vi, HgO, $HgCl_2$, acetone, H_2O; vii, benzyltriphenylphosphonium chloride, n-BuLi, THF, HMPA (57%, *E*:*Z* = 1:9); viii, PhSH, AIBN (75%, 7:3 = *E*:*Z*); ix, TFA–H_2O; x, $MeSO_2Cl$, Et_3N, CH_2Cl_2 (54%).

In 1988, Gillard *et al.* also confirmed the (*R*)-absolute stereochemistry of (+)-goniothalamin **11** by a total synthesis from 1,2-*O*-isopropylidene-3-deoxy-α-D-glucofuranose as shown in Scheme 2.[8]



Scheme 2 *Reagents* : i, $MeSO_3Cl$, pyridine (96%); ii, NaI, Zn, DMF (95%); iii, 9-BBN, THF, then NaOH, H_2O_2 (92%); iv, PDC, DMF; v, CH_2N_2, Et_2O (62%); vi, amberlite IR 120 resin; vii, benzyltriphenylphosphonium chloride, DMSO, then sodium methylsulfinylmethanide, then HCl (45% mixture of *Z* and *E*); viii, CH_2Cl_2, Et_3N, $MeSO_3Cl$, then HCl (85% mixture of *Z* and *E*).

Another styryl-lactone, shown in Figure 3, called (+)-altholactone **14** was first isolated from an unknown *Polyalthea* species in 1977 by Loder *et al.*[9] Recently, McLaughlin *et al.* also isolated **14** from the stem bark of *Goniothalamus giganteus* (Annonaceae).[10] (+)-Altholactone was tested to be bioactive and displayed BS LC_{50} 234 μg/ml, 9KB cytotoxicity ED_{50} 2 μg/ml and P388 toxicity at 45 mg/kg.

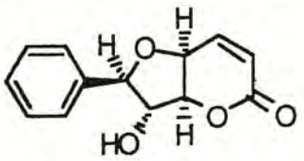
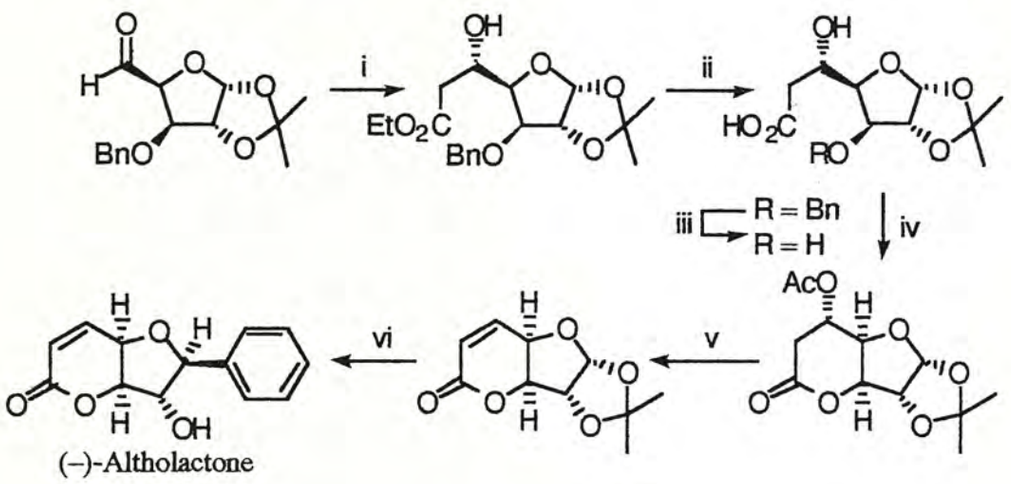
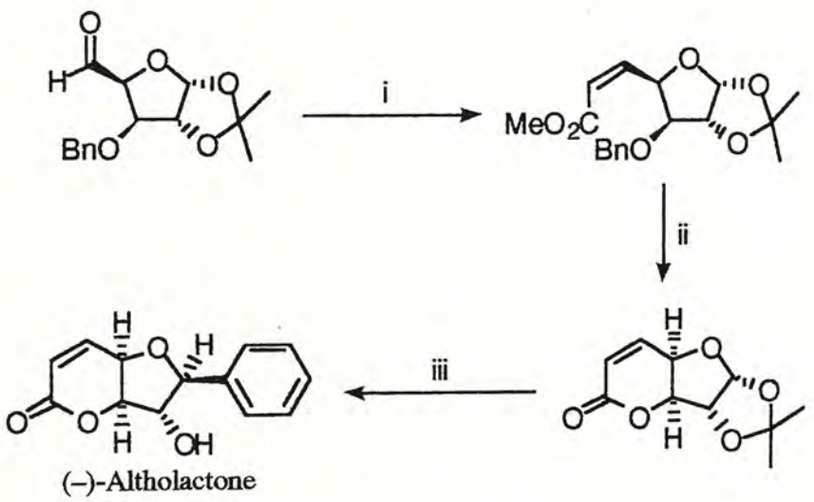


Figure 3. (+)-Altholactone **14**

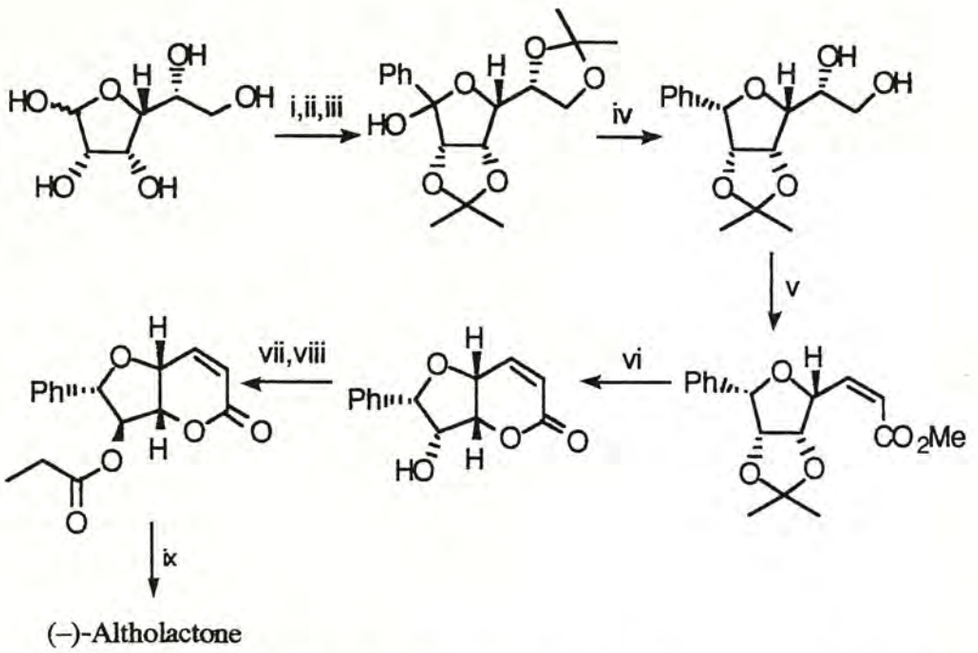
The structure of **14** was first determined by careful study of the ^{1}H, ^{13}C NMR spectra and by selective ^{1}H-^{1}H, ^{1}H-^{13}C decoupling experiments. The relative stereochemistry of all chiral centres were finally established by a single crystal X-ray analysis. The absolute stereochemistry of **14** was then corroborated by an unambiguous total synthesis of its (–)-enantiomer by Gesson *et al.* from D-glucose in 1987 as shown in Scheme 3 and 4.[11] Shing *et al.* also synthesized (–)-altholactone from D-mannose in 1988 as shown in Scheme 5.[12]



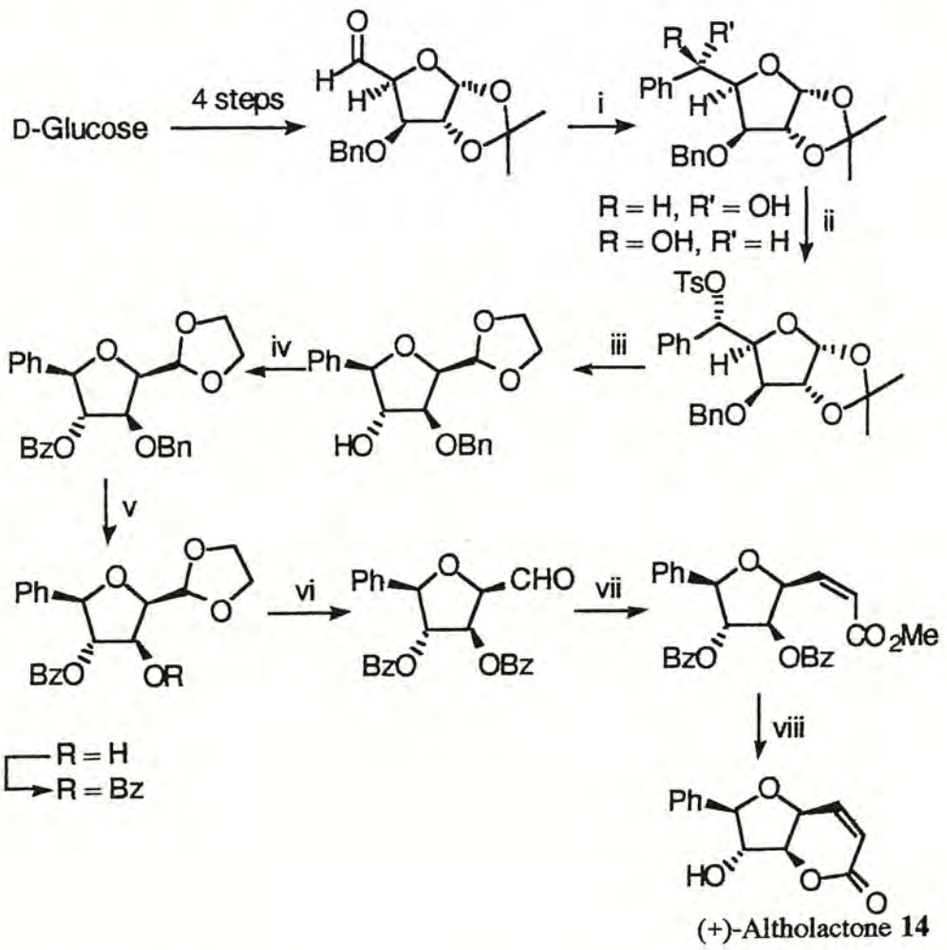
Scheme 3 *Reagents* : i, Zn, benzene, ethylbromoacetate, Et_2O, then H_2SO_4 (85%); ii, NaOH; iii, EtOAc, Pd/C, H_2 (85%); iv, pyridine, DCC then Ac_2O, cat. DMAP (79%); v, DBU, CH_2Cl_2; vi, HF, benzene (48%).



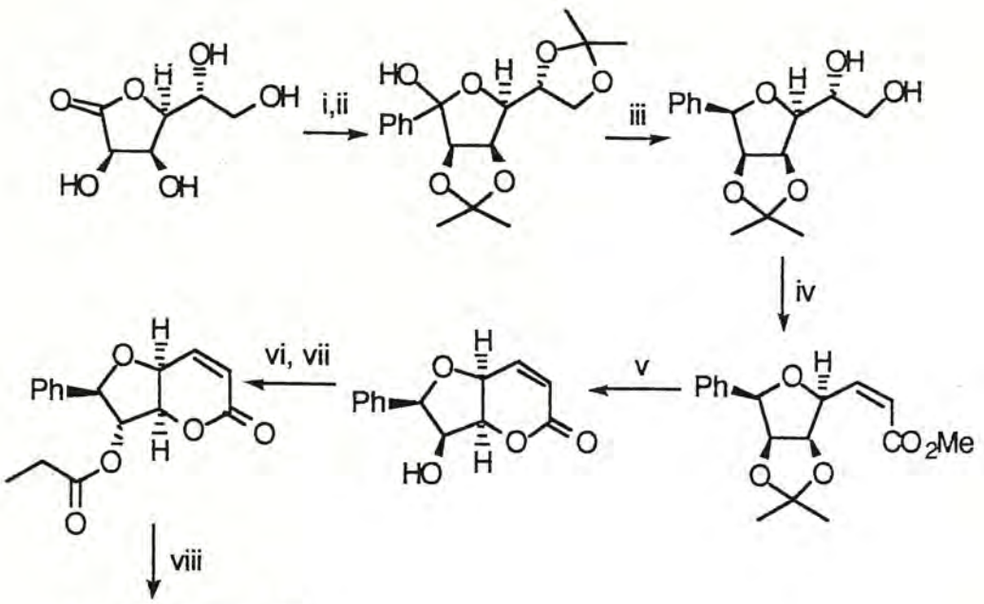
Scheme 4 *Reagents* : i, Ph_3P=$CHCO_2Me$, dry MeOH (71%); ii, NaOH, then H_2SO_4, then TFA-H_2O (66%); iii, HF, benzene (48%).



Scheme 5 *Reagents* : i, Me_2CO, H_2SO_4; ii, PCC, 3Å molecular sieves, CH_2Cl_2; iii, PhLi, THF, –78 °C (77%); iv, Et_3SiH, $BF_3.Et_2O$, MeCN, –20 °C (72%); v, $NaIO_4$, aq. MeOH; then $Ph_3P{=}CHCO_2Me$ (68%); vi, aq. TFA (93%); vii, $(CF_3SO_2)_2O$, CH_2Cl_2, pyridine, –10 °C; viii, $EtCO_2Cs$, $HCONMe_2$ (47%); ix, aq. NaOH, then TFA (62%).



Scheme 6 *Reagents* : i, PhMgBr, Et_2O (73%); ii, TsCl, pyridine (86%); iii, benzene, ethylene glycol, cat. TsOH (87%); iv, BzCl, pyridine (98%); v, CH_2Cl_2, TMSI (53%); vi, BzCl, pyridine (90%); vii, TFA-H_2O (86%); viii, $Ph_3P{=}CHCO_2Me$, dry MeOH (58%); ix, aq. NaOH, then H_2SO_4, then TFA-H_2O (55%).

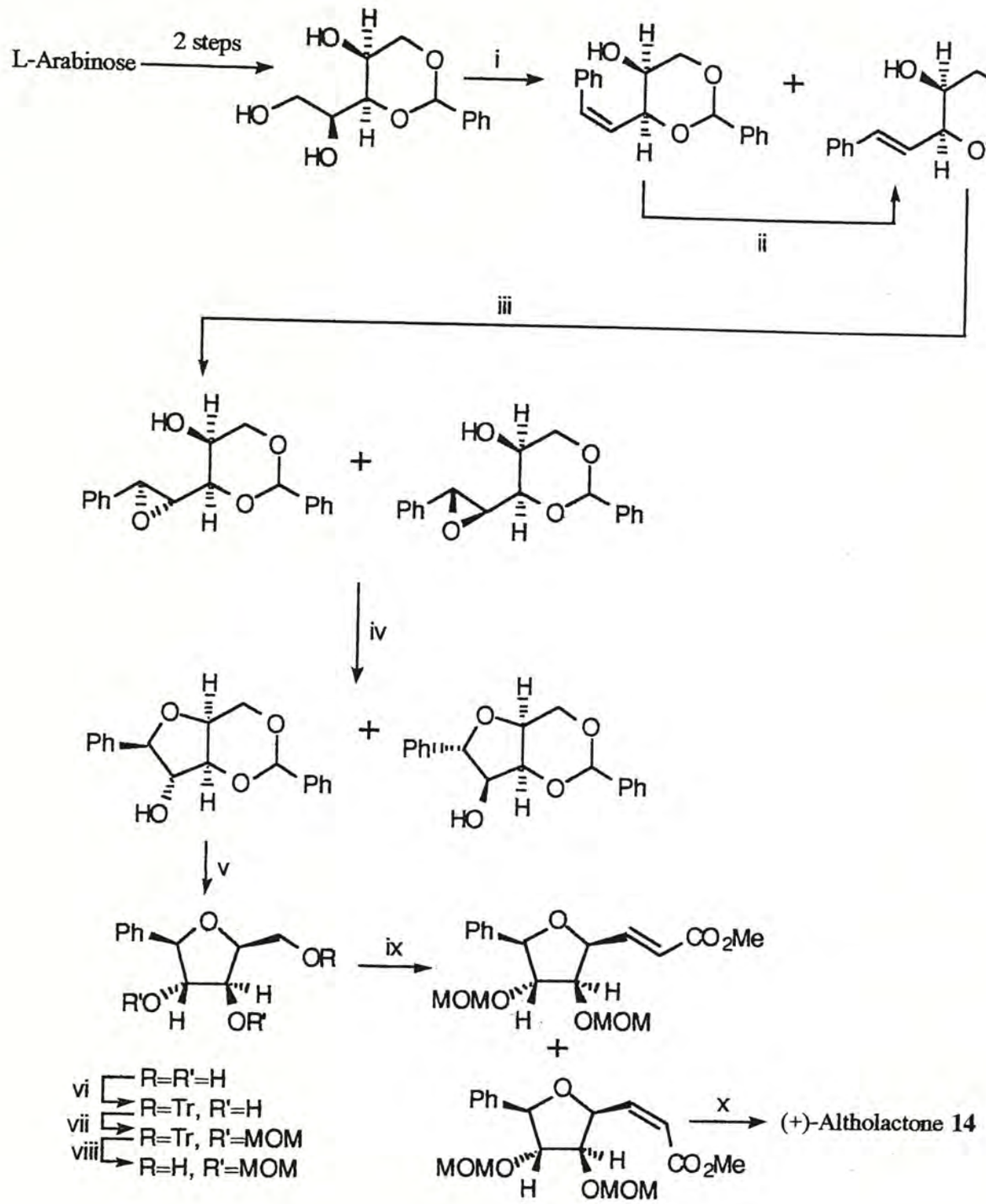


Scheme 7 *Reagents* : i, Me_2CO, H_2SO_4; ii, PhLi, THF, –78 °C (85%); iii, Et_3SiH, $BF_3.Et_2O$, MeCN, –20 °C (74%); iv, $NaIO_4$, aq. MeOH; then $Ph_3P{=}CHCO_2Me$ (70%); v, aq. TFA (92%); vi, $(CF_3SO_2)_2O$, CH_2Cl_2, pyridine, –10°C; vii, $EtCO_2Cs$, $HCONMe_2$ (53%); viii, aq. NaOH, then TFA (65%).

Total synthesis of **14** was accomplished independently by Gesson *et al.* from D-glucose in 1987 as shown in Scheme 6,[13] Shing *et al.* from D-gulonolactone in 1988 (Scheme 7)[12] and Ogawa *et al.* from 1,3-*O*-benzylidene-L-arabinitol in 1989 (Scheme 8).[14] These unambiguous syntheses thus confirmed the absolute stereochemistry of (+)-altholactone **14.**

Continuous investigation of the *Goniothalamus* genus led to the isolation of more styryl-lactones. 5-Acetoxy-6-methoxykawain **2** and (+)-goniothalamin **11**, which were isolated previously in other species, were also obtained from *Goniothalamus giganteus* (Annonaceae) in 1985 by McLaughlin *et al*. along with the (+)-altholactone **14.**[10]

(+)-Goniodiol **15**, (+)-goniotriol **16**, (+)-goniodiol monoacetate **17**, and (+)-goniodiol diacetate **18**, shown in Figure 4, were isolated from the petrol extracts of the air-dried, powdered leaves and twigs of *Goniothalamus sesquipedalis* Wall (Annonaceae) in 1985 by Talapatra *et al*.[3] The absolute configurations of these styryl



Scheme 8 *Reagents* : i, MeOH, $NaIO_4$, then benzyltriphenylphosphonium chloride, BuLi, THF; ii, PhSH, AIBN, benzene (81%); iii, MCPBA, CH_2Cl_2; iv, silica gel; v, 1,4-dioxane, HCl, then NaOH (89%); vi, pyridine, triphenylmethyl chloride, DMAP (75%); vii, THF, diisopropylethylamine, chloromethyl ether (89%); viii, AcOEt, MeOH, *p*-TsOH, then Et_3N (94%); ix, pyridine, CH_2Cl_2, CrO_3 then $Ph_3P{=}CHCO_2Me$, MeOH; x, HCl, 1,4-dioxane (96%).

-lactones were tentatively assigned to be (5*S*,6*S*,7*S*) by NMR spectral analysis and their chemical interconversions, based on the (*S*) configuration for C-5. However, the absolute stereochemistry of the (+)-goniothalamin **11** at C-5 was later confirmed to be

(*R*).[7,8] Therefore, the absolute stereochemistry of these styryl-lactones should be (5*R*,6*R*,7*R*).

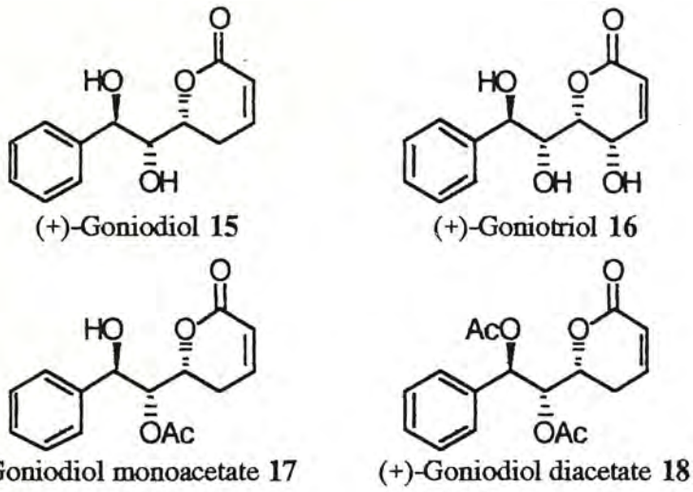
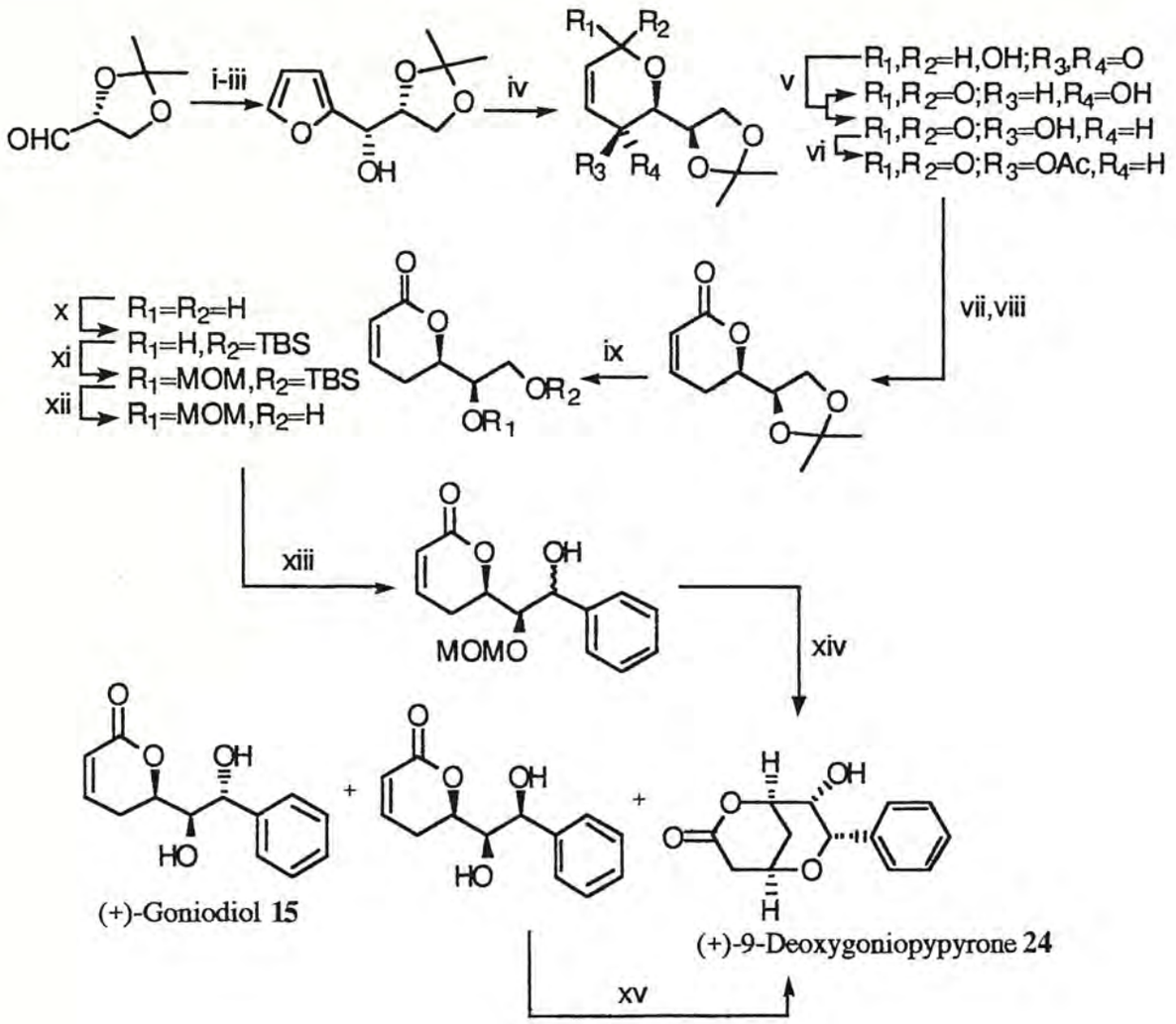


Figure 4

McLaughlin *et al.* isolated **15** from the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae) in 1991.[17] The structure and the relative stereochemistry of **15** were established by NMR spectral and single crystal X-ray crystallographic analysis of its diacetate **18**. Recently, Honda *et al.* confirmed the absolute stereochemistry of (+)-goniodiol **15** by a total synthesis from 2,3-*O*-isopropylidene-D-*glycero*-aldehyde as shown in Scheme 9.[18] In 1989, McLaughlin *et al.* also isolated **16** from the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae).[15] Based on NMR spectral analysis and single crystal X-ray analysis, the relative stereochemistry of **16** was unravelled. The absolute stereochemistry of **16** was recently established by Shing *et al.* based on an unambiguous total synthesis of its (–)-enantiomer from D-*glycero*-D-*gulo*-heptono-γ-lactone.[16] (+)-Goniodiol monoacetate **17** was also obtained by McLaughlin *et al.* in 1991.[2] The structure and the relative stereochemistry of **17** were unravelled by a single crystal X-ray crystallographic analysis.

In 1987, (+)-goniothalamin oxide **19** together with the known (+)-goniothalamin **11**, were obtained from the methanol extract of the roots and stems of *Goniothalamus macrophyllus* (Bl.) Hook fil. & Thomas (Annonaceae) by Sam *et al.*[4]



Scheme 9 *Reagents* : i, 2-lithiofuran, THF, –78 °C (92%); ii, MnO_2, MeCN, r.t., 3 days; iii, L-Selectride, THF, –78 °C [84% (2 steps)]; iv, NBS, 80% aq. THF, 0 °C (97%); v, CrO_3, AcOH, r.t., 0.5 h; then *i*-PrOH, $NaBH(OAc)_3$, –20 °C (41%); vi, Ac_2O, pyridine, cat. DMAP, CH_2Cl_2, r.t. (99%); vii, Zn, $CuSO_4.5H_2O$, AcONa, 50% aq. AcOH, THF, 0 °C to r.t., 1 h (92%); viii, cat. DBU, THF, r.t., 16 h (99%); ix, 75% aq. AcOH, THF, 40 °C, 2 h (99%); x, *t*-$BuMe_2SiCl$, Et_3N, cat. DMAP, CH_2Cl_2, r.t. (99%); xi, $MeOCH_2Cl$, *i*-Pr_2NEt, cat. DMAP, CH_2Cl_2, r.t. (99%); xii, 75% aq. AcOH, 50 °C, 5 h (89%); xiii, $(COCl)_2$, DMSO, CH_2Cl_2, –65 °C, Et_3N, then PhTi(O*i*-Pr)$_3$, Et_2O, 0 °C, 1 h (94%); xiv, 75% aq. AcOH, 65 °C, 4 h (97%); xv, cat. DBU, THF, r.t., 15 h (82%).

The structure of **19** was assigned first by spectral analysis. Then oxidation of (+)-goniothalamin **11** with *m*-chloroperbenzoic acid gave the corresponding diastereoisomeric epoxides in a ratio of 3 : 2. The major product showed spectral data in good agreement with the natural (+)-goniothalamin oxide **19**. The absolute stereochemistry of **19** was finally assigned to be (5*S*,6*R*,7*R*) by the authors based on the (*S*) configuration at C-5.

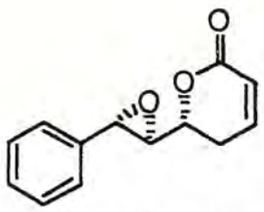
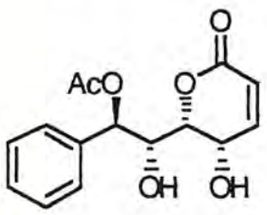
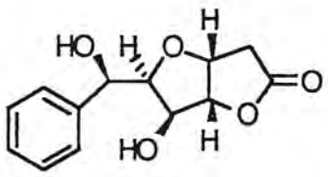


Figure 5. (+)-Goniothalamin oxide **19**

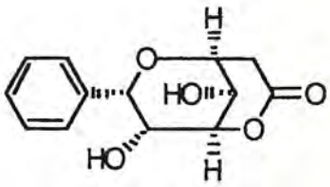
(+)-7-Acetylgoniotriol **20**, (+)-goniofufurone **21** and (+)-goniopypyrone **22**, shown in Figure 6, were isolated by McLaughlin *et al.* in 1990 from the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae).[19] Compounds **20**, **21** and **22** were tested to exhibit significant anti-tumor activities. For example, **22** showed ED_{50} of 0.7 μg/ml against the human tumors A-549, MCF-7 and HT-29. Relative stereochemistries of **21** and **22** were established by NMR spectral and X-ray crystallographic analyses.



(+)-7-Acetylgoniotriol **20**



(+)-Goniofufurone **21**

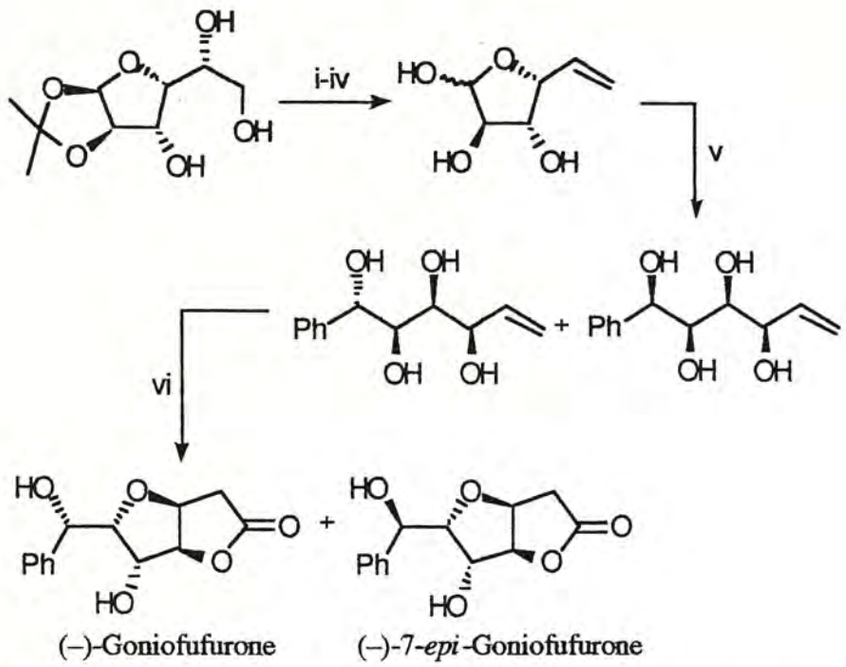


(+)-Goniopypyrone **22**

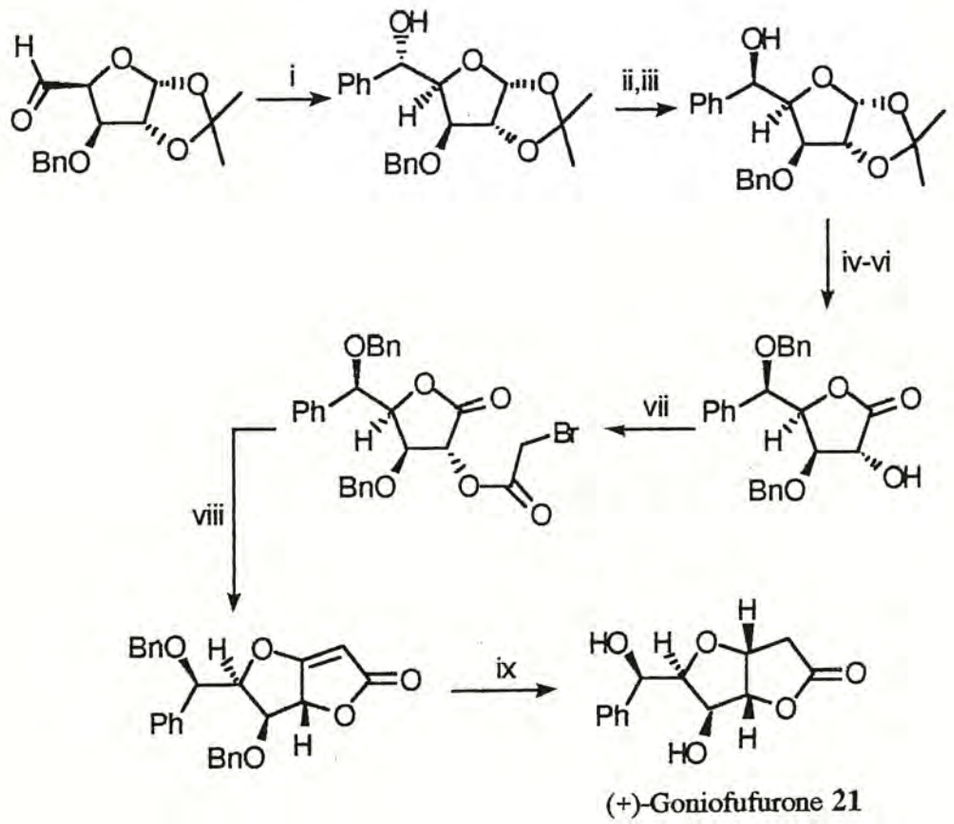
Figure 6

Total synthesis of **21**, its (–)-enantiomer and **22** were accomplished by our group recently from D-*glycero*-D-*gulo*-heptono-γ-lactone and the absolute stereochemistries of **21** and **22** were therefore established.[20–22] Gracza *et al.* completed the synthesis of (–)-goniofufurone and (–)-7-*epi*-goniofufurone from D-glucose using palladium(II)-catalyzed oxycarbonylation as the key step as shown in Scheme 10.[23]

Murphy also synthesized **21** from D-glucose.[24] The key step involved the Wittig cyclization of a stabilized phosphorane with a butyrolactone as shown in Scheme 11. In 1993, Rao *et al.* also completed the total synthesis of **21** from D-glucose using the bis-cyclization method as shown in Scheme 12.[25]



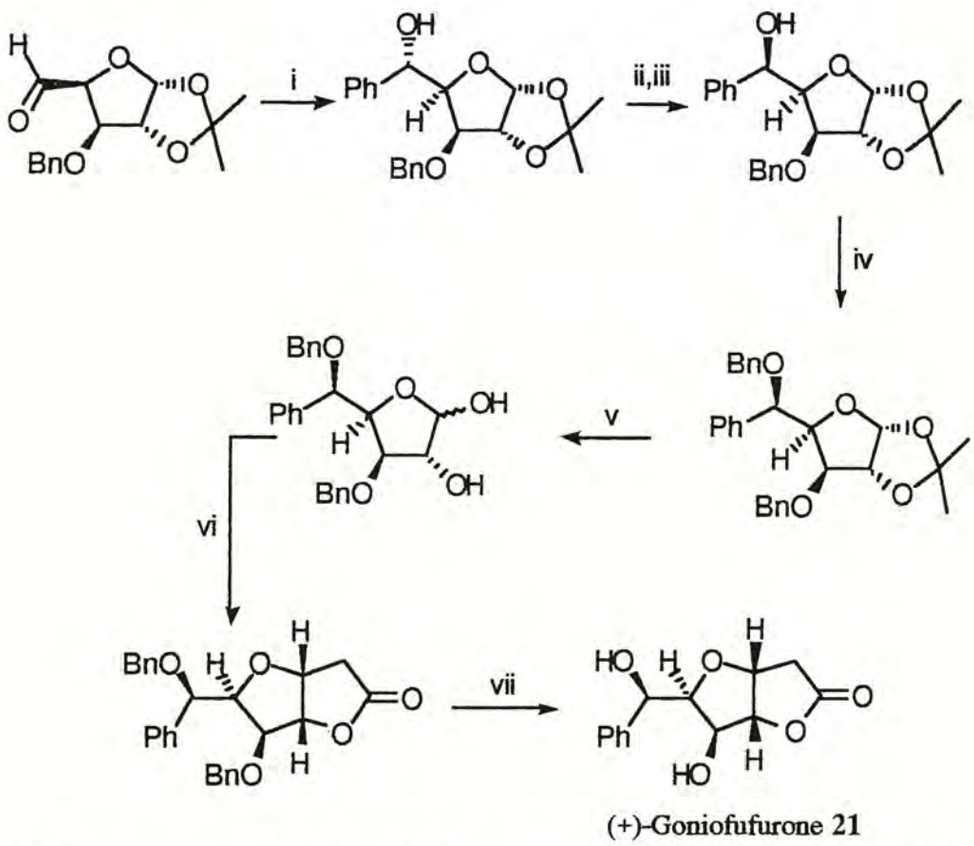
Scheme 10 *Reagents* : i, $MeSO_2Cl$, pyridine (83%); ii, NaI, acetone, (92%); iii, $LiAlH_4$, Et_2O, CH_2Cl_2 (94%); iv, AcOH, H_2O (87%); v, PhMgBr, THF (54%); vi, CO, $PdCl_2$, $CuCl_2$, NaOAc, AcOH (93%).



Scheme 11 *Reagents* : i, PhMgBr, Et_2O (78%); ii, PCC, CH_2Cl_2; iii, $NaBH_4$, $CeCl_3.7H_2O$, MeOH, –78 °C (67%); iv, BnBr, NaH, THF (87%); v, CF_3CO_2H-H_2O (85%); vi, Br_2-$BaCO_3$, dioxane, H_2O (54%); vii, $BrCOCH_2Br$, pyridine, Et_2O (87%); viii, PPh_3, MeCN, then DBU (88%); ix, H_2, 10% Pd-C (58%).

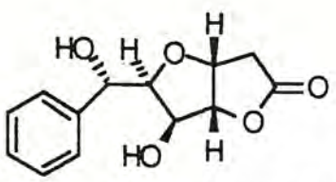
Stereochemistry of **20** was established by comparing the spectral data of its peracetyl-derivative with those of triacetyl derivative of the (+)-goniotriol **16** whose stereochemistry was already established by an X-ray crystallographic analysis.[15] Total synthesis of the (–)-enantiomer of **20** was reported recently by Shing *et al.*, thereby confirming its absolute stereochemistry.[26]

(+)-7-*epi*-Goniofufurone **23** and (+)-9-deoxygoniopypyrone **24** were recently isolated by McLaughlin *et al.* from the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae).[17] The structures of **23** and **24** are illustrated in Figure 7. Neither **23** nor **24** was tested to have significant biological activities. Relative stereochemistries of **23** and **24** were established by NMR spectral and X-ray crystallographic analyses.

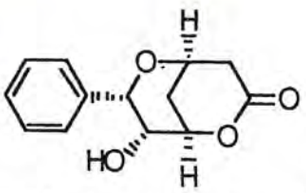


(+)-Goniofufurone **21**

Scheme 12 *Reagents* : i, PhMgCl, THF (89%); ii, PDC, CH_2Cl_2; iii, $NaBH_4$, MeOH (81%); iv, BnBr, NaH, DMF (93%); v, TFA–H_2O (63%); vi, $Ph_3P{=}CHCO_2Et$, MeOH (71%); vii, H_2, 10% Pd–C (58%).



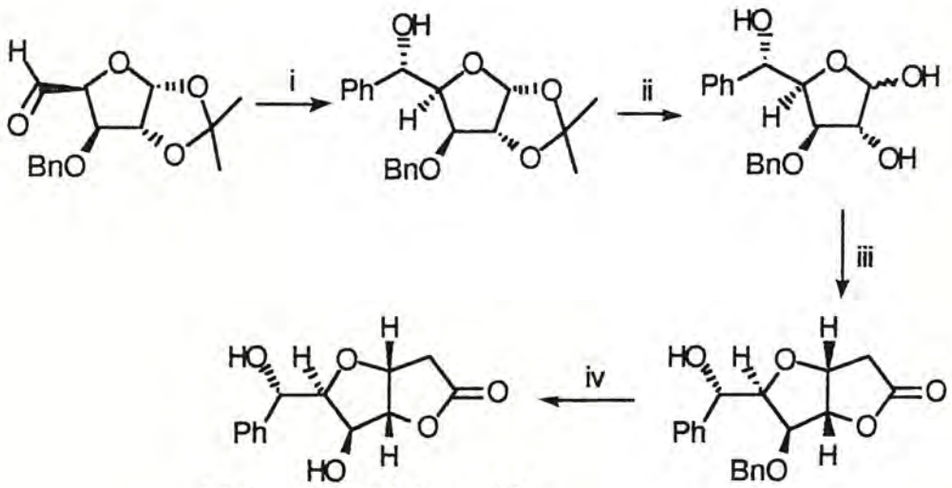
(+)-7-*epi*-Goniofufurone **23**



(+)-9-Deoxygoniopypyrone **24**

Figure 7

In 1992, Shing *et al.* established the absolute stereochemistry of **23** by a total synthesis of its (–)-enantiomer from D-*glycero*-D-*gulo*-heptono-γ-lactone.[25] Gracza *et al.* also reported the total synthesis of (–)-**23** from D-glucose in 1992.[23] Honda *et al.* confirmed the absolute stereochemistry of **24** by an unambiguous synthesis from (2*S*,3*R*)-1,2-*O*-isopropylidene-3-(2-furyl)glycerol as shown in Scheme 9.[18] Rao *et al.* synthesized **23** from D-glucose using the bis-cyclization process as the key step as shown in Scheme 13.[27]

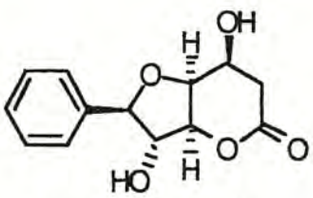


(+)-7-*epi*-Goniofufurone **23**

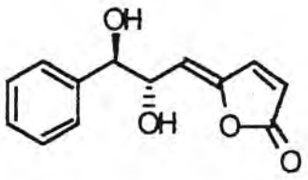
Scheme 13 *Reagents* : i, PhMgBr, THF (83%); ii, TFA-H_2O (88%); vi, $Ph_3P{=}CHCO_2Et$, MeOH (60%); vii, H_2, 10% Pd-C (93%).

(–)-Goniofupyrone **25**, (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27**, shown in Figure 8, were recently isolated from the ethanolic extracts of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae) by McLaughlin *et al.*[28] Structural determination was based on an NMR spectral analysis.

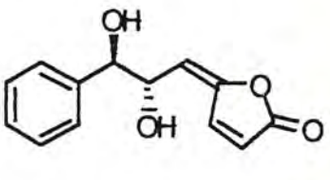
Very recently, Mclaughlin *et al.* reported the isolation of (+)-gonioheptolide A **28** and (+)-gonioheptolide B **29** from the *Goniothalamus giganteus* (Annonaceae).[29] The structure of **28** and **29** were illustrated in Figure 9. Both styryl-lactones possessed novel eight-membered-ring lactone which were elucidated by an NMR spectral analysis. Compounds **28** and **29** only exhibited marginal cytotoxicities against certain human tumors.[29]



Goniofupyrone **25**

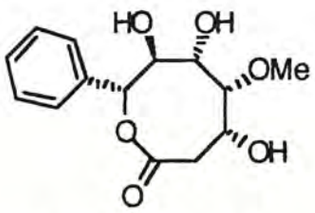


(+)-Goniobutenolide A **26**

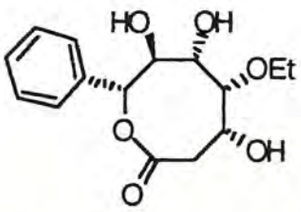


(–)-Goniobutenolide B **27**

Figure 8



Gonioheptolide A **28**

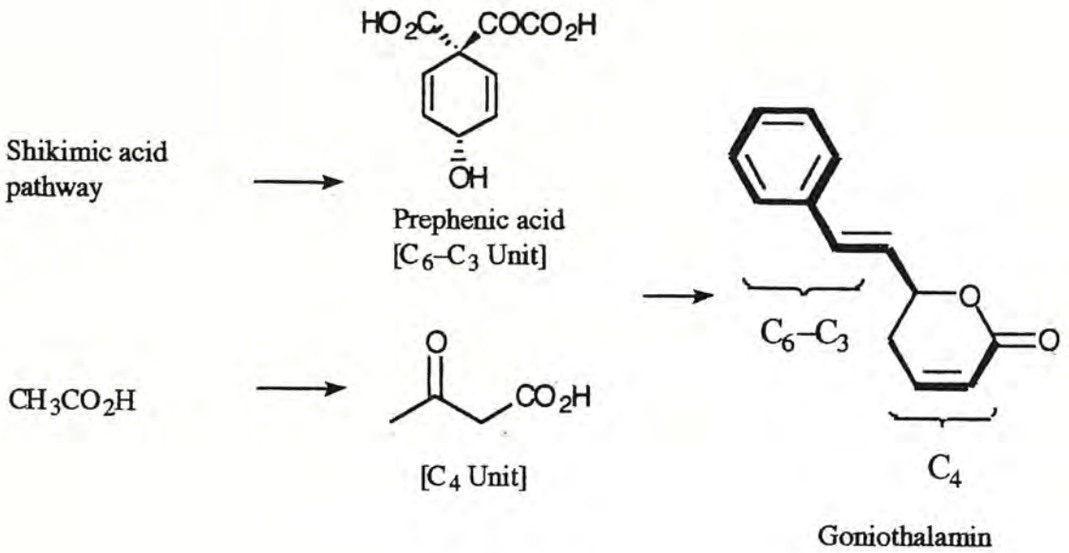


Gonioheptolide B **29**

Figure 9

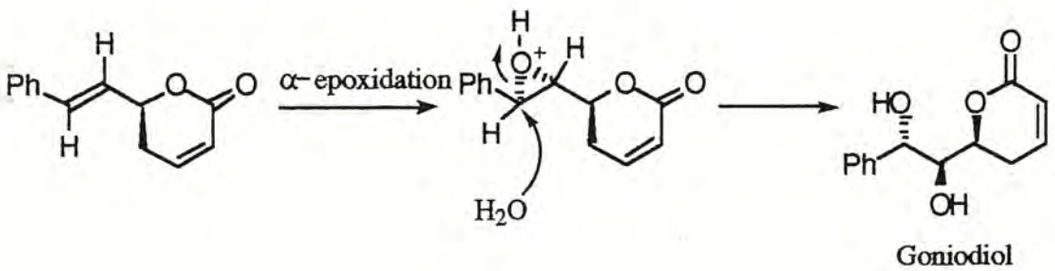
1.3 Biosynthetic pathways

All styryl-lactones isolated shared the same basic C_6–C_3–C_4 skeleton. The biosynthetic pathway would be expected to be of a mixed origin. The C_6–C_3 unit would be provided by the shikimic acid pathway and condensation of two acetyl-Coenzyme A would give the C_4 unit. Condensation of the two fragments then provided the basic skeleton of styryl-lactones as proposed by Gillhouley as shown in Scheme 14.[30]



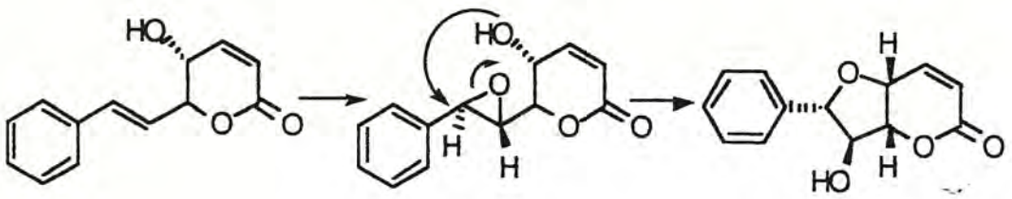
Scheme 14

In fact, along the discovery of the styryl-lactones, several authors have recognized their biosynthetic possibilities. In 1985, Talapatra *et al.* proposed that the (+)-goniothalamin **11** was the most logical biogenetic precursor of all the dihydropyrones by epoxidation and then *trans*-opening of the epoxide by an S_N2 type attack at the benzylic position (Scheme 15).[3]



Scheme 15

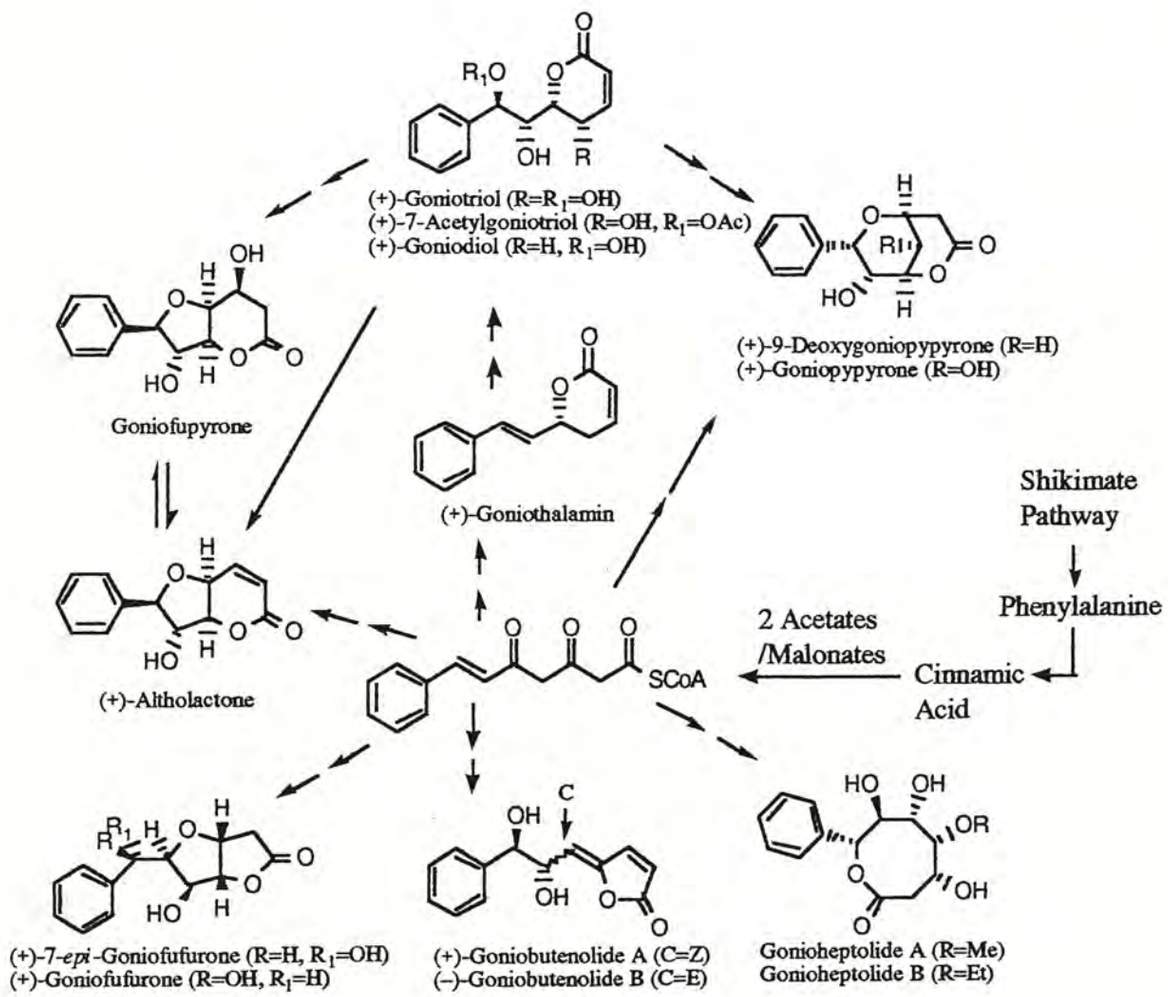
In 1987, Sam *et al.* proposed (+)-altholactone **14** could be obtained from an intramolecular cyclization of an unknown 5-hydroxygoniothalamin as shown in Scheme 16.[4] In 1989, Gesson *et al.* also proposed that the (+)-goniotriol **16** was the uncyclized form of (+)-altholactone **14**.[31]



Altholactone

Scheme 16

Recently, McLaughlin *et al.* proposed the biosynthetic pathways of all the fourteen isolated styryl-lactones from the *Goniothalamus* genus.[29] The authors proposed that the biosynthesis starts from the shikimic acid pathway with incorporation of two acetate units to form the basic carbon skeleton. Reductions, oxidations and cyclizations at different positions then generated all the different styryl-lactones (Scheme 17).



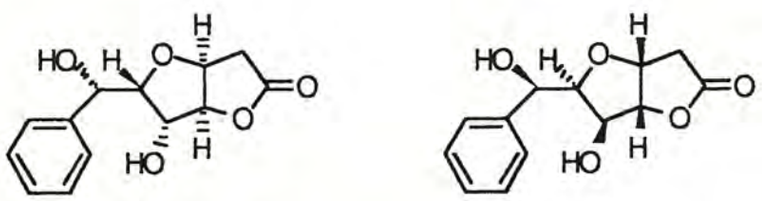
Scheme 17

2. Results and discussion

Initially, the synthesis and the absolute stereochemistry proof of goniofufurone **21** from D-*glycero*-D-*gulo*-heptono-γ-lactone **32** will be described. Total syntheses of (+)-goniofufurone **21b**, (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27**, (+)-goniopypyrone **22**, (+)-altholactone **14**, (+)-goniotriol **16** and (+)-7-acetylgoniotriol **20** from the same starting material will then be discussed in sequence.

2.1 Goniofufurone : Synthesis and absolute configuration[20,26,32]

Among all the styryl-lactones isolated from the genus *Goniothalamus*, we began our work on the total synthesis and the determination of the absolute stereochemistry of goniofufurone. At the very beginning, only the relative stereochemistry of goniofufurone was known from the reported X-ray crystallographic analysis.[19] Therefore, the natural (+)-goniofufurone might have the absolute configuration **21a** or **21b** as depicted in Figure 10. In our project, we arbitrarily selected **21a** as our first target molecule.



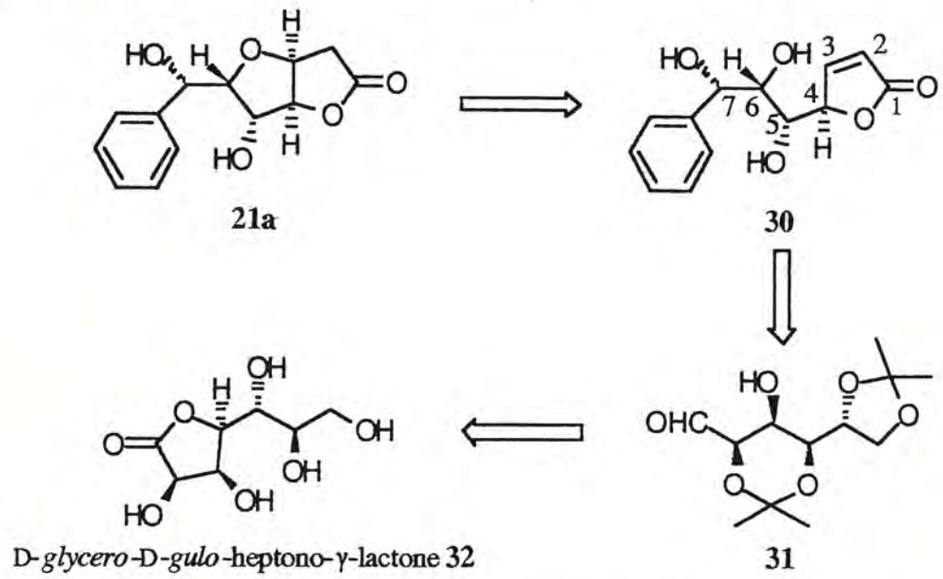
21a **21b**

Figure 10

Retrosynthetic analysis of **21a** indicates that the furanoid ring could be constructed by an intramolecular Michael addition of the OH-6 onto the unsaturated lactone **30** as shown in Scheme 18.[32] Hence, the chirality at C-3 could be controlled by the pre-existing stereochemistry at the adjacent carbon (C-4) due to geometrical constraint. The butenolide **30** could then be obtained from the aldehyde **31** which could be readily derived from the inexpensive and commerically available D-*glycero*-D-

gulo-heptono-γ-lactone **32** following the work of Brimacombe and Tucker with some modifications.[33]

The preparation of the aldehyde **31** is illustrated in Scheme 19. Isopropylidenation of D-*glycero*-D-*gulo*-heptono-γ-lactone **32** using acetone–zinc chloride–phosphoric acid at room temperature gave the desired diacetonide **33** as

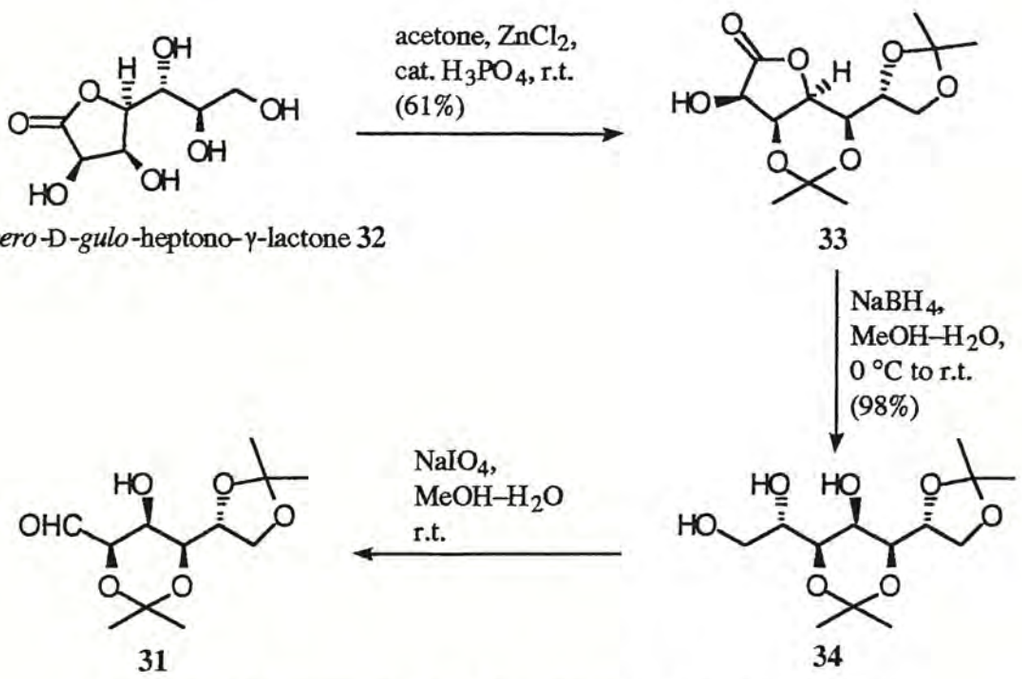


Scheme 18. Retrosynthetic analysis of Goniofufurone **21a**

colorless crystals after fractional crystallization from chloroform and hexane in 61% yield with m.p. 157—158 °C and $[\alpha]_D^{24}$ – 76 (*c* 1.1, chloroform); [lit.,[33] 153—154 °C and $[\alpha]_D^{30}$ – 76 (*c* 2, chloroform)]. The use of zinc chloride–phosphoric acid in this work gave cleaner products. The four singlets between 1.36–1.50 ppm in the ^{1}H NMR spectrum of **33** indicated the formation of two isopropylidenes and their positions on the skeleton were established by Brimacombe and Tucker using chemical transformations.[33] Moreover, the presence of two isopropylidenes in **33** was also evident from the two resonances for the ketal carbons of the isopropylidenes at 99.76 and 110.64 ppm in the ^{13}C NMR spectrum of **33**. The two resonances at 99.76 and 110.64 also suggested that the two isopropylidenes were in the form of a dioxane ring and a dioxolane ring, respectively.[34,35] As pointed out by Brimacombe and Tucker,[33] the formation of the dioxane ring at C-3 and C-5 in **33** instead of a more stable dioxolane ring at C-2 and C-3 was abnormal. Although the reasons for this

abnormality were not clear, the stability of this isopropylidene was very useful for our later purposes.

Reduction of the lactone moiety in **33** using sodium borohydride in aqueous methanol from 0 °C to room temperature afforded the triol **34** in quantitative yield with m.p. 62—64 °C and $[\alpha]_D^{25}$ – 6 (*c* 0.5, water); [lit.,[33] m.p. 67—68 °C and $[\alpha]_D$ – 6 (*c* 2, water)]. The disappearance of the strong absorption peak at 1788 cm^{-1} for the carbonyl absorption and the presence of the strong absorption peak at 3400 cm^{-1} for the hydroxy group in the i.r. spectrum of **34** showed the successful reduction of the lactone moiety to the alcohol. The aldehyde **31** was then obtained by oxidative cleavage of the terminal diol in **34** using sodium metaperiodate in aqueous methanol at room temperature.[36]



D-*glycero*-D-*gulo*-heptono-γ-lactone **32** — **33** — **34** — **31**

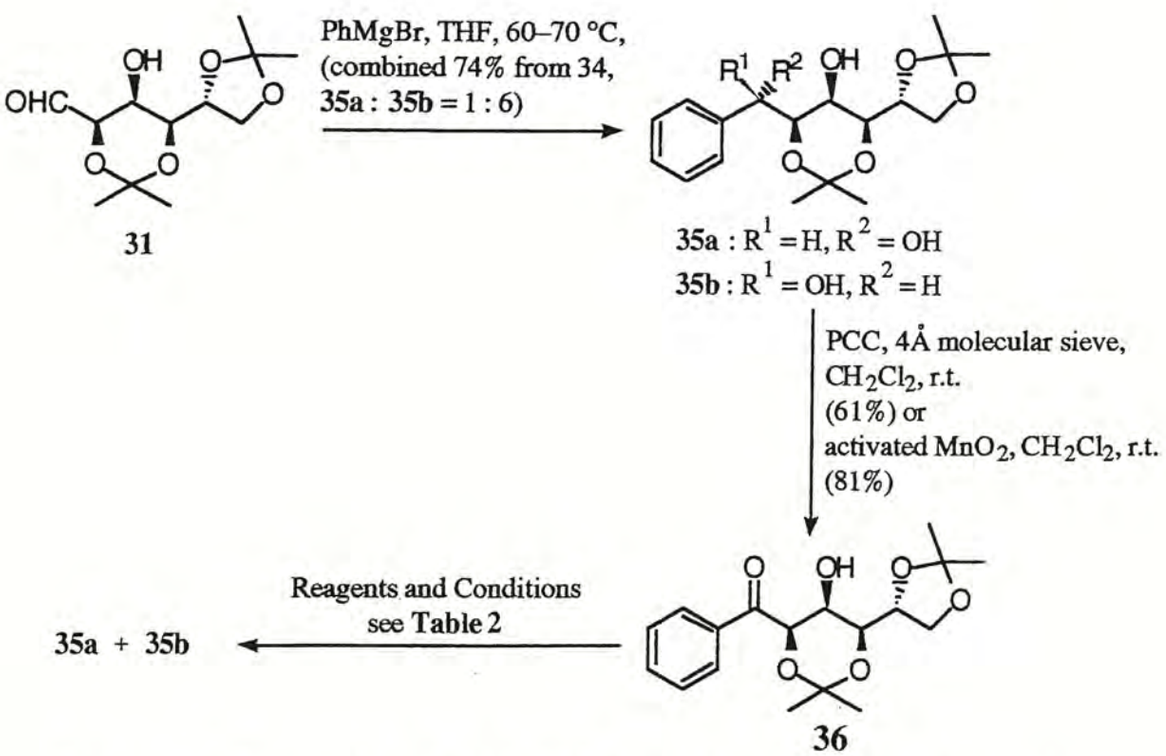
Scheme 19. Preparation of the aldehyde **31** by the modified Brimacombe and Tucker method

After the preparation of the aldehyde **31**, the addition of the phenyl group to the aldehyde **31** to produce a benzylic alcohol was then investigated. Unfortunately, we observed that predominant formation of the desired diastereoisomer **35a** was not possible after several conditions were attempted (Table 1).[32] The major isomer **35b**

obtained was in agreement with the transition state predicted by both the Cram's open chain model or the α-chelation model.[37,38] The absolute stereochemistry at the benzylic carbon in **35b** was confirmed by an X-ray crystallographic analysis of its 7-acetyl-derivative.[32] Because of this poor selectivity, synthesis of the alcohol **35a** by another method was then investigated. Finally, the predominant formation of **35a** proved successful by the oxidation–reduction strategy as shown in Scheme 20.

Table 1. Reaction of compound **31** with PhMgBr, PhCuCNMgBr or PhLi

Entry	Reagent	Temp.(°C)	Solvent	Yield(%)	Ratio **35a** : **35b**
1	PhMgBr	70	THF	73	1 : 6.0
2	PhMgBr	0	THF	74	1 : 8.0
3	PhMgBr	0	Et_2O	65	1 : 3.7
4	PhCuCNMgBr	0	THF	70	1 : 6.2
5	PhLi	0	THF	45	1 : 2.0
6	PhLi	– 78	THF	48	1 : 2.2
7	PhLi	0	Et_2O	47	1 : 3.2
8	PhLi	– 78	Et_2O	48	1 : 5.6



Scheme 20. Preparation of alcohol **35a** by oxidation–reduction strategy

The alcohols **35a** and **35b** were prepared by nucleophilic addition of phenylmagnesium bromide to the aldehyde **31** in refluxing THF under nitrogen to give the benzylic alcohols **35a** and **35b** with 74% overall yield from **34** and in a ratio of 1 to 6, respectively. The success of the Grignard reaction was evident from the ^{1}H NMR spectrum of the mixture of **35a** and **35b** which showed resonances for the aromatic protons between 7.30–7.50 ppm and the benzylic protons around 4.9 ppm.

Selective oxidation of the benzylic hydroxy group in **35a** and **35b** by PCC in dry dichloromethane at room temperature gave the ketone **36** in 61% yield as colorless crystals. The low, isolated yield of the ketone **36** using PCC as oxidant was attributed to the difficult workup procedure. Fortunately, the preparation of the ketone **36** was later improved by using activated manganese dioxide in dry dichloromethane at room temperature to 81% yield. Using manganese dioxide as the oxidant also provided an easier workup procedure. The i.r. spectrum of **36** provided evidence for the successful selective oxidation. A strong absorption peak at 1655 cm^{-1} indicated the presence of a conjugated carbonyl function and absorption at 3450 cm^{-1} showed the presence of hydroxy group. The continued existence of the hydroxy group at C-3 was also supported by the ^{1}H NMR spectrum of **36** in which the OH-3 hydrogen showed resonance at 2.73 ppm and was assigned based on the coupling constants. Furthermore, the identity of the ketone **36** was further corroborated by a correct elemental analysis.

Reduction of the ketone **36** back to the alcohols **35a** and **35b** was then examined. The best conditions for the production of **35a** as the major alcohol were the Luche's procedure as indicated in Table 2.[39] Under those conditions, the ketone **36** was treated with cerium trichloride heptahydrate and sodium borohydride in methanol at – 78 °C for 15 minutes. The alcohols **35a** and **35b** were obtained in 70% yield and in a ratio of 19 to 1, respectively. The identity of the alcohols obtained from the reduction of the ketone **36** was confirmed by comparing the spectroscopic data of the reduction

Table 2. Reduction of ketone **36** by DIBAL-H or $NaBH_4$

Entry	Reagent	Solvent	Temp.(°C)	Yield(%)	**35a:35b**
1	DIBAL-H	THF	– 78	43	1:7
2	$NaBH_4$	MeOH	0	74	1:1
3	$NaBH_4$-$CeCl_3.7H_2O$	MeOH	0	60	5:1
4	$NaBH_4$-$CeCl_3.7H_2O$	MeOH	– 78	70	19:1

products with those of the alcohols obtained directly from the Grignard reaction.

The high stereoselectivity observed for $NaBH_4$–$CeCl_3.7H_2O$ in MeOH at – 78 °C was tentatively rationalized by an internal hydride transfer mechanism through a six-membered chair-like transition state as shown in Figure 11. The alternate transition state (Figure 11a) which would lead to **35b** was destabilized by the 1,3-diaxial interaction between the OMe and the phenyl group. Interestingly, using DIBAL-H as the reducing agent provided the alcohol **35b** as the major isomer. The reversed stereoselectivity using DIBAL-H was best interpreted by an external hydride transfer mechanism as illustrated in Figure 12.[40,41]

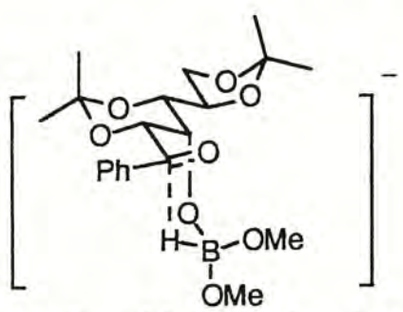


Figure 11. Transition state involved in the reduction of ketone **36** by $CeCl_3.7H_2O$-$NaBH_4$ to yield **35a**

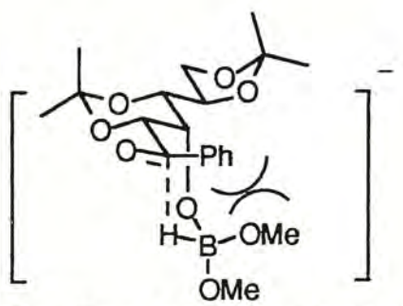


Figure 11a. Transition state involved in the reduction of ketone **36** by $CeCl_3.7H_2O$-$NaBH_4$ to yield **35b**

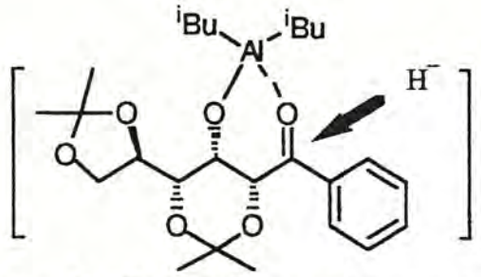
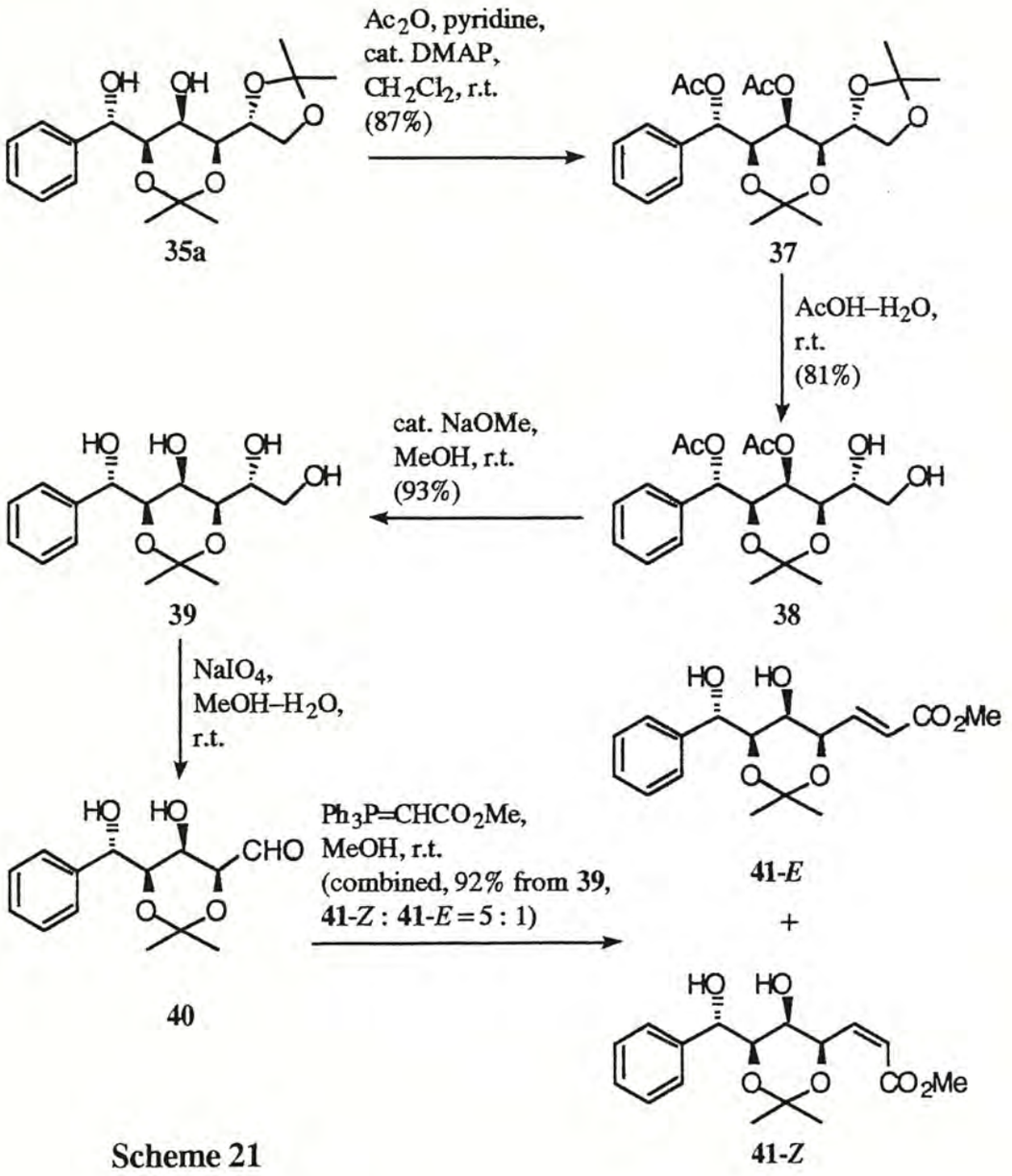


Figure 12. Transition state involved in the reduction of ketone **36** by DIBAL-H to yield **35b**

After obtaining the benzylic alcohol **35a** in good yields, we then proceeded to assemble the lactone moiety required in the target molecule. In order to prepare the tetraol **39**, acetylation of the alcohol **35a** to the diacetate **37** was performed using acetic anhydride–pyridine in dichloromethane at room temperature in 87% yield as shown in Scheme 21. The formation of the diacetate **37** was shown by the two methyl singlets at 2.03 and 2.15 ppm in the ^{1}H NMR spectrum of **37**. The resonances for H-1 and H-3 also exhibited a downfield shift from 4.90 and 3.87 ppm to 5.64 and 5.33 ppm, respectively. I.r. spectrum of **37** showed a carbonyl absorption at 1747 cm^{-1} indicating the presence of the acetate. No absorption around 3400 cm^{-1} supported the transformation of the hydroxy functions into the esters. The structure of **37** was further substantiated by a satisfactory elemental analysis. Pure alcohol **35a** was then obtained after deacetylation of the diacetate **37** by a catalytic amount of NaOMe in dry MeOH at room temperature.

Derivatization of **35a** to the corresponding diacetate **37** was essential and served two purposes. Firstly, selective hydrolysis of the terminal isopropylidene in **35a** directly to the tetraol **39** proved impractical and resulted in a mixture of products. Secondly, acetylation of the alcohols could help its separation by chromatography from the minor undesired alcohol **35b** produced from the reduction of the ketone **36**.



Scheme 21

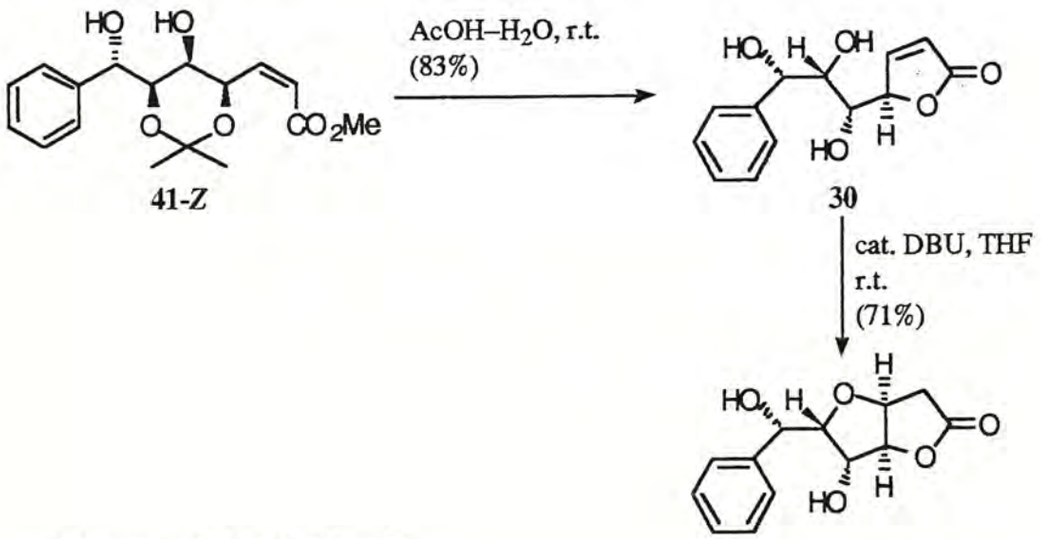
The required tetraol **39** was obtained effectively by the following reaction sequence. Selective hydrolysis of the terminal isopropylidene in **37** proceeded smoothly with 75% aqueous acetic acid at room temperature to give the diol **38** as a white foam in 81% yield. The successful hydrolysis of the terminal isopropylidene in **37** was evident from the ^{1}H NMR spectrum of **38** which exhibited two resonances at 1.29 and 1.34 ppm indicating that only one isopropylidene remained in **38**. An absorption at 3450 cm^{-1} in the i.r. spectrum of **38** indicated the presence of the hydroxy function. The structure of **38** was also substantiated by a correct elemental analysis. Deacetylation of **38** using catalytic amount of sodium methoxide in dry methanol at room temperature then afforded the tetraol **39** as colorless needles in 93% yield. Successful removal of the acetates from **38** was provided by the absence of the

two resonances at 2.02 and 2.23 ppm in the ^{1}H NMR spectrum of **39**. No absorption at 1750 cm^{-1} in the i.r. spectrum of **39** also supported the absence of the carbonyl function in **39**. A correct elemental analysis confirmed the identity of the alcohol **39**. The dioxane isopropylidene ring displayed no migration in the above steps was proved later by the successful glycol cleavage and then Wittig reaction as discussed below.

The terminal diol in **39** was oxidatively cleaved by sodium metaperiodate in aqueous methanol at room temperature to give the aldehyde **40**. Wittig alkenation of the aldehyde **40** with (methoxycarbonyl)methylenetriphenylphosphorane in methanol at room temperature gave a pair of isomers, **41**-*Z* and **41**-*E*, in a ratio of 5 to 1, respectively and in a combined overall yield of 92% from **39**.[42–44] The two isomers **41**-*Z* and **41**-*E* could be readily separated by chromatography as colorless needles and the geometry of the double bond could be easily identified by measuring the coupling constant between the two vinylic protons in their ^{1}H NMR spectra. The alkene with the smaller coupling constant of 12 Hz was assigned to the *Z*-alkene and that with the larger 16 Hz to the *E*-isomer.[45] The presence of the enonate moiety in **41**-*Z* was evident from the resonances of the methyl ester at 3.69 ppm and the two vinylic protons at 5.91 and 6.37 ppm in the ^{1}H NMR spectrum of **41**-*Z*. The enonate function in **41**-*E* was indicated by the resonances of the methyl ester at 3.70 ppm and the two vinylic protons at 6.09 and 6.96 ppm. An absorption at 1719 cm^{-1} in the i.r. spectrum of **41**-*Z* and 1725 cm^{-1} in the i.r. spectrum of **41**-*E* also indicated the presence of the unsaturated ester carbonyls. The identity of both **41**-*Z* and **41**-*E* was further corroborated by their correct elemental analyses. In addition, the *E*-isomer was deliberately prepared in larger quantity by employing toluene as the solvent in which the respective ratio of **41**-*Z* to **41**-*E* was 1 to 2 and with a combined overall 73% yield from **39**.

Removal of the remaining isopropylidene in **41**-*Z* by 75% aqueous acetic acid at room temperature proceeded with concomitant lactonization to give the

trihydroxy-butenolide **30** as colorless needles in 83% yield as shown in Scheme 22. Removal of the isopropylidene was evident from the absence of the six methyl protons at 1.34 ppm in the ^{1}H NMR spectrum of **30**. The most downfield methine hydrogen in the ^{1}H NMR spectrum of **30**, centered at 5.24 ppm (ddd) was assigned as H-4 from the coupling constants. Since lactonization was an intramolecular acylation reaction, the proton attached to the carbon bearing the *O*-acyl group is expected to be deshielded. The most downfield methine hydrogen at 5.24 ppm was H-4, hence compound **30** must be a γ-lactone. Absorption at 1733 cm^{-1} in the i.r. spectrum of **30** provided further evidence of the butenolide structure. The coupling constant of 5.8 Hz and the chemical shifts at 6.13 ppm and 7.80 ppm for the two vinylic protons also suggested a butenolide structure for **30**.[45]



41-*Z* **30** (–)-goniofufurone **21a**

Scheme 22. Synthesis of (–)-goniofufurone **21a**

Treating **30** with a catalytic amount of DBU in THF at room temperature induced the intramolecular Michael addition[46,47] and furnished the goniofufurone **21a** as colorless plates in 71% yield with m.p. 152—154 °C and $[\alpha]_D^{24}$ – 9 (*c* 0.8, ethanol); [lit.,[19] colorless plates with m.p. 152—154 °C and $[\alpha]_D^{22}$ + 9 (*c* 0.5, ethanol)]. Here, we envisaged that the formation of the five-membered furanoid ring in **21a** should be the most facile process and the resulting [3.3.0] bicycle should then be *cis*-fused; in this way, the desired stereochemistry at C-3 would be controlled by the

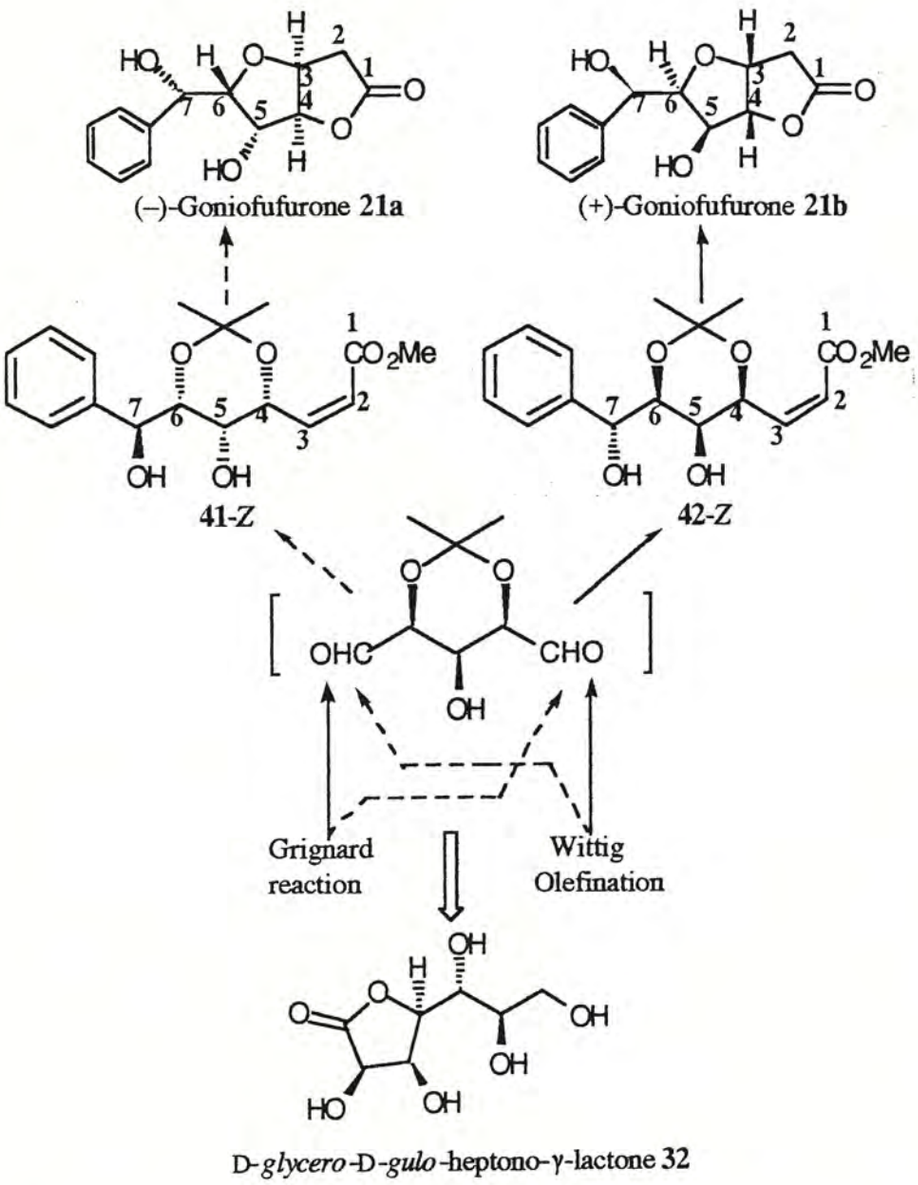
pre-existing chirality at C-4 of the butenolide **30**. The spectroscopic data of the synthetic goniofufurone **21a** are in accord with those reported, and since the reported $[\alpha]_D$ value of the natural goniofufurone is + 9 (*c* 0.5, ethanol), the absolute configuration of the natural goniofufurone must be **21b**. In conclusion, starting with the D-*glycero*-D-*gulo*-heptono-γ-lactone **32**, we completed the structure elucidation of the natural (+)-goniofufurone by synthesizing its enantiomer in 13 steps with 7.4% overall yield.

2.2 Synthesis of (+)-Goniofufurone 21b[21]

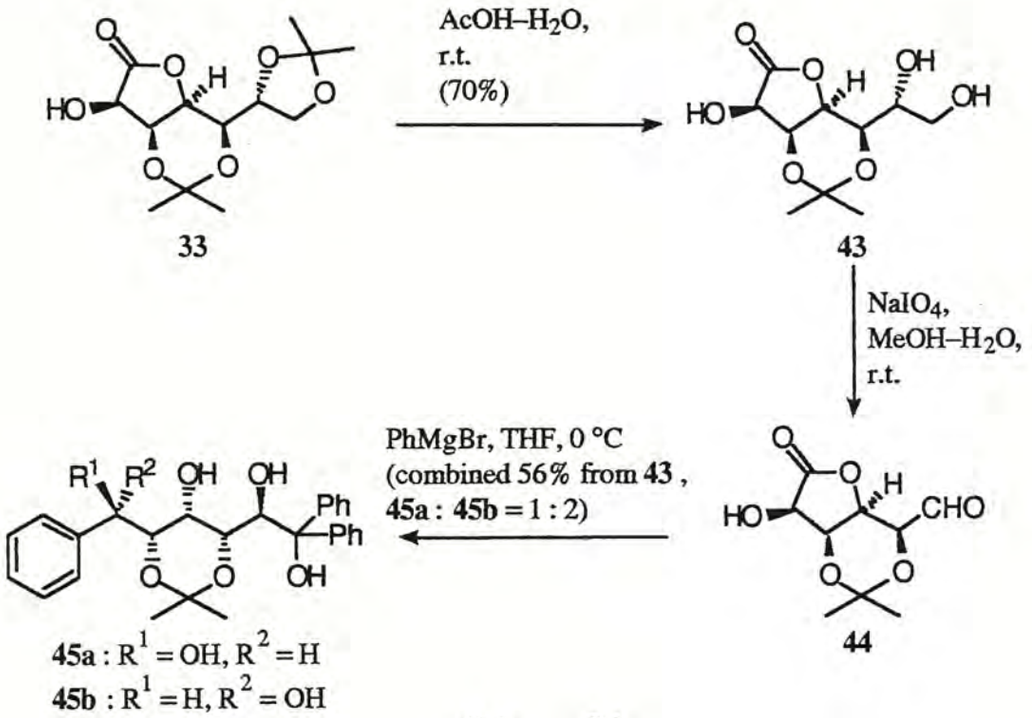
After the absolute stereochemistry of the (+)-goniofufurone was established as **21b**, work on its total synthesis was then initiated. Retrosynthetic analysis of **21b** using the same strategy for **21a** provides the intermediate enonate **42**-*Z* which was the mirror image of **41**-*Z*. Close inspection of **42**-*Z* reveals that the three chiral centres (C-4, C-5, C-6) are symmetrically disposed along the carbon skeleton. Moreover, both the α,β-unsaturated ester and the phenyl group could be introduced in sequence through the aldehyde intermediates as depicted in Scheme 23. The aldehydes could be generated at different stages from the same starting material, the D-*glycero*-D-*gulo*-heptono-γ-lactone **32**.

Therefore, as shown in Scheme 24, starting with the diacetonide **33**, selective hydrolysis of the terminal isopropylidene in **33** using aqueous acetic acid at room temperature provided the diol **43** in 70% yield as colorless needles with m.p. 160—161 °C and $[\alpha]_D^{24}$ – 77 (*c* 2.4, ethanol); [lit.,[48] m.p. 158 °C and $[\alpha]_D$ – 75 (*c* 1.0, ethanol)]. Selective hydrolysis of the terminal isopropylidene was evident from the ^{13}C NMR spectral analysis. The quarternary carbons of the dioxane ring and the dioxolane ring in **33** showed different resonances at 99.76 and 110.64 ppm, respectively. Removal of the terminal isopropylidene was indicated by the absence of the resonance at 110.64 ppm and the continued existence of the dioxane ring ketal

carbon at 99.73 ppm in the ^{13}C spectrum of **43**.[34,35]



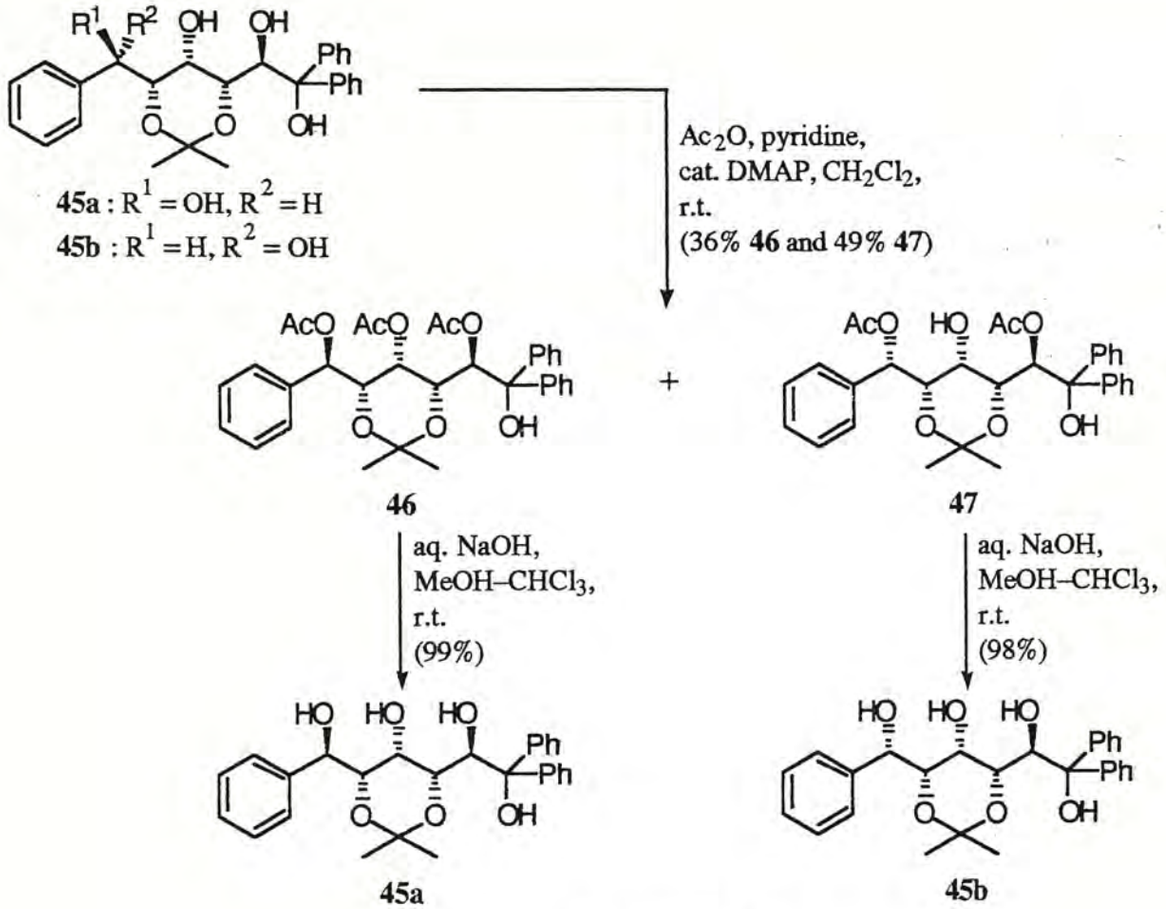
Scheme 23. Retrosynthetic analysis of (+)-goniofufurone **21b**



Scheme 24

Sodium metaperiodate oxidative cleavage of the terminal diol in **43** at room temperature gave the aldehyde **44** which immediately reacted with an excess of phenylmagnesium bromide in THF at 0 °C to provide the diastereoisomeric alcohols **45a** and **45b** in a ratio of 1 to 2, respectively with an overall yield of 56%. In this reaction, the excess of the Grignard reagent reacted with the lactone moiety to give an achiral tertiary alcohol which was important for the construction of the lactone moiety in the target molecule. However, the two diastereoisomeric alcohols proved difficult to separate by conventional chromatographic technique and they were derivatized to their corresponding acetates.

Fortunately, reacting the alcohols **45a** and **45b** with acetic anhydride–pyridine in dry dichloromethane at room temperature gave the triacetate **46** in 36% yield as colorless needles and the diacetate **47** in 49% yield as a white solid. Compounds **46** and **47** could now be easily separated by chromatography. The reasons why **45b** afforded only the diacetate **47** are not understood. The structure of the triacetate **46** was established as described below. Fifteen aromatic protons at 7.13–7.75 ppm in the ^1H NMR spectrum of **46** suggested the presence of three

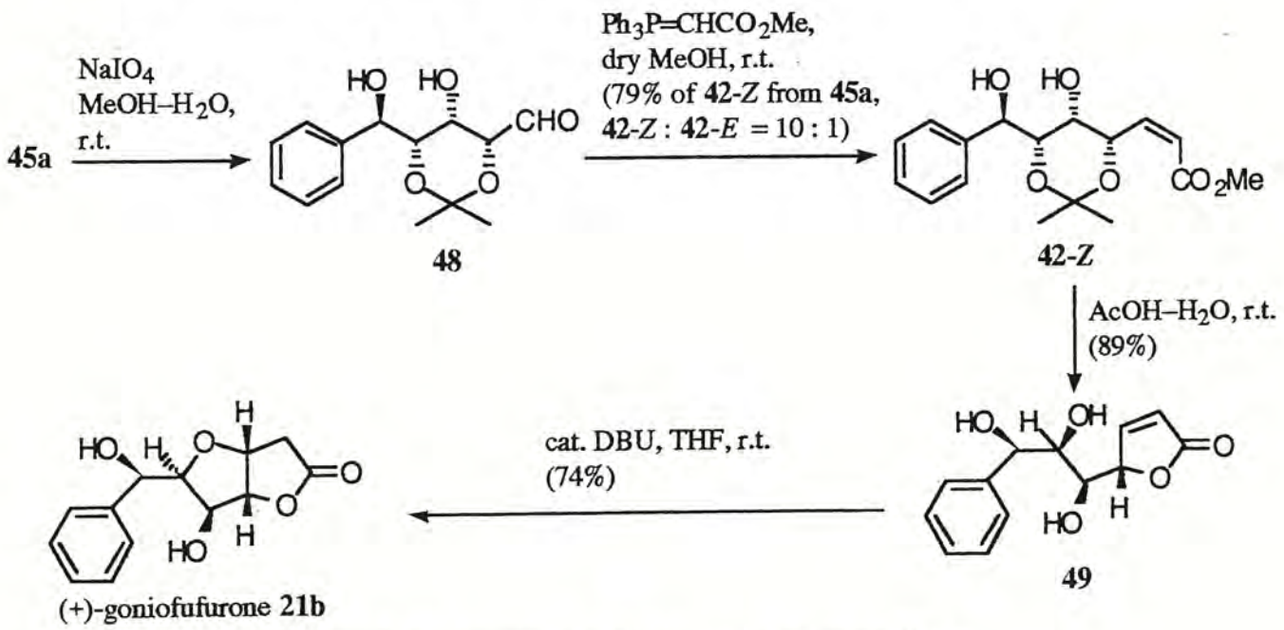


Scheme 25

phenyl groups. Three singlets at 1.85, 1.91 and 2.03 ppm showed the presence of three acetates in **46**. The positions of the acetates in **46** were evident from the down field shift of the protons from 4.47, 3.95 and 4.68 ppm to 5.43, 5.13 and 5.46 ppm for C-2, C-4 and C-6, respectively. This assignment also provided evidence that the dioxane isopropylidene ring showed no rearrangement in the above reactions. Carbonyl absorption at 1750 cm^{-1} in the i.r. spectrum of **46** confirmed the presence of the ester. The structure of **46** was further supported by a correct elemental analysis. The structure of **47** was assigned similarily to that of **46**. Two resonances at 2.00 and 2.04 ppm in the ^1H NMR spectrum of **47** suggested the diacetate structure. The downfield shift of the protons from 4.45 and 4.83 ppm to 5.04 and 5.97 ppm for C-2 and C-6, respectively in **47** provided evident for the positions of the two acetates. Carbonyl absorption at 1750 cm^{-1} in the i.r. spectrum of **47** showed the presence of the ester. The structure of **47** was also supported by a correct elemental analysis.

Pure **45a** and **45b** were regenerated from the respective acetates by hydrolysis with aqueous sodium hydroxide at room temperature in excellent yields. The structures of the alcohols **45a** and **45b** were evident from their ^{1}H NMR and i.r. spectral analysis. Absence of resonances for the acetate methyls in the ^{1}H NMR spectra of **45a** and **45b** showed the success of complete hydrolysis. Strong absorption at 3420 cm^{-1} and 3450 cm^{-1} in the i.r. spectrum of **45a** and **45b**, respectively indicated the presence of hydroxy function. Correct elemental analyses of **45a** and **45b** gave further support to their structures.

The absolute stereochemistry of the newly generated chiral centre at the benzylic position of **45a** and of **45b** was confirmed later by converting **45a** into the corresponding enonate as shown in Scheme 26.



Scheme 26. Synthesis of (+)-goniofufurone **21b**

Oxidative cleavage of the diol **45a** using sodium metaperiodate at room temperature gave the aldehyde **48** which immediately reacted with (methoxycarbonyl)methylenetriphenylphosphorane in dry methanol at room temperature to give **42-*Z*** as colorless needles in 79% yield.[42–44] Ratio of **42-*Z*** to **42-*E*** in this Wittig reaction was determined to be 10 to 1, respectively. Alkene **42-*Z*** with m.p. 135—136 °C and $[\alpha]_D^{24}$ + 71 (*c* 0.4, ethanol) showed all spectroscopic data in

accord with those of **41**-*Z* ; [lit.,[26] m.p. 135—136 °C and $[\alpha]_D^{24}$ – 65 (*c* 0.9, ethanol)], except for the sign of the optical rotation. Therefore, compound **42**-*Z* was enantiomeric to compound **41**-*Z*. In addition, the *E*-isomer was deliberately prepared in larger quantity by employing toluene as the solvent in which the respective ratio of **42**-*Z* to **42**-*E* was 1 to 2 and with a combined 83% overall yield.

The strong preference for the formation of *Z*-enonate **42**-*Z* in the Wittig reaction of stabilized ylides in anhydrous methanol was rationalized based on the report by S. Valverde *et al.* using the model depicted in Figure 13.[42] The requirement for the predominant formation of *Z*-enonate depended on both the solvent and the structure of the aldehyde. Absolute methanol was the best solvent. An alkoxy group at the carbon β to the carbonyl group of the aldehyde was required. The authors suggested that methanol was responsible for the stabilization of the "*anti*" betaine which would undergo *syn*-elimination to afford the *Z*-alkene. The presence of a β-alkoxy substituent can enhance the above mechanism through the participation of the alkoxy group in the solvation phenomena.

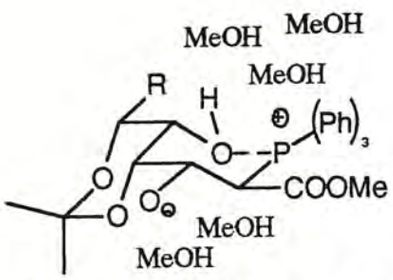


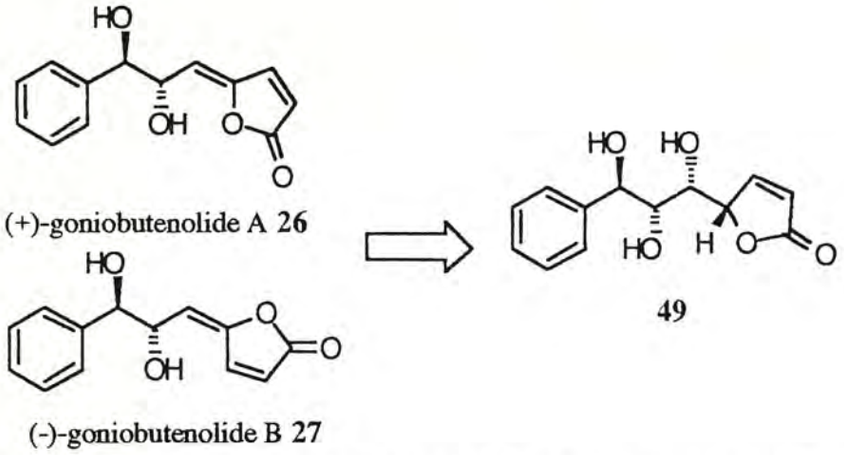
Figure 13. Transition state involved in the wittig reaction that led to the high *Z*-selectivity

After the preparation of the enonate **42**-*Z* (enantiomeric to **41**-*Z*) and following the same sequence of reaction as described previously for **40**-*Z*, we could obtain the natural (+)-goniofufurone **21b**. Hydrolysis of the remaining isopropylidene in **41**-*Z* proceeded with concomitant lactonization gave the trihydroxy-butenolide **49** in 89% yield as colorless needles with m.p. 109—111 °C and $[\alpha]_D^{24}$ – 68 (*c* 0.6,

ethanol). The structure of the butenolide **49** was evident by comparing the spectroscopic data with those of its enantiomer **30**; [lit.,[26] m.p. 109—111 °C and $[\alpha]_D^{23}$ + 72 (c 0.9, ethanol)]. The trihydroxy-butenolide **49** showed all spectroscopic data in accord with those of its enantiomer **30**, except for the sign of the optical rotation. Therefore, the butenolide **49** was enantiomeric to the butenolide **30**. Intramolecular Michael addition induced by DBU in dry THF at room temperature gave the natural (+)-goniofufurone **21b** in 74% yield as colourless plates with m.p. 152—154 °C and $[\alpha]_D^{24}$ + 10 (*c* 1.1, ethanol); [lit.,[19] m.p. 152—154 °C; $[\alpha]_D^{22}$ + 9 (*c* 0.5, ethanol)]. Synthetic **21b** showed all spectroscopic data in accord with those of the natural compound, including the sign of the optical rotation, and gave a correct elemental analysis. Therefore, the absolute stereochemistry of the natural (+)-goniofufurone must be **21b**. In conclusion, the natural (+)-goniofufurone **21b** was synthesized from D-*glycero*-D-*gulo*-heptono-γ-lactone **32** in 10 steps with an overall 4.4% yield.

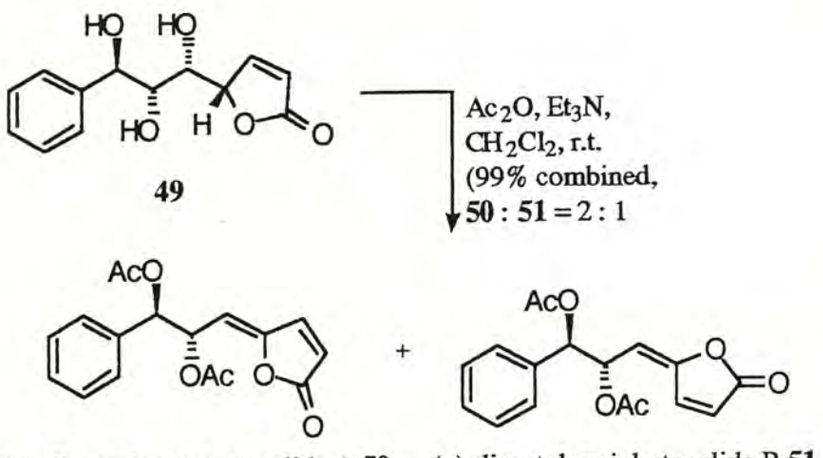
2.3 Syntheses of (+)-Goniobutenolide A 26 and (–)-Goniobutenolide B 27

At a first glance, (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27** could be regarded as the dehydrated analogs of the trihydroxy-butenolide **49** as shown in Scheme 28. In fact, the syntheses of the (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27** seem possible because the hydroxy group at C-5 may be easily eliminated under the acetylation conditions presumably *via* the E1-cb mechanism.[49] However, the generation of compounds **26** and **27** *via* the respective *anti*-E2 and the *syn*-E2 mechanism could not be ruled out.[49]



Scheme 28. Retrosynthetic analysis of (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27**

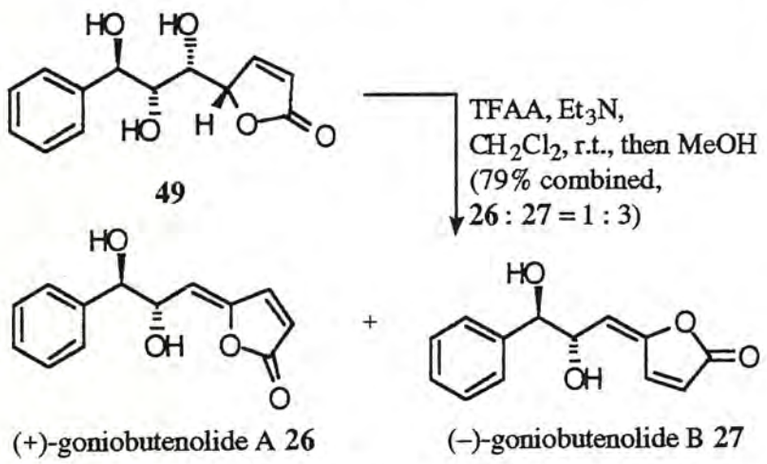
Hence, as shown in Scheme 29, treatment of the trihydroxy-butenolide **49** with acetic anhydride–triethylamine in dry dichloromethane at room temperature gave the (+)-diacetylgoniobutenolide A **50** and (–)-diacetylgoniobutenolide B **51** with a combined overall 99% yield and in a ratio of 2 to 1, respectively. Both compounds **50** and **51** were separated by chromatography as yellowish oils. Synthetic (+)-diacetylgoniobutenolide A **50** and (–)-diacetylgoniobutenolide B **51** in this work showed all spectroscopic data in accord with those of the diacetylgoniobutenolide A and diacetylgoniobutenolide B derived from the natural (+)-goniobutenolide A and (–)-goniobutenolide B, respectively.[28] Structures of both **50** and **51** were further substantiated by their correct elemental analyses.



Scheme 29

At this stage, the syntheses of **26** and **27** were obvious and should be completed simply by deacetylation. However, attempts to remove the acetates from **50** and **51** *via* alkaline hydrolysis proved detrimental because of the highly reactive α,β and γ,δ-unsaturated lactone moiety in both compounds. Decomposition was also observed using LiOH-THF-H_2O and no desired products were isolable.

Fortunately, the synthesis of **26** and **27** were finally realized from **49** by the fact that trifluoroacetyl ester could be easily hydrolyzed under mild conditions.[50] Therefore, the conversion of the trihydroxy-butenolide **49** into (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27** was accomplished by first reacting **49** with trifluoroacetic anhydride and triethylamine (dehydration) and then *in situ* methanol hydrolysis to remove the esters as shown in Scheme 30. Compounds **26** and **27** were



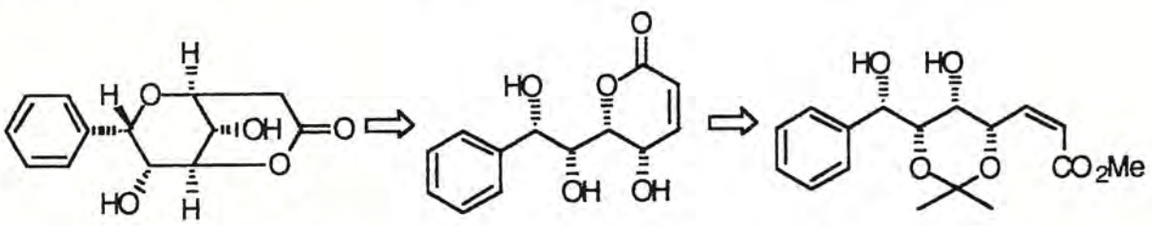
Scheme 30. Synthesis of (+)-goniobutenolide A 26 and (–)-goniobutenolide B 27

obtained with a combined overall yield of 79% from **49** and in a ratio of 1 to 3, respectively. Both synthetic **26** and **27** showed all spectroscopic data in accord with those of the natural compounds, including the sign of the optical rotation.[28] Therefore, the absolute stereochemistry of the natural (+)-goniobutenolide A and (–)-goniobutenolide B must be **26** and **27**, respectively. However, goniobutenolide B **27** was obtained as colorless needles with m.p. 148—149 °C (lit.,[28] yellowish oil) and exhibited limited solubility in chloroform. Interestingly, using trifluoroacetic anhydride to mediate the dehydration gave **26** and **27** in a ratio of 1 to 3 which was reversed

when acetic anhydride was used to produce the diacetate **50** and **51** (2 : 1). This observation was in contrast to our expectation that trifluoroacetyl ester could be easily eliminated through the *anti*-E2 mechanism which would give the (+)-goniobutenolide A **26** as the major product. Therefore, elimination *via* the E1-cb or *syn*-E2 mechanism was possible with trifluoroacetic anhydride.[49] In conclusion, both (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27** were easily synthesized from the D-*glycero*-D-*gulo*-heptono-γ-lactone **32** in 10 steps with an overall 1.2% and 3.6% yield, respectively.

2.4 Synthesis of (+)-Goniopypyrone 22[22]

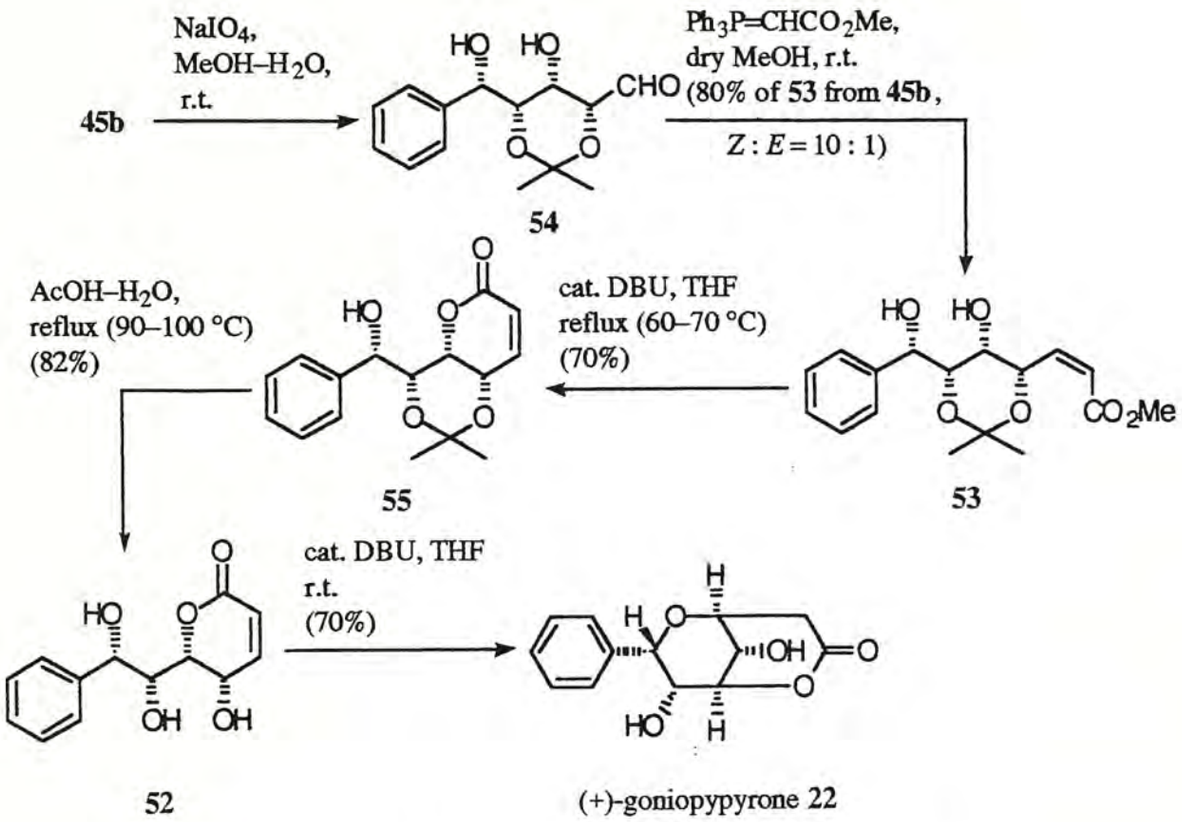
Based on the above works and assuming all the stryl-lactones have the same biosynthetic origin, the absolute stereochemistry of the (+)-goniopypyrone **22** was tentatively assigned as shown in Scheme 31.



(+)-goniopypyrone **22** **52** **53**

Scheme 31. Retrosynthetic analysis of (+)-goniopypyrone **22**

Retrosynthetic analysis of the goniopypyrone **22** using the similar intramolecular Michael strategy for the goniofufurone gives the trihydroxy-pyrone **52**. The trihydroxy-pyrone **52** could be made from the *Z*-enonate **53** through δ-lactonization. The *Z*-enonate **53** might then be obtained by the same reaction sequence as for **45a** to **42**-*Z* discussed previously (Scheme 26).



Scheme 32. Synthesis of (+)-goniopypyrone 22

As shown in Scheme 32, oxidative cleavage of the 1,2-diol in **45b** using sodium metaperiodate provided the aldehyde **54** which reacted with (methoxycarbonyl)methylenetriphenylphosphorane in anhydrous methanol furnished the *Z*-enonate **53** in 80% yield. The idenitity of the enonate **53** was confirmed using the same argument as discussed before for its diastereoisomer **42**-*Z*. The *Z*-geometry of the double bond was indicated by the 12 Hz coupling constant for the two vinylic protons in the ^{1}H NMR spectrum of **53**.

Lactonization induced by DBU in dry THF under reflux gave the pyrone **55** as colorless needles in 70% yield. Absence of the methyl protons at 3.61 ppm and the downfield shift of the C-5 hydrogen from 3.25 ppm to 3.63 ppm in the ^{1}H NMR spectrum of **55** indicated that it is a δ-lactone. The chemical shifts at 6.79 and 6.18 ppm and the coupling constant of 9.6 Hz for the two vinylic protons were in accord with the pyrone structure in **55**. Further evidences were provided by the carbonyl absorption at 1732 cm^{-1} in the i.r. spectrum of **55**, suggesting the presence of the

α,β−unsaturated δ-lactone moiety. Base induced intramolecular Michael addition of **55** proved impossible. Decomposition was observed using LDA in THF and no cyclized products were isolable. The failure of the cyclization was reasoned to the large ring strain in the cyclized product. Therefore, the isopropylidene in **55** was removed first. Hydrolysis of the isopropylidene in **55** by aqueous acetic acid under reflux then generated the trihydroxy-pyrone **52** in 81% yield as colorless needles. The removal of the isopropylidene in **55** was evident from the absence of resonances at 1.53 and 1.56 ppm in the ^{1}H NMR spectrum of **52**. The pyrone moiety in **52** showed no rearrangement to the expected more stable butenolide structure was evident from the continuing existence of the two resonances at 6.02 and 7.06 ppm and the 9.7 Hz coupling constant for the two vinylic protons which is characteristic of the pyrone structure.[45] The structure of **52** was further supported by a correct elemental analysis.

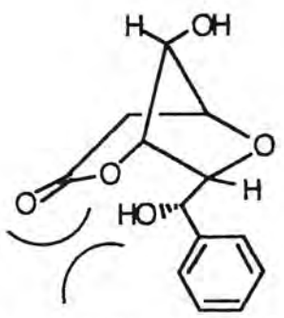


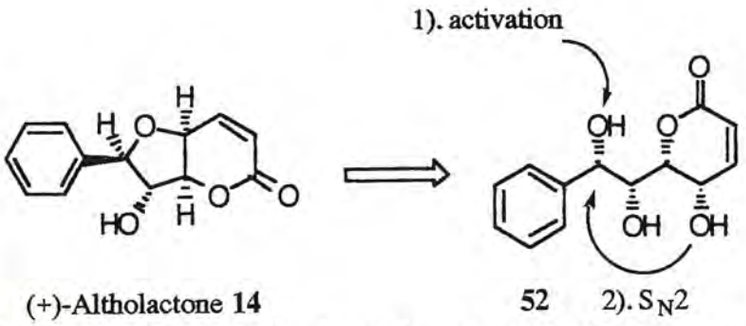
Figure 14. Intramolecular Michael addition by OH-6 of **52**

Intramolecular Michael addition catalyzed by DBU in dry THF at room temperature gave the goniopypyrone **22** with m.p. 178—179 °C and $[\alpha]_D^{22}$ + 53 (*c* 0.6, ethanol); [lit.,[19] 182—184 °C and $[\alpha]_D^{22}$ + 54 (*c* 0.4 ethanol)]. The participation of the OH-6 of **52** in the intramolecular Michael reaction to form the corresponding furanoid ring was reasoned to be unfavorable, being attributable to severe steric interation between the lactone ring and the benzyl moiety as shown in Figure 14. The synthetic goniopypyrone **22** showed all spectroscopic data in accord with those of the natural compound, including the sign of the optical rotation, and gave a correct elemental analysis. Therefore, the structure and the absolute stereochemistry of the natural (+)-goniopypyrone must be **22**. In conclusion, (+)-goniopypyrone **22** was

effectively synthesized from the D-*glycero*-D-*gulo*-heptono-γ-lactone **32** in 11 steps with an overall 3.7% yield.

2.5 Synthesis of (+)-Altholactone 14

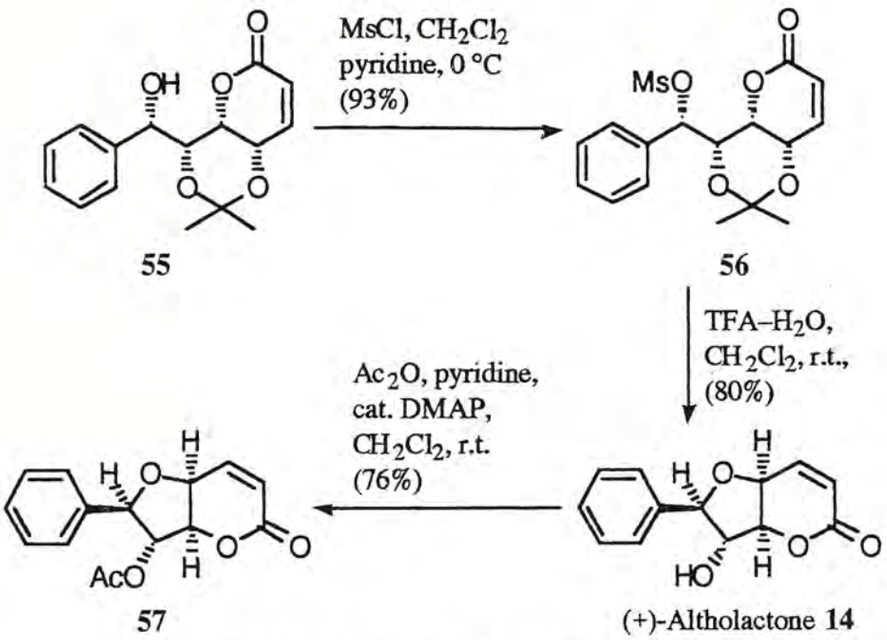
Several reports on the synthesis of the (+)-altholactone **14** had already appeared and the absolute stereochemistry of **14** was shown in Scheme 34.[12–14,31] (+)-Althoactone **14** was regarded as the anhydro analog of the corresponding triol as proposed by several authors.[4, 30, 31] Retrosynthetic analysis of (+)-altholactone **14** using the above idea gives the pyrone **52** as the key intermediate.



Scheme 34. Retrosynthetic analysis of (+)-altholactone **14**

Therefore, activating the hydroxy group as mesylate by treating the pyrone **55** with methanesulfonyl chloride in pyridine–dry dichloromethane at 0 °C gave the unstable mesylate **56** as shown in Scheme 35.

The mesylate **56** was obtained in 93% yield as colorless needles. The presence of the mesylate was evident from the resonance of the methyl singlet at 3.01 ppm in the ^{1}H NMR spectrum of **56**. Furthermore, the downfield shift of the C-7 hydrogen from 5.15 ppm to 5.83 ppm suggested that the mesylate was attached to OH-7. The mesylate was chosen as the activating group because displacement of the mesylate is well established to undergo S_N2 mechanism predominantly.[51]



Scheme 35. Synthesis of (+)-altholactone **14**

Gratifyingly, hydrolysis of the isopropylidene in **56** using TFA–H_2O–CH_2Cl_2 at room temperature occurred with concomitant S_N2 ring closure to give the (+)-altholactone **14** in 80% yield. The synthetic (+)-altholactone **14** showed all spectroscopic data in accord with those of the natural compound. However, the (+)-altholactone **14** produced by the present method was obtained as a colorless oil with $[\alpha]_D^{23}$ + 177 (*c* 1.5, ethanol); [lit.,[10] colorless needles with m.p. 110 °C and $[\alpha]_D^{25}$ + 187 (ethanol)]. The identity of **14** was further proved by converting it into the corresponding acetate. Acetylation of (+)-altholactone **14** using acetic anhydride and pyridine in dry dichloromethane at room temperature gave the (+)-acetylaltholactone **57** as colorless needles with m.p. 141—142 °C and $[\alpha]_D^{25}$ + 204 (*c* 0.3, ethanol); [lit.,[11] m.p. 142 °C; $[\alpha]_D$ + 208 (*c* 1.0, ethanol)]. Furthermore, compound **57** showed all spectroscopic data in accord with those of the acetylaltholactone derived from the natural (+)-altholactone and gave a correct elemental analysis. In conclusion, (+)-altholactone **14** was synthesized from the D-*glycero*-D-*gulo*-heptono-γ-lactone **32** in 11 steps with an overall 4.8% yield.

2.6 Synthesis of (+)-Goniotriol 16 and (+)-7-Acetylgoniotriol 20

The absolute stereochemistries of (+)-goniotriol **16** and (+)-7-acetylgoniotriol **20** had already been established by synthesizing their enantiomers from D-*glycero*-D-*gulo*-heptono-γ-lactone **32**.[15]

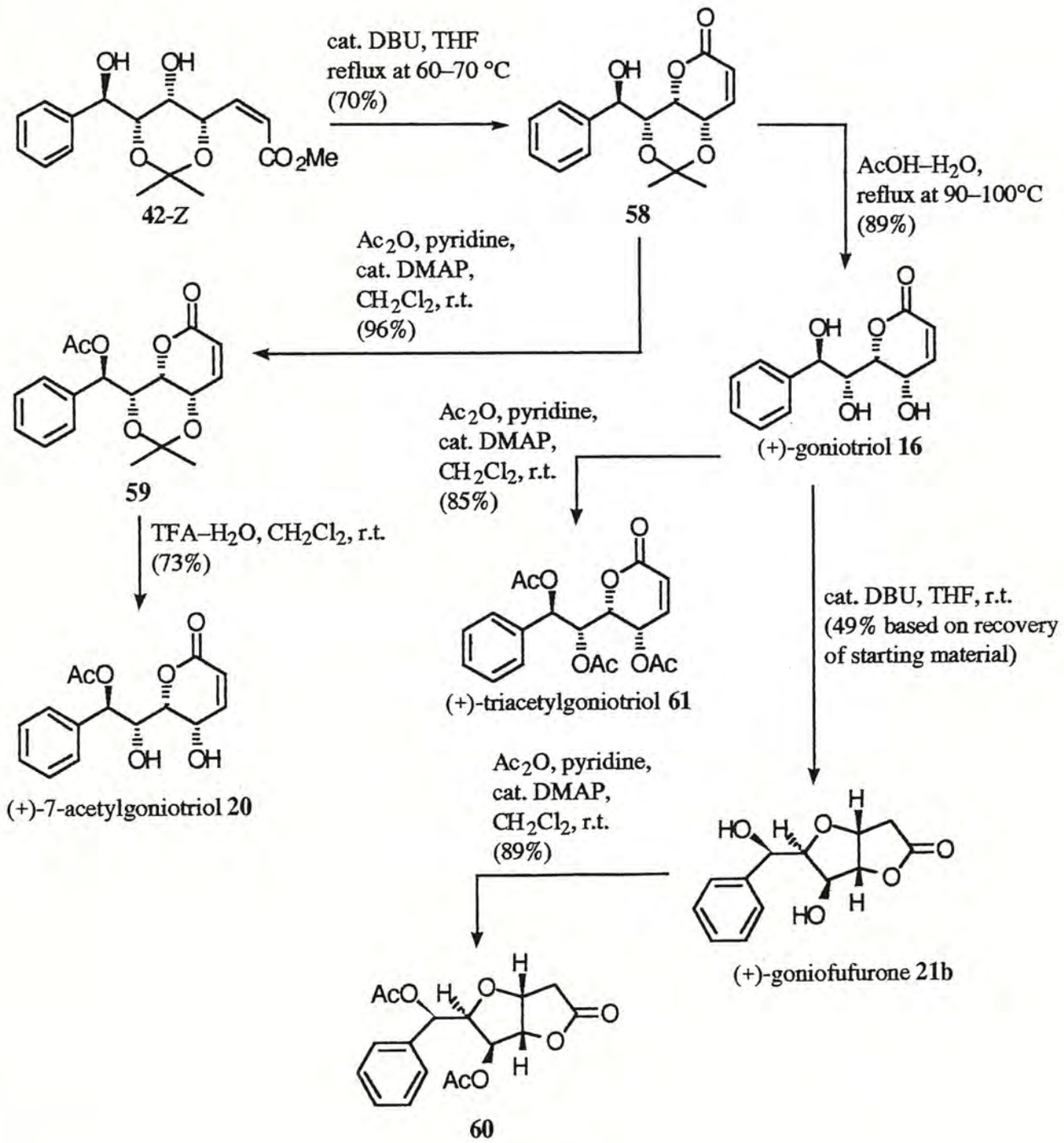
Therefore, the natural (+)-goniotriol **16** and (+)-7-acetylgoniotriol **20** could be easily obtained from the enonate **42**-*Z*, and following the same reaction sequence for their enantiomers. As shown in Scheme 36, lactonization induced by DBU in refluxing THF gave the pyrone **58** in 81% yield as colorless needles. The chemical shifts at 6.25 and 6.89 ppm and the 9.6 Hz coupling constant for the two vinylic protons in the ^{1}H NMR spectrum of **58** were in accord with the pyrone structure as discussed before. Structure of **58** was further substantiated by a satisfactory elemental analysis.

Hydrolysis of the isopropylidene in **58** using aqueous acetic acid at refluxing temperature gave the (+)-goniotriol **16** as colorless needles with m.p. 178—180 °C and $[\alpha]_D^{24}$ + 118 (*c* 0.9, methanol); [lit.,[3] m.p. 173 °C and $[\alpha]_D^{30}$ + 161 (pyridine); for (–)-goniotriol : lit.,[16] m.p. 178—180 °C, $[\alpha]_D^{23}$ – 116 (*c* 0.3, methanol)]. (+)-Goniotriol **16** showed all spectroscopic data in accord with those of the natural compound and gave a correct elemental analysis. The (+)-goniotriol **16** was further characterized by converting it into the corresponding triacetate. Acetylation of **16** using acetic anhydride and pyridine gave the (+)-triacetylgoniotriol **61** as a white solid with m.p. 95—97 °C and $[\alpha]_D^{24}$ + 121 (*c* 0.8 MeOH); [lit.,[3] m.p. 90—93 °C]. Compound **61** showed all spectroscopic data in accord with those of the triacetate derived from the natural (+)-goniotriol and its structure was further substantiated by a correct elemental analysis.

For the synthesis of (+)-7-acetylgoniotriol **20**, acetylation of the pyrone **58** using acetic anhydride and pyridine in dry dichloromethane at room temperature nicely

introduced the acetyl function onto the benzylic hydroxy group to give the 7-acetylpyrone **59**. The presence of the acetate on C-7 in **59** was evident from its ^{1}H NMR spectral analysis. The acetate methyl group showed resonance at 2.03 ppm and the downfield shift of the C-7 proton from 5.11 ppm to 5.99 ppm. Carbonyl absorption at 1725 cm^{-1} in the i.r. spectrum of **59** showed the presence of the acetate. Hydrolysis of **59** using TFA–H_2O in dichloromethane at room temperature gave the (+)-7-acetylgoniotriol **20** as colorless needles with m.p. 159—160 °C and $[\alpha]_D^{24}$ + 38 (*c* 0.9, ethanol); [lit.,[19] m.p. 158—159 °C and $[\alpha]_D^{22}$ + 30 (*c* 0.4, ethanol)]. The synthetic (+)-7-acetylgoniotriol **20** showed all spectroscopic data in accord with those of the natural compound, including the sign of the optical rotation, and gave a satisfactory elemental analysis. In conclusion, (+)-goniotriol **16** and (+)-7-acetylgoniotriol **20** were synthesized from the D-*glycero*-D-*gulo*-heptono-γ-lactone **32** in 10 and 11 steps with overall yield of 4.3% and 3.2%, respectively.

Interestingly, as shown in Scheme 36, when (+)-goniotriol **16** was treated with DBU in THF at room temperature, (+)-goniofufurone **21b** was isolated together with some unreacted starting material **16**. Rearrangement of the pyrone **16** to the butenolide **30** followed by Michael addition was the feasible explanation. The goniofufurone obtained by this rearrangement showed all spectroscopic data in accord with those of the (+)-goniofufurone **21b** prepared previously. The identity of the (+)-goniofufurone **21b** was further supported by derivatizing it to the corresponding diacetate. Acetylation of **21b** using acetic anhydride and pyridine in dry dichloromethane at room temperature gave the (+)-diacetylgoniofufurone **60** as colorless needles, m.p. 184—185 °C and $[\alpha]_D^{24}$ + 22 (0.5, chloroform); [lit.,[19] m.p. 130—132 °C]. Synthetic (+)-diacetylgoniofufurone **60** showed all spectroscopic data in accord with those of the acetylgoniofufurone derived from the natural (+)-goniofufurone. The structures of (+)-goniofufurone **21b** and (+)-diacetylgoniofufurone **60** obtained from the (+)-goniotriol **16** were further substantiated by their correct elemental analyses.


cat. DBU, THF
reflux at 60–70 °C
(70%)
42-Z
58
AcOH–H2O,
reflux at 90–100°C
(89%)
Ac2O, pyridine,
cat. DMAP,
CH2Cl2, r.t.
(96%)
59
(+)-goniotriol 16
Ac2O, pyridine,
cat. DMAP,
CH2Cl2, r.t.
(85%)
TFA–H2O, CH2Cl2, r.t.
(73%)
(+)-triacetylgoniotriol 61
cat. DBU, THF, r.t.
(49% based on recovery
of starting material)
(+)-7-acetylgoniotriol 20
Ac2O, pyridine,
cat. DMAP,
CH2Cl2, r.t.
(89%)
(+)-goniofufurone 21b
60

Scheme 36

3. Conclusions

From the above results, we had devised an effective way for the syntheses of a number of styryl-lactones with various structural complexities from the inexpensive and commerically available D-*glycero*-D-*gulo*-heptono-γ-lactone **32**. The absolute stereochemistries of some of the styryl-lactones have been established. We could also predict that other styryl-lactones (see introduction), which have not been synthesized, should have the same chiralities by assuming that they have a common biosynthetic origin. Moreover, the unnatural enantiomers of these styryl-lactones can also be prepared for biological evaluation.

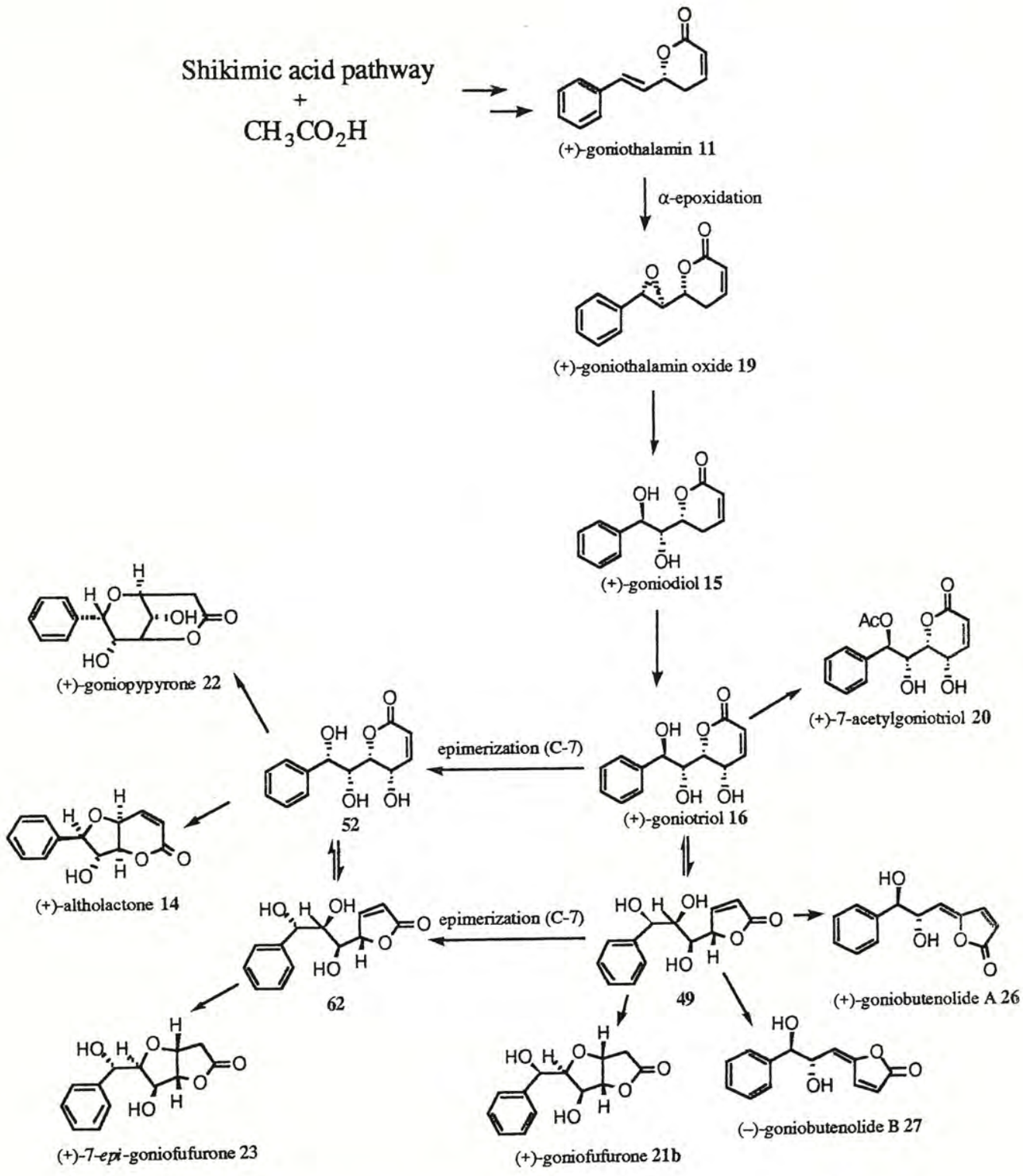
This work has given some hints about the possible biosynthetic pathway of the styryl-lactones (Scheme 37). As discussed previously, the biosynthesis of the styryl-lactones is predicted to be of mixed origin (see page 15). The C_6–C_3 unit comes from the shikimic acid pathway and the C_4 unit comes from two acetyl-Coenzyme A. Coupling of the two units followed by lactonization gives the (+)-goniothalamin **11** as the key intermediate (Scheme 14). α-Epoxidation of the double bond in (+)-goniothalamin **11** gives the (+)-goniothalamin oxide **19**.† *trans*-Opening of the epoxide at the benzylic carbon in **19** gives (+)-goniodiol **15** (see page 16). Allylic hydroxylation of **15** gives (+)-goniotriol **16**. Acetylation at the benzylic hydroxy group gives (+)-7-acetylgoniotriol **20**.

Rearrangement of the pyrone in **16** to the butenolide **49** is evident from our synthetic work (see page 43). Therefore, biosynthetic origin of the five-membered lactone analogues may come from the pyrone intermediates. Thus, (+)-goniofufurone **21b** may be derived from the rearrangement of (+)-goniotriol **16** to the butenolide **49**

† the absolute stereochemistry of **19** has not been confirmed by synthesis.

followed by intramolecular Michael addition. Both the (+)-goniobutenolide A **26** and the (–)-goniobutenolide B **27** may be generated by the elimination of the OH-5 in **49**.

Some styryl-pyrones have the opposite stereochemistry at the benzylic carbon and this stereochemistry is expected through the epimerization of the corresponding hydroxy-pyrones at C-7. Thus, (+)-goniopypyrone **22** may be produced from the (+)-goniotriol **16** through epimerization at the benzylic carbon to give the (+)-7-*epi*-goniotriol **52** followed by an intramolecular Michael addition. (+)-Altholactone **14** can also be regarded as the anhydro analog of the (+)-7-*epi*-goniotriol **52** *via* an intramolecular ring closure with inversion at the benzylic carbon. The (+)-7-*epi*-goniofufurone **23** can be obtained through two possible pathways. The first pathway involves the epimerization of (+)-goniotriol **16** to the pyrone **52** which isomerizes to the butenolide **62** and is followed by an intramolecular Michael addition to give (+)-7-*epi*-goniofufurone **23**. The second pathway towards (+)-7-*epi*-goniofufurone **23** involves the epimerization of the butenolide **49** followed by an intramolecular Michael addition. We propose that butenolides **49** and **62** may be the key intermediates for the biosyntheses of (+)-goniofufurone **21b**, (+)-7-*epi*-goniofufurone **23**, (+)-goniobutenolide A **26** and (–)-goniobutenolide B **27**, although they have not been isolated or reported.



Scheme 37. Proposed biosynthetic pathways for some styryl-lactones.

4. Experimental

Melting points (m.p.)

Melting points were determined with a Reichert apparatus and are reported in degrees Centigrade uncorrected.

Specific optical rotation ($[\alpha]_D^t$)

All optical rotations were measured with a JASCO, DIP-300 automatic digital polarimeter, operating at 589 nm and temperature t.

Infrared absorption spectra (ν_{max}/cm^{-1})

All spectra were recorded on a Nicolet 205 FT-IR spectrometer. The spectra were measured as thin films on sodium chloride discs. All absorption maxima (ν_{max}) are given in wave numbers (cm^{-1}).

^1H Nuclear magnetic resonance spectra (δ_H)

Unless stated to the contrary, all spectra were measured in solutions of deuteriated chloroform on a Brucker WM250 spectrometer at 250 MHz. All chemical shifts were recorded in p.p.m. on the δ scale and measured directly from the spectra. Tetramethylsilane was used as the internal standard for organic solutions. Spin-spin coupling constants are indicated by the symbol *J* which are reported in Hertz and were measured directly from the spectra. The following abbreviations are reported for the multiplicities of the signals : s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad).

^{13}C Nuclear magnetic resonance spectra ($\delta^{13}C$)

Unless stated to the contrary, all spectra were measured in solutions of deuteriated chloroform on a Brucker WM250 spectrometer at 62.9 MHz. All chemical shifts were recorded in p.p.m. on the δ scale and measured directly from the spectra.

Elemental analyses

Carbon and hydrogen elemental analyses were carried out at either the Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, China or the MEDAC Ltd., Department of Chemistry, Brunel University, Uxbridge.

Thin-layer chromatography

All reactions were monitored by thin-layer chromatography (t.l.c.) on aluminum precoated with silica gel $60F_{254}$ (E. Merck) and compounds were visualized with a spray of either 5% w/v dodecamolybdophosphoric acid in ethanol or 5% v/v concentrated sulfuric acid in ethanol and subsequent heating.

Column chromatography

All columns were packed wet using silica gel (230–400 mesh, E. Merck) as the stationary phase and eluted using flash chromatographic technique.[52]

Drying and purification of solvents

Pyridine was distilled over barium oxide and stored in the presence of potassium hydroxide pellets. Absolute methanol was distilled over magnesium and stored in the presence of 4Å molecular sieves. THF was distilled over sodium using benzophenone as indicator. Dichloromethane was distilled over phosphorous pentoxide and stored in the presence of 4Å molecular sieves.

(+)-*Altholactone* **14**.—A solution of the mesylate **56** (215 mg, 0.58 mmol) in trifloroacetic acid and water [10 cm^3 (9 : 1 v/v)] was stirred at room temperature for 1 h. The solvent was then removed *in vacuo* to give a yellow oil. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] afforded the (+)-*altholactone* **14** as a colorless oil (108 mg, 80%), R_f 0.47 [ethyl acetate–hexane (1 : 1 v/v)]; $[\alpha]_D^{23}$ + 177 (*c* 1.5 in EtOH) {lit.,[10] $[\alpha]_D^{25}$ + 187 (EtOH)}; ν_{max}/cm^{-1} 1717, 1733 (α,β-unsaturated δ-lactone), 3400 (OH); δ_H 3.48 (1 H, d, *J* 4.1, 6-OH), 4.44 (1 H, m, 6-H), 4.62 (1 H, t, *J* 5.1, 4-H), 4.73 (1 H, d, *J* 5.6, 7-H), 4.92 (1 H, dd, *J* 2.2 and 5.2, H-5), 6.22 (1 H, d, *J* 9.9, 2-H), 7.00 (1 H, dd, *J* 5.0 and 9.9, 3-H), 7.29–7.35 (5 H, m, Ph); δ^{13}_C 68.15, 83.44, 86.05, 86.53, 123.46, 126.04, 128.17, 128.52, 138.29, 140.52, 161.52; *m/z* (EI) 97 (100%), 91 (43.37), 107 (84.63, $PhCHOH^+$ or M^+ – PhCHOH – H_2O), 232 (27.10, M^+).

(+)-*Goniotriol* **16**.—A solution of the unsaturated lactone **58** (261 mg, 0.90 mmol) in acetic acid (8 cm^3) and water (2 cm^3) was stirred at 90–100 °C for 2 h. The solvents were then removed *in vacuo* to give **16** as a white solid. Purification by flash chromatography (ethyl acetate) then afforded the *triol* **16** (200 mg, 89%) as white crystals. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 178—180 °C (lit.,[3] m.p. 173 °C); R_f 0.41 (ethyl acetate); (Found: C, 62.5; H, 5.7. $C_{13}O_5H_{14}$ requires C, 62.4; H, 5.6%); $[\alpha]_D^{24}$ + 118 (*c* 0.8 in MeOH) {lit.,[3] $[\alpha]_D^{30}$ + 161 (pyridine) and for (–)-goniotriol, lit.,[16] m.p. 178—180 °C and $[\alpha]_D^{23}$ – 116 (*c* 0.3 in MeOH)}; ν_{max}/cm^{-1} 1719 (α,β-unsaturated δ-lactone) and 3400 (OH); δ_H (acetone-d_6) 4.15 (1 H, ddd, *J* 3.1, 4.1 and 8.0, 6-H), 4.35 (1 H, d, *J* 4.2, OH), 4.55 (1 H, m, 4-H), 4.71–4.81 (3 H, m, 5-H, 7-H and OH), 5.10 (1 H, d, *J* 4.9, OH), 6.05 (1 H, d, *J* 9.7, 2-H), 7.05 (1 H, dd, *J* 5.8 and 9.7, 3-H), 7.25–7.49 (5 H, m, Ph); *m/z* (EI) 107 (100%, $PhCHOH^+$), 126 (33.42, M^+ – PhCHOH), 144 (25.49, MH^+ – PhCHOH).

(+)-*7-Acetylgoniotriol* **20**.—A solution of the acetate **59** (357 mg, 1.07 mmol) in dichloromethane (20 cm^3) was stirred at room temperature. Trifluoroacetic acid (10

cm^3) and water (10 cm^3) were added to the solution. After being stirred at room temperature for 16 h, solvents were then removed *in vacuo* to give a yellow oil. Purification by flash chromatography (diethyl ether) then afforded crude **20** (222 mg, 71%) as a white solid. Recrystallization from ethyl acetate–hexane gave **20** as colorless needles, m.p. 159—160 °C (lit.,[19] 158—159 °C); R_f 0.26 (diethyl ether); (Found: C, 61.65; H, 5.4. $C_{15}H_{16}O_6$ requires C, 61.6; H, 5.4); $[\alpha]_D$ + 38 (*c* 0.91 in EtOH) {lit.,[19] $[\alpha]_D^{22}$ + 30 (*c* 0.4, ethanol)}; ν_{max}/cm^{-1} 1725 (ester and α,β-unsaturated δ-lactone), 3400 (OH); δ_H 1.89 (3 H, s, Ac), 4.31–4.81 (4 H, m, 4-H, 5-H, 6-H and OH); 5.01 (1 H, dd, *J* 1.1 and 5.6, OH), 5.75 (1 H, d, *J* 7.3, 7-H), 5.89 (1 H, d, *J* 9.7, 2-H), 6.90 (1 H, dd, *J* 5.6 and 9.7, 3-H), 7.16–7.39 (5 H, m, Ph); *m/z* (EI) 143 (17.43%, M^+ – PhCHOAc), 144 (6.95, MH^+ – PhCHOAc), 149 (8.47, $PhCHOAc^+$), 215 (0.19, M^+ – Ph), 233 (0.42, MH^+ – HOAc).

(–)-*Goniofufurone* **21a**.—A solution of the unsaturated lactone **30** (75 mg, 0.3 mmol) was stirred in dry THF (20 cm^3) containing 0.05% (v/v) DBU at room temperature for 1 d. The solution was then filtered through a short column of silica topped with Celite. Removal of solvent from the filtrate *in vacuo* gave a white solid which was flash chromatographed (diethyl ether) to give (–)-*goniofufurone* **21a** (53mg, 71%) as colorless crystals. Recrystallization from ethyl acetate–hexane gave colorless plates, m.p. 152—154 °C (lit.,[19] m.p. 152—154 °C); R_f 0.24 (diethyl ether); (Found: C, 62.3; H, 5.5. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%); $[\alpha]_D^{24}$ – 9 (*c* 0.8 in EtOH) {lit.,[19] $[\alpha]_D^{22}$ + 9 (*c* 0.5 in EtOH)}; ν_{max}/cm^{-1} 1757 (γ-lactone), 3406 (OH); δ_H 2.64–2.83 (3 H, m, 3-H_a, 3-H_b and 8-OH), 4.10 (1 H, dd, *J* 2.9 and 4.5, 7-H), 4.13 (1 H, d, *J* 2.8, 6-OH), 4.40 (1 H, m, 6-H), 4.87 (1 H, br d, *J* 4.3, 5-H), 5.12 (1 H, dt, *J* 1.3 and 5.1, 4-H), 5.21 (1 H, dd, *J* 3.3 and 4.5, 8-H), 7.33–7.43 (5 H, m, Ph); *m/z* (EI) 107 (100%, $PhCHOH^+$), 232 (9.85, $M^+ - H_2O$).

(+)-*Goniofufurone* **21b**.—A solution of the unsaturated lactone **49** (213 mg, 0.85 mmol) in dry tetrahydrofuran (20 cm^3) containing 0.05% (v/v) DBU was stirred at room temperature for 24 h. The solution was then filtered through a bed of silica gel

topped with Celite. Removal of solvent from the filtrate *in vacuo* gave a white solid which was flash chromatographed [ethyl acetate–hexane (2 : 1 v/v)] to give (+)-*goniofufurone* **21b** (158 mg, 74%) as colorless crystals. Recrystallization from ethyl acetate–hexane gave colorless plates, m.p. 152—154 °C (lit.,[19] m.p. 152—154 °C); R_f 0.55 (ethyl acetate); (Found: C, 62.35; H, 5.4. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%); $[\alpha]_D^{24}$ + 10 (*c* 1.1 in EtOH) {lit.,[19] $[\alpha]_D^{22}$ + 9 (*c* 0.5, EtOH)}; ν_{max}/cm^{-1} 1786 (γ-lactone), 3410 (OH); δ_H 2.64–2.82 (3 H, m, 3-H_a, 3-H_b and 8-OH), 4.10 (1 H, br t, *J* 3.0, 7-H), 4.17 (1 H, d, *J* 2.8, 6-OH), 4.40 (1 H, br s, 6-H), 4.87 (2 H, d, *J* 4.3, 5-H), 5.12 (1 H, br t, *J* 5.0, 4-H), 5.21 (2 H, br t, *J* 3.6, 8-H), 7.35–7.43 (5 H, m, Ph); *m/z* (EI) 107 (100%, PhCHOH), 126 (50.86, M^+ – PhCHOH – OH), 233 (12.30, $MH^+ - H_2O$), 251 (1.73, MH^+).

(+)-*Goniofufurone* **21b** *prepared from* (+)-*goniotriol* **16**.—A solution of the (+)-goniotriol **16** (470 mg, 1.88 mmol) in dry THF (30 cm^3) containing a catalytic amount of DBU was stirred at room temperature for 48 h. The solution was then filtered through a bed of silica gel topped with Celite. Removal of solvents *in vacuo* gave a white solid. Purification by flash chromatography (diethyl ether) afforded **21b** (177 mg, 49% based on recovery of the triol **16**) as colorless crystals and the starting *triol* **16** (111 mg, 24%). Recrystallization of **21b** from ethyl acetate–hexane gave colorless plates, m.p. 152—154 °C (lit.,[19] m.p. 152—154 °C); R_f 0.55 (ethyl acetate); (Found: C, 62.5 ; H, 5.55. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6); $[\alpha]_D^{25}$ + 10 (*c* 0.5 in EtOH) {lit.,[19] $[\alpha]_D^{22}$ + 9 (c 0.5, EtOH)}; ν_{max}/cm^{-1} 1782 (γ-lactone), 3400 (OH); δ_H 2.68 (1 H, dd, *J* 1.5 and 18.8, 2-H_a), 2.81 (1 H, dd, *J* 5.4 and 2-H_b), 4.10 (1 H, dd, *J* 2.9 and 4.7, 6-H), 4.39 (1 H, d, *J* 2.3, 5-H), 4.87 (1 H, d, *J* 4.2, 4-H), 5.12 (1 H, td, *J* 1.5 and 5.4, 3-H), 5.20 (1 H, d, *J* 4.7, 7-H), 7.33–7.45 (5 H, m, Ph); $\delta^{13}C$ 36.42, 71.94, 74.49, 77.91, 84.82, 88.63, 127.61, 128.07, 128.73, 143.31, 176.61; *m/z* (EI) 107 (100%, PhCHOH), 126 (50.86, M^+ – PhCHOH – OH), 233 (12.30, $MH^+ - H_2O$), 251 (1.73, MH^+).

(+)-*Goniopypyrone* **22**.—A solution of the triol **52** (108 mg, 0.43 mmol) in dry THF (20 cm^3) containing a catalytic amount of DBU was stirred at room temperature for 4 h. The solution was then filtered through a bed of silica gel topped with Celite. Removal of solvents *in vacuo* gave a white solid. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] afforded **22** (76 mg, 70%) as white crystals. Recrystallization from ethyl acetate–hexane gave (+)-*goniopypyrone* **22** as colorless needles, m.p. 178—179 °C (lit.,[19] m.p. 182—184 °C); R_f 0.37 [ethyl acetate–hexane (1:1 v/v)]; (Found: C, 62.4; H, 5.6. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%); $[\alpha]_D^{22}$ + 53 (*c* 0.6 in EtOH) {lit.,[19] $[\alpha]_D^{22}$ + 54 (*c* 0.4 in EtOH)}; ν_{max}/cm^{-1} 1746 (lactone), 3330 (OH); δ_H (acetone-d_6) 2.97 (1 H, dd, *J* 1.5 and 19.4, 3-H_b), 3.16 (1 H, dd, *J* 5.2 and 19.4, 3-H_a), 4.04 (1 H, m, 7-H), 4.22 (1 H, m, 5-H), 4.42 (1 H, m, 4-H), 4.65 (1 H, m, 6-H), 4.74 (1 H, br s, 5-OH), 4.97 (1 H , br s, 8-H), 5.18 (1 H, br s, 7-OH), 7.22–7.48 (5 H, m, Ph); δ^{13}_C (acetone-d_6) 35.58, 64.89, 70.47, 71.40, 71.61, 74.32, 127.61, 128.06, 128.62, 139.29, 169.23; *m/z* (EI) 107 (100%, $PhCHOH^+$), 126 (10.72, $MH^+ - PhCHOH - H_2O$), 144 (9.55, $MH^+ - PhCHOH$), 250 (7.73, M^+).

(+)-*Goniobutenolide A* **26** and (–)-*Goniobutenolide B* **27**.—A solution of the triol **49** (599 mg, 2.4 mmol) in dry dichloromethane (20 cm^3) was stirred at room temperature. Triethylamine (1.7 cm^3), trifluoroacetic anhydride (1.7 cm^3) were added to the solution. After the solution was stirred at room temperature for 2 h, methanol (20 cm^3) was then added. The solution was stirred at room temperature for 5 h then filtered through a bed of silica gel topped with Celite. Evaporation of the filtrate *in vacuo* gave a yellow solid. Purification by flash chromatography [diethyl ether–hexane (4 : 1 v/v)] gave (+)-*goniobutenolide A* **26** and (–)-*goniobutenolide B* **27** (437 mg, 79%) as a yellow solid. Pure **26** and **27** were obtained by repeated chromatography. The less polar (–)-*goniobutenolide B* **27** was obtained as colorless needles, m.p. 148—149 °C; R_f 0.31 [diethyl ether–hexane (4 : 1 v/v)]; (Found: C, 67.1; H, 5.2. $C_{13}H_{12}O_4$ requires C, 67.2; H, 5.2%); $[\alpha]_D^{27}$ – 112 (*c* 0.2 in $CHCl_3$) {lit.,[28] $[\alpha]_D^{24}$ – 37 (*c* 0.2 in $CHCl_3$)}; ν_{max}/cm^{-1} 1670 (C=C), 1742 (C=O), 3404 (OH); δ_H 2.35 (1 H, d, *J* 4.9, 6-OH), 2.42 (1 H, d, *J* 3.3, 7-OH), 4.65 (1 H, dt, *J* 4.6 and 7.8, 6-H), 4.89

(1 H, dd, *J* 3.3 and 4.6, 7-H), 5.79 (1 H, ddd, *J* 0.7, 1.8 and 7.8, 5-H), 6.14 (1 H, dd, *J* 1.8 and 5.7, 2-H), 7.28–7.37 (5 H, m, Ph), 7.51 (1 H, d,*J* 0.7 and 5.7, 3-H); *m/z* (EI) 77 (37.98%), 79 (44.39), 97 (14.29), 107 (43.16), 126 (100).

The more polar (+)-*Goniobutenolide A* **26** was obtained as a yellowish oil, R_f 0.28 [diethyl ether–hexane (4 : 1 v/v)]; $[\alpha]_D^{27}$ + 187 (*c* 0.4 in $CHCl_3$) {lit.,[28] $[\alpha]_D^{24}$ + 82 (*c* 0.3 in $CHCl_3$)}; ν_{max}/cm^{-1} 1678 (C=C), 1748, 1777 (C=O), 3426 (OH); δ_H 4.92–4.99 (2 H, m, 2-H and 6-H), 5.30 (1 H, d, *J* 8.3, 7-H), 6.13 (1 H, d, *J* 5.4, 2-H), 7.24–7.33 (6 H, m, Ph and 3-H); $\delta^{13}C$ 70.77, 76.11, 112.99, 120.41, 126.50, 128.06, 128.35, 139.26, 143.51, 150.57, 169.00; *m/z* (EI) 77 (29.19%), 79 (28.86), 91 (3.38), 97 (8.37), 107 (23.86), 126 (47.17). The ratio of **26** : **27** (*ca.* 1 : 3) was determined by ^1H NMR spectral analysis.

(*Z*)-7-C-*Phenyl*-L-gluco-*hept*-2-*enono*-γ-*lactone* **30**.—A solution of the enonate **41**-*Z* (101 mg, 0.31 mmol) in acetic acid (8 cm^3) and water (2 cm^3) was stirred at room temperature for 2 d. The solvents were then removed by azeotropic distillation with toluene *in vacuo* to give a white solid. Purification by flash chromatography [diethyl ether–hexane (1 : 1 v/v)] afforded the *unsaturated lactone* **30** (65 mg, 83%) as a colorless solid. Recrystallization from diethyl ether–hexane gave colorless needles, m.p. 109—111 °C; R_f 0.20 [diethyl ether–hexane (1 : 1 v/v)]; $[\alpha]_D^{23}$ + 72 (*c* 0.9 in EtOH); ν_{max}/cm^{-1} 1733 (α,β-unsaturated γ-lactone), 3400 (OH); δ_H (acetone-d_6) 3.70 (1 H, br dd, *J* 2.1 and 7.7, 6-H), 4.08 (1 H, br d, *J* 2.1 and 5.5, 5-H), 4.77 (1 H, d, *J* 7.7, 7-H), 5.24 (1 H, ddd, *J* 1.7, 1.9 and 5.5, 4-H), 6.13 (1 H, dd, *J* 1.9 and 5.8, 2-H), 7.24–7.46 (5 H, m, Ph), 7.80 (1 H, dd, *J* 1.7 and 5.8, 3-H); *m/z* (EI) 107 (100%, $PhCHOH^+$), 143 (1.17, M^+ – PhCHOH).

2,4:5,6-*Di*-O-*isopropylidene*-D-*glucose* **31**.—Sodium metaperiodate (3.7 g, 0.017 mol) was added in one portion to a stirred solution of the triol **34** (5 g, 0.017 mol) in methanol (50 cm^3) and water (5 cm^3) at room temperature. After being stirred at room temperature for 3 h, the white suspension was filtered. Solvent removal from the

filtrate gave the crude *aldehyde* **31** as a colorless oil. The aldehyde was dried by concentrating several times with toluene *in vacuo*. The dried aldehyde was used for the next step without further purification.

3,5:6,7-*Di*-O-*isopropylidene*-D-glycero-D-gulo-*heptono*-γ-*lactone* **33**.—Anhydrous zinc chloride (6.54 g, 0.048 mol) and a few drops of 85% phosphoric acid were added to a stirred suspension of D-*glycero*-D-*gulo*-heptono-γ-lactone **32** (10.0 g, 0.048 mol) in dry acetone (200 cm^3) at room temperature. After being stirred at room temperature for 24 h, the solution was adjusted with aqueous ammonia solution (S.G. 0.88) to pH 8–9. The white solid was filtered through a bed of Celite and solvent removal from the filtrate gave a pale yellow syrup. The syrup was then dissolved in chloroform (250 cm^3) and washed with water (100 cm^3). The aqueous layer was extracted with chloroform (2 × 20 cm^3) and the combined organic extracts were dried ($MgSO_4$) and filtered. The filtrate was concentrated to approximate 250 cm^3 and hexane was added until precipitation of the *title compound*. The precipitate was filtered to give a white solid. Recrystallization from chloroform–hexane afforded the *diacetonide* **33** as colorless needles (8.5 g, 61%), m.p. 157—158°C (lit.,[33] m.p. 153—154 °C); R_f 0.31 (ether); $[\alpha]_D^{24}$ − 76 (*c* 1.1 in $CHCl_3$) {lit.,[33] $[\alpha]_D^{30}$ − 76 (*c* 2 in $CHCl_3$) ; ν_{max}/cm^{-1} 3450 (OH) and 1788 (γ-lactone); δ_H 1.36 (3 H, s, Me), 1.41 (3 H, s, Me), 1.44 (3 H, s, Me), 1.50 (3 H, s, Me), 3.01 (1 H, d, *J* 9.8, 2-OH), 3.85 (1 H, dd, *J* 1.9 and 8.5, 5-H), 3.93 (1 H, dd, *J* 4.1 and 9.0, 7-H_a), 4.11 (1 H, dd, *J* 6.2 and 8.8, 7-H_b), 4.29–4.36 (2 H, m, 6-H and 4-H), 4.51 (1 H, dd, *J* 4.0 and 9.7, 2-H), 4.26 (1 H, dd, *J* 2.2 and 4.1, 3-H); $\delta^{13}C$ (d_4-methanol) 19.78 (Me), 25.43 (Me), 27.09 (Me), 29.33 (Me), 67.88, 70.31, 70.50, 70.74, 72.49, 74.89 (2-C, 3-C, 4-C, 5-C, 6-C and 7-C), 99.76 (dioxane), 110.64 (dioxolane) and 177.46 (carbonyl); *m/z* (EI) 273 (30.05%, M^+ – Me).

1,2:3,5-*Di*-O-*isopropylidene*-D-glycero-L-gulo-*heptitol* **34**.—Sodium borohydride (5.3 g, 0.14 mol) was added in portions to a stirred solution of the lactone **33** (20 g, 0.069 mol) in methanol (100 cm^3) at 0 °C. After being stirred overnight and with the

temperature rising from 0 °C to room temperature, the reaction was quenched with a few drops of acetic acid. Evaporation of solvent *in vacuo* gave a colorless syrup. The syrup was then dissolved in chloroform (100 cm^3), dried ($MgSO_4$) and filtered. Removal of solvent from the filtrate gave the *triol* **34** (20g, 98%) as a white foam. Crystallization from chloroform–hexane afforded the *triol* **34** as white plates, m.p. 62—64°C (lit.,[33] m.p. 67—68 °C); R_f 0.31 (ethyl acetate); $[\alpha]_D^{25}$ – 6 (*c* 0.5 in H_2O); {lit.,[33] $[\alpha]_D$ – 6 (*c* 2 in H_2O)}; ν_{max}/cm^{-1} 3400 (OH); δ_H 1.36 (3 H, s, Me), 1.39 (3 H, s, Me), 1.42 (6 H, s, 2 × Me), 3.66 (1 H, d, *J* 8.4), 3.73–3.92 (5 H, m), 4.08 (1 H, dd, *J* 6.4 and 8.7), 4.26 (1 H, ddd *J* 4.7, 6.1 and 8.2, 2-H); *m/z* (EI) 277 (8.02%, M^+ – Me).

2,4:5,6-*Di*-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-gulo-*hexitol* **35a** and 2,4:5,6-*di*-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-ido-*hexitol* **35b**.—Bromobenzene (9.0 cm^3) was added dropwisely to a stirred suspension of magnesium turnings (2.1 g) in dry THF (100 cm^3) under nitrogen at room temperature. After the addition of bromobenzene, the solution was then stirred at room temperature until most of the magnesium dissolved. The aldehyde **31** prepared from the previous experiment was dissolved in dry THF (50 cm^3) and added dropwise to the Grignard reagent at 60–70 °C. The mixture was stirred at 60–70 °C for a further 3h. The solution was then cooled to room temperature and quenched by cold saturated ammonium chloride. The solid was filtered off and the filtrate was extracted with chloroform (50 cm^3, then 2 × 20 cm^3). The combined organic extracts were dried ($MgSO_4$) and filtered. Evaporation of solvent from the filtrate gave a yellow oil. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] gave a diastereoisomeric mixture of **35a** and **35b** as a white foam (4.3 g, 74%). The ratio of **35a** : **35b** (*ca.* 1 : 6) was estimated by ^1H NMR spectral analysis.

Stereoselective reduction of ketone **36** *to the mixture of alcohols* **35a** *and* **35b**.—*Method A*. Cerium trichloride heptahydrate (2.8 g, 7.6 mmol) was added to a stirred solution of the ketone **36** (1.3 g, 3.8 mmol) in methanol (200 cm^3) at room

temperature. The solution was cooled in a dry ice-acetone bath and sodium borohydride (0.15 g, 3.8 mmol) was added. After 15 min, the mixture was quenched with a few drops of acetic acid. The temperature was then raised to room temperature gradually. The methanol was removed *in vacuo* and the residue extracted with chloroform (100 cm^3). The extract was dried ($MgSO_4$) and filtered. Removal of the solvent gave a mixture of diastereoisomeric alcohols (**35a** : **35b**, *ca.* 19 : 1) as a white solid (0.90 g, 70%). The ratio of diastereoisomers was determined by ^1H NMR spectral analysis.

Method B. Sodium borohydride (8 mg, 0.21 mmol) was added to a stirred solution of the ketone **36** (70 mg, 0.21 mmol) in methanol (10 cm^3) at 0 °C for 15 min, a few drops of acetic acid was added to quench the reaction. The methanol was removed *in vacuo* and the residue extracted with chloroform (20 cm^3). The extract was dried ($MgSO_4$) and the filtrate was concentrated. A mixture of diastereoisomers (**35a** : **35b**, *ca.* 1 : 1) was obtained as a white solid (52 mg, 74%). The ratio was estimated by t.l.c.

Method C. Cerium trichloride heptahydrate (11 mg, 0.030 mmol) was added to a stirred solution of the ketone **36** (5 mg, 0.015 mmol) in methanol (10 cm^3) at room temperature. The mixture was cooled to 0 °C and sodium borohydride (0.6 mg, 0.016 mmol) was added. After being stirred for 15 min, the solution was quenched with a few drops of acetic acid. The temperature of the mixture was raised to room temperature gradually. The methanol was removed and the residue was extracted with chloroform (20 cm^3). The extract was dried ($MgSO_4$) and filtered. Removal of the solvent gave a mixture of diastereoisomers (**35a** : **35b**, *ca.* 5 : 1) as a white solid (3 mg, 60%). The ratio of diastereoisomers was estimated by t.l.c.

Method D. Diisobutylaluminum hydride in toluene (1.0 dm mol^{-1} ; 0.12 cm^3, 0.12 mmol) was added to a solution of the ketone **36** (10 mg, 0.03 mmol) in dry THF (10 cm^3) at – 78 °C. After being stirred for 15 min at – 78 °C, a few drops of acetic acid

was added to quench the reaction. The temperature was recovered to room temperature and the solvent was removed *in vacuo*. The residue was extracted with chloroform (20 cm^3), dried ($MgSO_4$) and filtered. Removal of the solvent gave a mixture of diastereoisomers (**35a** : **35b**, *ca.* 1 : 7) as a white solid (4.3 mg, 43%). The ratio of diastereoisomers was also estimated by t.l.c.

2,4:5,6-*Di*-O-*isopropylidene*-1-C-*phenyl*-D-gluco-*hex*-1-*ulose* **36**.—*Method A*. Pyridinium chlorochromate (0.64 g, 2.96 mmol) was added in one portion to a stirred solution of the mixture **35a** and **35b** (0.50 g, 1.48 mmol) in dry dichloromethane (20 cm^3) containing powdered 4Å molecular sieve (0.5 g) at room temperature. The reaction was stirred at room temperature for 3 h and then Celite (1.0 g) and diethyl ether (100 cm^3) were added. The mixture was stirred at room temperature for a further 15 min and then filtered through a bed of silica gel topped with Celite. Removal of the solvent from the filtrate *in vacuo* gave crude **36** as a yellow solid. Fractionation by flash chromatography [ethyl acetate–hexane (1 : 2 v/v)] afforded a white solid. Recrystallization from diethyl ether–hexane afforded the *ketone* **36** (0.30 g, 61%) as colorless needles, m.p. 201—202 °C; R_f 0.38 [ethyl acetate–hexane (1 : 2 v/v)]; (Found: C, 63.9; H, 7.0. $C_{18}H_{24}O_6$ requires C, 64.3; H, 7.2%); $[\alpha]_D^{23}$ + 10 (*c* 0.7 in EtOAc); ν_{max}/cm^{-1} 1655 (conjugated C=O), 3450 (OH); δ_H 1.30–1.60 (12 H, 4s, 4 × Me), 2.73 (1 H, d, *J* 9.2, 3-OH), 3.84 (1 H, dd, *J* 1.2 and 8.1, 4-H), 4.07 (1 H, ddd, *J* 1.2, 1.3 and 9.2, 3-H), 4.09 (1 H, dd, *J* 6.2 and 8.7, 6-H), 4.29 (1 H, ddd, *J* 4.7, 6.2 and 8.1, 5-H), 5.22 (1 H, d, *J* 1.3, 2-H), 7.40–8.00 (5 H, m, Ph); *m/z* (EI) 105 (100%, $C_6H_5C{=}O^+$), 231 (7.52, $M^+ - C_6H_5C{=}O$).

Method B. Manganese dioxide (15.7 g, 0.18 mol) was added in one portion to a stirred solution of the mixture **35a** and **35b** (3.6 g, 0.011 mol) in dry dichloromethane (50 cm^3) at room temperature. After being stirred at room temperature for 48 h, the mixture was then filtered through a bed of silica gel topped with Celite. Evaporation of solvent *in vacuo* gave the *ketone* **36** (3.0 g, 85%) as white crystals. The crystals could be used in the next step without further purification.

1,3-*Di*-O-*acetyl*-2,4:5,6-*di*-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-gulo-*hexitol* **37**.—A solution of **35a** (1.03 g, 3.04 mmol) in dry dichloromethane (20 cm^3) was stirred at room temperature. Pyridine (7.4 cm^3, 0.091 mol), acetic anhydride (8.6 cm^3, 0.091 mmol) and a catalytic amount of DMAP were added. After being stirred at room temperature for 48 h, the mixture was washed with water (20 cm^3). The organic layer was dried ($MgSO_4$) and filtered. Concentration of the filtrate under reduced pressure followed by flash chromatography [ethyl acetate–hexane (1 : 4 v/v)] afforded the *acetate* **37** (1.11 g, 87%) as a white foam. Crystallization from chloroform-hexane gave colorless prisms, m.p. 88—89 °C; R_f 0.32 [ethyl acetate–hexane (1 : 4 v/v)]; (Found: C, 62.0; H, 7.3. $C_{19}H_{26}O_8$ requires C, 62.55; H, 7.2%);$[\alpha]_D^{24}$ – 8 (*c* 0.9 in EtOAc); ν_{max}/cm^{-1} 1747 (ester C=O); δ_H 1.28 (3 H, s, Me), 1.32 (6 H, s, 2 × Me), 1.41 (3 H, s, Me), 2.03 (3 H, s, Ac), 2.15 (3 H, s, Ac), 3.87–4.06 (4 H, m, 4-H, 5-H, 6-H_a and 6-H_b), 4.26 (1 H, dd, *J* 1.5 and 9.5, 2-H), 5.33 (1 H, t, *J* 1.5, 3-H), 5.64 (1 H, d, *J* 9.5, 1-H), 7.28–7.36 (5 H, m, Ph); *m/z* (EI) 407 (10.6%, M^+ – Me).

2,4:5,6-*Di*-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-gulo-*hexitol* **35a**.—A solution of diacetate **37** (0.50 g, 1.2 mmol) in dry methanol (5.0 ml) was treated with a catalytic amount of sodium methoxide at room temperature for 1 h. The mixture was passed through a pad of silica gel. Concentration of the filtrate yielded the *alcohol* **35a** (0.40 g, 100%) as a white solid. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 133—135 °C; R_f 0.10 [chloroform–ethanol (98 : 2 v/v)], 0.30 [ethyl acetate–hexane (1 : 1 v/v)]; $[\alpha]_D^{23}$ + 11 (*c* 1.0 in EtOAc); ν_{max}/cm^{-1} 3442 (OH); δ_H 1.30 (3 H, s, Me), 1.35 (3 H, s, Me), 1.37 (3 H, s, Me), 1.40 (3 H, s, Me), 3.05 (1 H, d, *J* 7.8, 3-OH), 3.22 (1 H, d, *J* 5.5, 1-OH), 3.60 (1 H, dd, *J* 1.3 and 8.1, 4-H), 3.85 (1 H, dd, *J* 0.9 and 4.9, 2-H), 3.87 (1 H, ddd, *J* 0.9, 1.3 and 7.8, 3-H), 3.88 (1 H, dd, *J* 4.8 and 8.5, 6-H_b), 4.10 (1 H, dd, *J* 6.4 and 8.6, 6-H_a), 4.26 (1 H, ddd, *J* 4.8, 6.2 and 8.1, 5-H), 4.90 (1 H, dd, *J* 5.6 and 5.0, 1-H), 7.30–7.43 (5 H, m, Ph); *m/z* (EI) 101 (100%, $C_5O_2H_9^+$), 107 (13.46, $PhCHOH^+$), 231 (3.20, M^+ – PhCHOH), 323 (1.9, M^+ – Me).

1,3-*Di*-O-*acetyl*-2,4-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-gulo-*hexitol* **38**.—A solution of the diacetate **37** (500 mg, 1.18 mmol) in acetic acid (20 cm^3) and water (20 cm^3) was stirred at room temperature for 15 h. The solvents were removed by azeotropic distillation with toluene *in vacuo* to give a yellow syrup residue. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] afforded the *diol* **38** (367 mg, 81%) as a white foam, R_f 0.43 (diethyl ether); (Found: C, 59.7; H, 6.8. $C_{19}H_{26}O_8$ requires C, 59.7; H, 6.85%); $[\alpha]_D^{24}$ + 19 (*c* 1.0 in EtOAc); ν_{max}/cm^{-1} 1750 (ester C=O), 3450 (OH); δ_H 1.29 (3 H, s, Me), 1.34 (3 H, s, Me), 2.02 (s, 3 H, Ac), 2.23 (3 H, s, Ac), 3.40–3.49 (1 H, m, 5-H), 3.64 (1 H, br dd, *J* 5.0 and 11, 6-H_a), 3.82 (1 H, br dd, *J* 3.2 and 11, 6-H_b), 3.92 (1 H, dd, *J* 1.1 and 9.4, 4-H), 4.25 (1 H, dd, *J* 1.5 and 9.4, 2-H), 5.09 (1 H, br t, *J* 1.4, 3-H), 5.83 (1 H, d, *J* 9.4, 1-H), 7.31–7.38 (5 H, m, Ph); *m/z* (EI) 310 (5%, $M^+ - 2 \times Me - C_3H_6$), 325 (100, $M^+ - Me - C_3H_6$).

2,4-O-*Isopropylidene*-1-C-*phenyl*-D-*glycero*-D-gulo-*hexitol* **39**.—A catalytic amount of sodium methoxide was added to a stirred solution of diol **38** (512 mg, 1.34 mmol) in methanol (10 cm^3) at room temperature. After being stirred at room temperature for 2 h, the solution was filtered through a short column of silica gel topped with Celite. Removal of solvent from the filtrate *in vacuo* gave a solid residue which was flash chromatographed (diethyl ether) to give the *tetraol* **39** (370 mg, 93%) as a white solid. Recrystallization from diethyl ether–hexane gave colorless needles, m.p. 169—172 °C; R_f 0.14 (diethyl ether); (Found: C, 60.2; H, 7.2. $C_{15}H_{22}O_6$ requires C, 60.4; H, 7.4%); $[\alpha]_D^{24}$ + 6 (*c* 0.5 in EtOH); ν_{max}/cm^{-1} 3400 (OH); δ_H 1.27 (3 H, s, Me), 1.30 (3 H, s, Me), 3.47–3.96 (5 H, m), 4.80 (1 H, d, *J* 7.5, 1-H), 7.23–7.44 (5 H, m, Ph); *m/z* (EI) 107 (41%, $PhCHOH^+$), 191 (4, $M^+ - PhCHOH$).

2,4-O-*Isopropylidene*-5-C-*phenyl*-L-gluco-*pentose* **40**.—Sodium metaperiodate (300 mg, 1.40 mmol) was added in one portion to a stirred solution of the tetraol **39** (300 mg, 1.01 mmol) in methanol (20 cm^3) and water (10 cm^3) at room temperature. After being stirred at room temperature for 30 min, the mixture was filtered through a bed of

silica gel. Methanol in the filtrate was then removed *in vacuo*. The residue was partitioned between chloroform (20 cm^3) and saturated ammonium chloride (10 cm^3). The aqueous solution was further extracted with chloroform (7 × 10 cm^3). The combined organic extracts were dried ($MgSO_4$) and filtered. Removal of solvent from the filtrate *in vacuo* gave the *aldehyde* **40** as a colorless syrup. This compound was used in the next step without further purification.

(*Z*)-*Methyl* 4,6-O-*isopropylidene*-7-C-*phenyl*-L-gluco-*hept*-2-*enonate* **41**-*Z* and (*E*)-*Methyl* 4,6-O-*isopropylidene*-7-C-*phenyl*-L-gluco-*hept*-2-*enonate* **41**-*E*.—*Method A*. Methoxycarbonylmethylenetriphenylphosphorane (405 mg, 1.21 mmol) was added in one portion to a stirred solution of the aldehyde **40** from the previous experiment in methanol (20 cm^3) at room temperature. After being stirred at room temperature for 2 h, the reaction was concentrated *in vacuo*. Fractionation of the residue by flash chromatography [diethyl ether–hexane (2 : 3 v/v)] gave firstly the *enonate* **41**-*Z* (248 mg, 76%) as a white solid. Recrystallization from diethyl ether–hexane gave colorless needles, m.p. 135—136 °C; R_f 0.20 [diethyl ether–hexane (1 : 1 v/v)]; (Found: C, 63.1; H, 6.9. $C_{17}H_{22}O_6$ requires C, 63.3; H, 6.9%); $[\alpha]_D^{24}$ – 65 (*c* 0.9 in EtOH); ν_{max}/cm^{-1} 1650, 1719 (α,β-unsaturated ester), 3475 (OH); δ_H (acetone-d_6) 1.29 (3 H, s, Me), 1.33 (3 H, s, Me), 3.69 (3 H, s, $CO_2\underline{Me}$), 3.91 (1 H, br s, 5-H), 4.00 (1 H, dd, *J* 1.4 and 7.8, 6-H), 4.78 (1 H, br d, *J* 7.8, 7-H), 5.48 (1 H, m, 4-H), 5.91 (1 H, dd, *J* 1.4 and 12, 2-H), 6.37 (1 H, dd, *J* 7.0 and 12, 3-H), 7.24–7.45 (5 H, m, Ph); *m/z* (EI) 307 (6%, M^+ – Me).

The more polar *enonate* **41**-*E* was also obtained as a white solid (50 mg, 16%). Recrystallization from diethyl ether–hexane gave colorless needles, m.p. 114—115 °C; R_f 0.15 [diethyl ether–hexane (1 : 1 v/v)]; (Found: C, 63.3; H, 6.8. $C_{17}H_{22}O_6$ requires C, 63.3; H, 6.9%); $[\alpha]_D^{22}$ – 20 (*c* 0.6 in EtOH); ν_{max}/cm^{-1} 1725 (α,β-unsaturated ester), 3433 (OH); δ_H (acetone-d_6) 1.34 (6 H, s, 2 × Me), 3.70 (3 H, s, $CO_2\underline{Me}$), 3.84 (1 H, br s, 5-H), 4.00 (1 H, dd, *J* 1.2 and 7.8, 6-H), 4.71 (1 H, m, 4-H), 4.79 (1 H, br d, *J* 7.8, 7-H), 6.07 (1 H, dd, *J* 1.9 and 16, 2-H), 6.96 (1 H, dd,

J 4.2 and 16, 3-H), 7.24–7.44 (5 H, m, Ph); *m/z* (EI) 307 (5.81%, M^+ – Me). The ratio of **41**-*Z* : **41**-*E* (*ca.* 5 : 1) was estimated by isolated yield.

Method B. Methoxycarbonylmethylenetriphenylphosphorane (893 mg, 2.67 mmol) was added in one portion to a stirred solution of the aldehyde **40** from the previous experiment in toluene (20 cm^3) at room temperature. After being stirred at room temperature for 12 h, the reaction was concentrated *in vacuo*. Fractionation of the residue by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] gave firstly the *enonate* **41**-*Z* (154 mg, 22%) as a colorless solid. The more polar *enonate* **41**-*E* was obtained as a white solid (364 mg, 51%). The ratio of **41**-*Z* : **41**-*E* (*ca.* 1 : 2) was estimated by isolated yield.

(*Z*)-*Methyl* 4,6-O-*isopropylidene*-7-C-*phenyl*-D-gluco-*hept*-2-*enonate* **42**-*Z*.—*Method A.* Methoxycarbonylmethylenetriphenylphosphorane (843 mg, 2.52 mmol) was added in one portion to a stirred solution of the aldehyde **48** in anhydrous methanol (50 cm^3) at room temperature. After being stirred at room temperature for a further 2 h, the solution was concentrated under reduced pressure. Fractionation of the residue by flash chromatography [diethyl ether–hexane (2 : 3 v/v)] gave the *enonate* **42**-*Z* (531 mg, 79%) as a white solid. Recrystallization from diethyl ether–hexane gave colorless needles, m.p. 135—136 °C; R_f 0.25 [diethyl ether–hexane (3 : 2 v/v)]; (Found: C, 63.1; H, 6.8. $C_{17}H_{22}O_6$ requires C, 63.3; H, 6.9%); $[\alpha]_D^{24}$ + 71 (*c* 0.4 in EtOAc); ν_{max}/cm^{-1} 1658, 1722 (α,β-unsaturated ester), 3400 (OH); δ_H 1.44 (3 H, s, Me), 1.46 (3 H, s, Me), 2.83 (1 H, d, *J* 4.5, 7-OH), 3.09 (1 H, d, *J* 9.4, 5-OH), 3.69 (3 H, s, $CO_2\underline{Me}$), 3.85 (1 H, br d, *J* 9.4, 5-H), 4.00 (1H, d, *J* 6.3, 6-H), 4.88 (1 H, br t, *J* 6.3, 7-H), 5.48 (1 H, br d, *J* 7.2, 4-H), 5.92 (1 H, dd, *J* 1.4 and 12, 2-H), 6.32 (1 H, dd, *J* 7.2 and 12, 3-H), 7.13–7.30 (5 H, m, Ph); *m/z* (EI) 59 (65.88%, CO_2Me^+), 77 (59.00, Ph^+), 307 (2.03, M^+ – Me). Ratio of **42**-*Z* : **42**-*E* (*ca.* 10 : 1) was determined by ^1H NMR spectral analysis.

Method B. Methoxycarbonylmethylenetriphenylphosphorane (625 mg, 1.87 mmol) was added in one portion to a stirred solution of the *aldehyde* **48** in toluene (25 cm^3) at room temperature. After being stirred at room temperature for a further 16 h, the solution was concentrated under reduced pressure. Fractionation of the residue by flash chromatography [diethyl ether–hexane (1 : 1 v/v)] gave firstly the less polar **42**-*Z* (142 mg, 28%) as a white solid. The more polar compound **42**-*E* (284mg, 57%) was obtained as a white solid. Crystallization from diethyl ether–hexane gave **42**-*E* as colorless needles, m.p. 114—115 °C ; R_f 0.15 [diethyl ether–hexane (1 : 1 v/v)]; (Found: C, 63.5; H, 6.7. $C_{17}H_{22}O_6$ requires C, 63.3; H, 6.9%); $[\alpha]_D^{25}$ + 22 (*c* 1.3 in EtOH); ν_{max}/cm^{-1} 1727 (α,β-unsaturated ester), 3438 (OH); δ_H 1.40 (3 H, s, Me), 1.48 (3 H, s, Me), 2.97 (1 H, br s, OH), 3.16 (1 H, br s, OH), 3.73 (4 H, m, $CO_2\underline{Me}$ and 5-H), 3.91, (1 H, dd, *J* 1.1 and 6.1, 6-H), 4.48 (1 H, m, 4-H), 4.91 (1 H, br d, *J* 6.0, 7-H), 6.13 (1 H, dd, *J* 1.9 and 15.7, 2-H), 6.87 (1 H, dd, *J* 3.9, 15.7, 3-H), 7.28–7.42 (5 H, m, Ph); *m/z* (EI) 307 (8.03%, M^+ – Me). The ratio of **42**-*Z* : **42**-*E* (*ca.* 1 : 2) was determined by the isolated yield.

3,5-O-*Isopropylidene*-D-glycero-D-gulo-*heptono*-γ-*lactone* **43**.—A solution of 3,5:6,7-di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptono-γ-lactone **33** (5.0 g, 17.4 mmol) was stirred to dissolve in acetic acid (50 cm^3) at room temperature. Water (50 cm^3) was then added and the solution was stirred at room temperature for a further 48 h. Solvent was removed *in vacuo* to give a white residue. The residue was recrystallized from methanol–diethyl ether to give the *triol* **43** (3.0 g, 70%) as colorless prisms, m.p. 160—161 °C (lit.,[48] m.p. 158 °C); R_f 0.39 [methanol–chloroform (1 : 4 v/v)]; $[\alpha]_D^{24}$ – 77 (*c* 2.4 in ethanol) {lit.,[48] $[\alpha]_D$ – 75 (*c* 1.0, ethanol); ν_{max}/cm^{-1} 1779 (γ-lactone), 3450 (OH); δ_H (d_4-methanol) 1.37 (3 H, s, Me), 1.51 (3 H, s, Me), 3.58 (1 H, dd, *J* 4.8 and 11.4, 6-H_b), 3.70–3.82 (2 H, m, 5-H and 6-H_a), 4.05 (1 H, dd, *J* 1.5 and 9.0, 4-H), 4.44 (1 H, br t, 3-H), 4.61–4.66 (2 H, m, 1-H and 2-H); $\delta_{^{13}C}$ (d_4-methanol) 18.34 (Me), 29.39 (Me), 63.90, 69.16, 70.56, 70.63, 72.64 (2-C, 3-C, 4-C, 5-C, 6-C), 99.73 (dioxane ring), 177.84 (C=O); *m/z* (EI) 233 (16.61%, M^+ – Me), 249 (1.15, MH^+).

Aldehyde **44**.—Sodium periodate (1.0 g, 4.8 mmol) was added in one portion to a stirred solution of the triol **43** (1.0 g, 4.0 mmol) in methanol (50 cm^3) and water (4 cm^3) at room temperature. After being stirred at room temperature for 30 min, the mixture was filtered through a bed of silica gel topped with Celite. Evaporation of the filtrate under reduced pressure gave crude *aldehyde* **44.** The aldehyde was then pumped dry with toluene (5 × 10 cm^3). This compound was used in the next step without further purification.

3,5-O-*Isopropylidene*-1,1,6-*tri*-C-*phenyl*-D-glycero-D-gulo-*hexitol* **45a** and 3,5-O-*isopropylidene*-1,1,6-*tri*-C-*phenyl*-L-glycero-D-gulo-*hexitol* **45b**.—A solution of the aldehyde **44** in dry THF (20 cm^3) was stirred at 0 °C under nitrogen while a solution of phenylmagnesium bromide (prepared from 0.73 g magnesium and 3.2 cm^3 bromobenzene in 30 cm^3 dry THF) was added dropwise at 0 °C. The mixture was stirred at 0 °C for a further 2 h, quenched with ice-water mixture (50 cm^3) and chloroform (50 cm^3). The mixture was then filtered through Celite. The filtrate was then washed with saturated ammonium chloride (50 cm^3). The aqueous layer was further extracted with chloroform (2 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and filtered. Solvent removal gave a mixture of diastereoisomers **45a** and **45b** as a yellow syrup. Fractionation of the syrup by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] yielded a mixture of alcohols **45a** and **45b** (1.0 g, 56%) as a white solid. The ratio of **45a** : **45b** (*ca.* 1 : 2) was estimated by ^1H NMR spectral analysis.

3,5-O-*Isopropylidene*-1,1,6-*tri*-C-*phenyl*-D-glycero-D-gulo-*hexitol* **45a**.—A solution of the triacetate **46** (583 mg, 1.01 mmol) in chloroform (5 cm^3) and methanol (10 cm^3) was stirred at room temperature. Aqueous sodium hydroxide (1.0 dm mol^{-1}, 5 cm^3) was added and the mixture was stirred at room temperature for a further 1 h. The solution was diluted with chloroform (50 cm^3) and washed with saturated ammonium chloride (10 cm^3). The aqueous layer was further extracted with chloroform (2 × 10 cm^3). The combined organic extracts were dried ($MgSO_4$) and

filtered. Concentration of the filtrate yielded the *tetraol* **45a** as a white solid. Purification by flash chromatography [diethyl ether–hexane (2 : 1 v/v)] afforded **45a** (450 mg, 99%) as a white solid, m.p. 200—205 °C; R_f 0.28 [chloroform–methanol (98 : 2 v/v)]; (Found: C, 71.6; H, 6.4. $C_{27}H_{30}O_6$ requires C, 72.0; H, 6.7%); $[\alpha]_D^{24}$ + 110 (*c* 1.8 in EtOAc); ν_{max}/cm^{-1} 3450 (OH); δ_H 0.67 (3 H, s, Me), 1.25 (3 H, s, Me), 2.28 (1 H, d, *J* 3.4, 6-OH), 3.39 (1 H, d, *J* 4.1, 2-OH), 3.47 (1 H, d, *J* 8.2, 4-OH), 3.66 (1 H, d, *J* 6.9, 5-H), 3.84 (1 H, d, *J* 8.0, 3-H), 3.95 (1 H, d, *J* 8.2, 4-H), 4.19 (1 H, s, 1-OH), 4.68 (1 H, dd, *J* 3.4 and 6.9, 6-H), 7.02–7.78 (15 H, m, Ph); *m/z* (EI) 77 (54.18%, Ph^+), 105 (89.62, $PhCO^+$), 183 (100, Ph_2COH^+), 249 (5.30, $M^+ - Ph_2COH - H_2O$), 435 (0.25, $M^+ - Me$).

3,5-O-*Isopropylidene*-1,1,6-*tri*-C-*phenyl*-L-glycero-D-gulo-*hexitol* **45b**.—A solution of the diacetate **47** (2.4 g, 4.5 mmol) in chloroform (10 cm^3) and methanol (30 cm^3) was stirred at room temperature. Aqueous sodium hydroxide (1.0 dm mol^{-1}, 10 cm^3) was added and the mixture was stirred at room temperature for a further 5 h. The solution was diluted with chloroform (100 cm^3) and was washed with saturated ammonium chloride (10 cm^3). The aqueous layer was further extracted with chloroform (2 × 50 cm^3). The combined organic extracts were dried by $MgSO_4$ and filtered. Concentration of the filtrate yielded the *tetraol* **45b** as a white solid. Purification by flash chromatography [diethyl ether–hexane (2 : 1 v/v)] afforded **45b** (2.0 g, 98%) as a white solid, m.p. 166—168 °C; R_f 0.34 [chloroform–methanol (98 : 2 v/v)]; (Found: C, 71.7; H, 6.5. $C_{27}H_{30}O_6$ requires C, 72.0; H, 6.7%); $[\alpha]_D^{24}$ + 122 (*c* 1.3 in EtOAc); ν_{max}/cm^{-1} 3420 (OH); δ_H 0.84 (3 H, s, Me), 1.36 (3 H, s, Me), 2.57 (1 H, d, *J* 11.5, 4-OH), 2.62 (1 H, d, *J* 3.8, 2-OH), 2.73 (1 H, d, *J* 1.2, 6-OH), 3.32 (1 H, d, *J* 11.5, 4-H), 3.60 (1 H, d, *J* 8.6, 5-H), 3.75 (1 H, d, *J* 7.7, 3-H), 3.93 (1 H, s, 1-OH), 4.45 (1 H, dd, *J* 3.8 and 7.7, 2-H), 4.83 (1 H, br d, *J* 8.0 , 6-H), 7.11–7.70 (15 H, m, Ph); *m/z* (EI) 77 (30.38%, Ph^+), 105 (55.66, $PhCO^+$), 183 (100, Ph_2COH^+), 249 (3.74, $M^+ - Ph_2COH - H_2O$).

2,4,6-*Tri*-O-*acetyl*-3,5-O-*isopropylidene*-1,1,6-*tri*-C-*phenyl*-D-glycero-D-gulo-*hexitol* **46** and 2,6-*di*-O-*acetyl*-3,5-O-*isopropylidene*-1,1,6-*tri*-C-*phenyl*-L-glycero-D-gulo-*hexitol* **47**.—A solution of alcohols **45a** and **45b** (1.70 g, 3.8 mmol) in dry dichloromethane (40 cm^3) was stirred at room temperature. Pyridine (8.9 cm^3, 0.09 mol), acetic anhydride (7.6 cm^3, 0.09 mmol) and a catalytic amount of DMAP were added. After being stirred at room temperature for 48 h, the mixture was washed with water (10 cm^3), then saturated ammonium chloride (10 cm^3). The organic layer was dried ($MgSO_4$) and filtered. Concentration of the filtrate under reduced pressure followed by flash chromatography [ethyl acetate–hexane (1 : 3 v/v)] first afforded the less polar *triacetate* **46** (788 mg, 36%) as a white solid. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 237—239 °C; R_f 0.55 [ethyl acetate–hexane (1 : 2 v/v)]; (Found: C, 68.7; H, 6.3. $C_{33}H_{36}O_9$ requires C, 68.7 ; H, 6.3%); $[\alpha]_D^{24}$ + 77 (*c* 0.9 in EtOAc); ν_{max}/cm^{-1} 1750 (C=O ester); δ_H 0.54 (3 H, s, Me), 1.19 (3 H, s, Me), 1.85 (3 H, s, Ac), 1.91 (3 H, s, Ac), 2.03 (3 H, s, Ac), 4.03 (1 H, dd, *J* 1.4 and 9.5, 5-H), 4.27 (1 H, dd, *J* 1.4 and 9.5, 3-H), 4.38 (1 H, s, 1-OH), 5.13 (1 H, br s, 4-H), 5.45 (2 H, t, *J* 9.2, 2-H and 6-H), 7.13–7.75 (15 H, m, Ph); *m/z* (EI) 77 (16.07%, Ph^+), 105 (44.25, $PhCO^+$), 183 (89.42, Ph_2COH^+), 561 (0.65, $M^+ - Me$).

The more polar *diacetate* **47** (981 mg, 49%) was also obtained as a white solid. Recrystallization from ethyl acetate–hexane gave a white solid, m.p. 183—185 °C; R_f 0.45 [ethyl acetate–hexane (1 : 2 v/v)]; (Found: C, 69.8; H, 6.2. $C_{31}H_{34}O_8$ requires C, 69.7; H, 6.4%); $[\alpha]_D^{24}$ + 114 (*c* 0.8 in EtOAc); ν_{max}/cm^{-1} 1750 (C=O ester), 3500 (OH); δ_H 0.78 (3 H, s, Me), 1.41 (3 H, s, Me), 2.00 (3 H, s, Ac), 2.04 (3 H, s, Ac), 4.13 (1 H, br d, *J* 7.3, 5-H), 4.23 (1 H, br d, *J* 9.4, 3-H), 4.45 (1 H, s, 1-OH), 4.69 (1 H, br s, 4-H), 5.04 (1 H, d, *J* 9.4, 2-H), 5.97 (1 H, d, *J* 9.0, 6-H), 7.18–7.77 (15 H, m, Ph); *m/z* (EI) 77 (19.94%, Ph^+), 105 (54.16, $PhCO^+$), 183 (100, Ph_2COH^+), 233 (1.45, $M^+ - Ph_2COH - 2 \times OAc$), 339 (0.98, $M^+ - Ph - 2 \times OAc$).

2,4-O-*Isopropylidene*-5-C-*phenyl*-D-gluco-*pentose* **48**.—Sodium metaperiodate (539 mg, 2.52 mmol) was added in one portion to a stirred solution of tetraol **45a** (945 mg, 2.10 mmol) in methanol (40 cm^3) and water (10 cm^3) at room temperature. After being stirred at room temperature for 30 min, the mixture was filtered through a bed of silica gel topped with Celite. Removal of solvent from the filtrate *in vacuo* gave the *aldehyde* **48** as a colorless syrup. The *aldehyde* **48** was dried by concentration with toluene several times. This compound was used in the next step without further purification.

(*Z*)-7-C-*Phenyl*-L-gulo-*hept*-2-*enono*-γ-*lactone* **49**.—A solution of enonate **42**-*Z* (307 mg, 0.95 mmol) in acetic acid (25 cm^3) and water (25 cm^3) was stirred at room temperature for 24 h. The solvents were then removed *in vacuo* to give a white solid. Purification by flash chromatography [diethyl ether–hexane (1 : 1 v/v)] afforded **49** (213 mg, 89%) as a white solid. Recrystallization from diethyl ether–hexane gave colorless needles, m.p. 109—111 °C; R_f 0.42 (ethyl acetate); (Found: C, 62.4 ; H, 5.8. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%); $[\alpha]_D^{24}$ – 68 (*c* 0.6 in EtOAc); ν_{max}/cm^{-1} 1750, 1778 (α,β-unsaturated γ-lactone), 3400 (OH); δ_H (acetone-d_6) 3.71 (1 H, br t, *J* 7.4, 6-H), 3.88 (1 H, d, *J* 7.6, 7-OH), 4.10 (1 H, br t , *J* 6.2, 5-H), 4.50 (1 H, d, *J* 6.5, 5-OH), 7.79 (1 H, br d, *J* 5.7, 3-H), 4.70 (1 H, d, *J* 4.6, 6-OH), 4.78 (1 H, br t, *J* 7.4, 7-H), 5.24 (1 H, br d, *J* 6.2, 4-H), 6.12 (1 H, br d, *J* 5.7, 2-H), 7.24–7.45 (5 H, m, Ph); *m/z* (EI) 83 (23.80%, $C_4O_2H_3^+$), 107 (100, $PhCHOH^+$), 126 (22.22, M^+ – PhCHOH – OH), 232 (0.32, $M^+ - H_2O$).

Di-acetylgoniobutenolide A **50** and *Di-acetylgoniobutenolide B* **51**.—A solution of the triol **49** (201 mg, 0.80 mmol) in dry dichloromethane (20 cm^3) was stirred at room temperature. Triethylamine (0.6 cm^3), acetic anhydride (0.4 cm^3) and a catalytic amount of DMAP were added to the solution. The solution was stirred at room temperature for 21 h and then filtered through a bed of silica gel topped with Celite. Evaporation of the filtrate *in vacuo* gave a yellow oil. Purification by flash chromatography [diethyl ether–hexane (1 : 1 v/v)] gave **50** and **51** as yellow oils (253 mg, 99%). Separation by flash chromatography gave firstly the *butenolide* **51** as a

yellow oil, R_f 0.28 [diethyl ether–hexane (1 : 1 v/v)]; (Found: C, 64.4; H, 5.3. $C_{17}H_{16}O_6$ requires C, 64.55; H, 5.1%); $[\alpha]_D^{24}$ – 63 (*c* 0.7 in $CHCl_3$); ν_{max}/cm^{-1} 1744 (ester) and 1790 (conjugated α,β and γ,δ-unsaturated γ-lactone); δ_H 2.02 (3 H, s, Ac), 2.12 (3 H, s, Ac), 5.66 (1 H, dd, *J* 1.5 and 9.9, 5-H), 5.83 (1 H, dd, *J* 4.3 and 9.9, 6-H), 6.05 (1 H, d, *J* 4.3, 7-H), 6.18 (1 H, dd, *J* 1.7 and 5.7, 2-H), 7.22–7.41 (5 H , m, Ph), 7.47 (1 H, d, *J* 5.7, 3-H); $\delta_{^{13}C}$ 20.66, 20.71, 70.65, 75.56, 107.00, 122.02, 126.99, 128.49, 128.66, 135.40, 139.81, 153.22, 168.45, 169.39, 169.55; *m/z* (CI, isobutane) 257 (100%, M^+ – OAc).

The *butenolide* **50** was also obtained as a yellow oil, R_f 0.17 [diethyl ether–hexane (1 : 1 v/v)]; (Found: C, 64.2; H, 5.3. $C_{17}H_{16}O_6$ requires C, 64.55; H, 5.1%); $[\alpha]_D^{24}$ + 75 (*c* 1.7 in $CHCl_3$); ν_{max}/cm^{-1} 1746 (ester), 1785 (conjugated α,β and γ,δ-unsaturated γ-lactone); δ_H 2.02 (3 H, s, Ac), 2.12 (3 H, s, Ac), 5.25 (1 H, dt, *J* 2.4 and 8.7, 6-H), 6.06–6.11 (2 H, m, 2-H and 5-H), 6.20 (1 H, d, *J* 5.5, 7-H), 7.26–7.36 (6 H, m, 3-H and Ph); $\delta_{^{13}C}$ 20.16, 20.25, 69.79, 74.55, 107.25, 120.86, 126.52, 127.90, 128.08, 135.28, 143.11, 151.11, 168.02, 168.84, 168.99; *m/z* (CI, isobutane) 257 (69.06%, M^+ – OAc), 317 (1.16, MH^+). The ratio of **50** : **51** (*ca.* 2 : 1) was determined by ^1H NMR spectral analysis.

(*Z*)- 7-C-*phenyl*-L-ido-hept-2-*enono*-δ-*lactone* **52**.—A solution of lactone **55** (157 mg, 0.54 mmol) in acetic acid (20 cm^3) and water (5 cm^3) was stirred at 90–100 °C for 3 h. The solvents were then removed *in vacuo* to give **52** as a white solid. Purification by flash chromatography then afforded the *triol* **52** (111 mg, 82%) as a white solid. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 127—129 °C; R_f 0.28 (ethyl acetate); (Found: C, 62.0 ; H, 5.1. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%); $[\alpha]_D^{22}$ + 88 (*c* 0.8 in EtOH); ν_{max}/cm^{-1} 1719 (α,β-unsaturated δ-lactone), 3373 (OH); δ_H (acetone-d_6) 4.18 (1 H, dd, *J* 3.7 and 6.2, 6-H), 4.31 (1 H, dd, *J* 2.8 and 6.2, 5-H), 4.51 (1 H, dd, *J* 2.8 and 5.8, 4-H), 5.04 (1 H, br d, *J* 3.3, 7-H), 6.02 (1 H, d, *J* 9.7, 2-H), 7.06 (1 H, dd, *J* 5.8 and 9.7, 3-H), 7.22–7.49 (5 H, m, Ph); *m/z* (EI) 107 (100%, $PhCHOH^+$), 126 (10.72, $MH^+ - PhCHOH - H_2O$), 144 (9.55, $MH^+ - PhCHOH$), 250 (7.73, M^+).

(*Z*)-*Methyl* 4,6-O-*isopropylidene*-7-C-*phenyl*-L-ido-*hept*-2-*enonate* **53**.—Methoxycarbonylmethylenetriphenylphosphorane (1.74 g, 5.20 mmol) was added in one portion to a stirred solution of the aldehyde **54** in anhydrous methanol (30 cm^3) at room temperature. After being stirred at room temperature for a further 3 h, the solution was concentrated under reduced pressure. Fractionation of the residue by flash chromatography [diethyl ether–hexane (2 : 3 v/v)] gave the *enonate* **53** (1.12g, 80%) as a colorless oil, R_f 0.46 [ethyl acetate–hexane (2 : 1 v/v)]; $[\alpha]_D^{22}$ + 121 (*c* 0.8 in EtOAc); ν_{max}/cm^{-1} 1657, 1724 (α,β-unsaturated ester), 3476 (OH); δ_H 1.54 (3 H, s, Me), 1.56 (3 H, s, Me), 2.64 (1 H, d, *J* 11.8, 5-OH), 2.84 (1 H, d, *J* 1.5, 7-OH), 3.25 (1 H, dt, *J* 1.3 and 11.8, 5-H), 3.61 (3 H, s, Me), 3.89 (1 H, dd, *J* 1.0 and 8.1, 6-H), 4.88 (1 H, dd, *J* 1.4 and 8.1, 7-H), 5.40 (1 H, dt, *J* 1.4 and 7.3, 4-H), 5.78 (1 H, dd, *J* 1.4 and 11.7, 2-H), 6.25 (1 H, dd, *J* 7.3 and 11.7, 3-H), 7.30–7.48 (5 H, m, Ph); *m/z* (EI) 307 (15.48%, M^+ – Me), 323 (2.72, MH^+). The ratio of *Z* : *E* isomers (*ca.* 10 : 1) was determined by ^1H NMR spectral analysis.

2,4-O-*Isopropylidene*-5-C-*phenyl*-D-gluco-*pentose* **54**.—Sodium metaperiodate (1.40 g, 6.50 mmol) was added in one portion to a stirred solution of the tetraol **45b** (1.95 g, 4.33mmol) in methanol (150 cm^3) and water (20 cm^3) at room temperature. After being stirred at room temperature for 30 min, the mixture was filtered through a bed of silica gel topped with Celite. The filtrate was then concentrated *in vacuo* to give the *aldehyde* **54** as a colorless syrup. The aldehyde was dried by evaporation with toluene several times. This compound was used in the next step without further purification.

(*Z*) 4,6-O-*Isopropylidene*- 7-C-*phenyl*-L-ido-*hept*-2-*enono*-δ-*lactone* **55**.—A solution of the unsaturated ester **53** (278 mg, 0.86 mmol) in dry THF (30 cm^3) containing a catalytic amount of DBU was stirred at 60–70 °C for 24 h. The solution was then filtered through a bed of silica gel topped with Celite. Removal of solvent *in vacuo* gave a white solid (176 mg, 70%). Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] afforded **55** as white crystals. Recrystallization from ethyl

acetate–hexane gave colorless needles, m.p. 192 °C (sublim.); R_f 0.36 [ethyl acetate–hexane (2 : 1 v/v)]; (Found: C, 65.9 ; H, 6.1. $C_{16}H_{18}O_5$ requires C, 66.2; H, 6.25%); $[\alpha]_D^{22}$ – 89 (*c* 0.9 in EtOH); ν_{max}/cm^{-1} 1732 (α,β-unsaturated δ-lactone), 3500 (OH); δ_H 1.53 (3 H, s, Me), 1.56 (3 H, s, Me), 2.84 (1 H, d, *J* 1.3, 7-OH), 3.63 (1 H, t, *J* 1.8, 5-H), 3.91 (1 H, dd, *J* 1.7 and 8.7, 6-H), 4.18 (1 H, dd, *J* 1.9 and 6.1, 4-H), 5.15 (1 H, br d, *J* 8.7, 7-H), 6.18 (1 H, d, *J* 9.6, 2-H), 6.79 (1 H, dd, *J* 6.1 and 9.6, 3-H), 7.31–7.55 (5 H, m, Ph); *m/z* (EI) 107 (44.93%, $PhCHOH^+$), 126 (10.43, MH^+ – PhCHOH), 275 (2.05, M^+ – Me).

(Z) 4,6-O-*Isopropylidene*-7-O-*mesyl*-7-C-*phenyl*-L-ido-*hept*-2-*enono*-δ-*lactone* **56.**—A solution of the alcohol **55** (209 mg, 0.67 mmol) in dry dichloromethane (10 cm^3) was stirred at 0 °C. Pyridine (0.6 cm^3) and methanesulfonyl chloride (0.6 cm^3) were added at 0 °C. The solution was then stirred at 0 °C for 24 h. The solution was diluted with ethyl acetate (50 cm^3)and washed with saturated ammonium chloride solution (20 cm^3), then water (20 cm^3). The organic layer was dried by anhydrous $MgSO_4$ and filtered. Removal of solvent *in vacuo* gave a yellow oil. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] affored the *mesylate* **56** (248 mg, 93%) as a white solid. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 97—98°C; R_f 0.52 [methanol–chloroform (2 : 98 v/v)]; $[\alpha]_D^{22}$ – 3.8 (*c* 0.5 in EtOAc); δ_H 1.51 (3 H, s, Me), 1.55 (3 H, s, Me), 3.01 (3 H, s, Ms), 3.51 (1 H, br s, 5-H), 4.22–4.30 (2 H, m, 4-H and 6-H), 5.83 (1 H, d, *J* 9.0, 7-H), 6.16 (1 H, d, *J* 9.7, 2-H), 6.78 (1 H, dd, *J* 6.0, 9.7, 3-H), 7.38–7.56 (5 H, m, Ph); *m/z* (EI) 90 (35.90%, $PhCHOMs^+$ – OMs), 91 (100, $PhCHOMsH^+$ – OMs), 95 (42.77, OMs), 183 (5.84, M^+ – PhCHOMs), 185 (8.03, $PhCHOMs^+$), 215 [8.98, M^+ – $(CH_3)_2CO_2$ – Ms]. The unstable mesylate was used immediately after chromatography.

(+)-*Acetylaltholactone* **57**.—A solution of the (+)-altholactone **14** (56 mg, 0.24 mmol) in dry dichloromethane (20 cm^3) was stirred at room temperature. Pyridine (0.1 cm^3), acetic anhydride (0.1 cm^3) and a catalytic amount of DMAP were added to the solution. The solution was stirred at room temperature for 14 h and then filtered

through a bed of silica gel topped with Celite. Evaporation of the filtrate *in vacuo* gave **57** (50 mg, 76%) as a white solid. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] gave the *title compound* **57** as white crystals. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 141—142 °C (lit.,[11] m.p. 142 °C); R_f 0.39 [ethyl acetate–hexane (1 : 1 v/v)]; (Found: C, 65.6; H, 4.9. $C_{13}H_{14}O_5$ requires C, 65.7; H, 5.15%); $[\alpha]_D^{25}$ + 204 (*c* 0.3 in EtOH) {lit.,[11] $[\alpha]_D$ + 208 (EtOH)}; ν_{max}/cm^{-1} 1702 (α,β-unsaturated δ-lactone), 1744 (ester); δ_H 2.16 (3 H, s, Ac), 4.63 (1 H, t, *J* 4.4 and 5.1, 4-H), 4.96 (1 H, dd, *J* 4.1, 5-H), 4.98 (1 H, d, *J* 3.6, 7-H), 5.40 (1 H, d, *J* 3.0, 6-H), 6.28 (1 H, d, *J* 9.8, 2-H), 7.04 (1 H, dd, *J* 5.3 and 9.8, 3-H), 7.29–7.34 (5 H, m, Ph); *m/z* (EI) 214 (7.36%, $M^+ - HOAc$) and 275 (4.30, MH^+).

(*Z*) 4,6-O-*Isopropylidene*-7-C-*phenyl*-D-gluco-*hept*-2-*enono*-δ-*lactone* **58**.—A solution of the unsaturated ester **42**-*Z* (517 mg, 1.61 mmol) in dry THF (30 cm^3) containing a catalytic amount of DBU was stirred at 60–70 °C for 24 h. The solution was then filtered through a bed of silica gel topped with Celite. Removal of solvent *in vacuo* gave a white solid. Purification by flash chromatography [diethyl ether–hexane (2 : 1 v/v)] afforded the *unsaturated lactone* **58** (325 mg, 70%) as white crystals. Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 190—191 °C; R_f 0.23 [diethyl ether–hexane (2 : 1 v/v)]; (Found: C, 66.1; H, 6.1. $C_{16}H_{18}O_5$ requires C, 66.2; H, 6.25%); $[\alpha]_D^{24}$ + 100 (*c* 1.2 in MeOH); ν_{max}/cm^{-1} 1727 (α,β-unsaturated δ-lactone) and 3401 (OH); δ_H 1.34 (6 H, s, 2 × Me), 2.89 (1 H, d, *J* 4.6, 7-OH), 4.05 (1 H, dd, *J* 1.8 and 8.6, 6-H), 4.34 (1 H, dd, *J* 2.0 and 6.0, 4-H), 4.50 (1 H, t, *J* 1.9, 5-H), 5.11 (1 H, dd, *J* 4.5 and 8.5, 7-H), 6.25 (1 H, d, *J* 9.6, 2-H), 6.89 (1 H, dd, *J* 6.1 and 9.6, 3-H), 7.29–7.45 (5 H, m, Ph); *m/z* (EI) 107 (48.23%, $PhCHOH^+$), 184 (10.30, $MH^+ - PhCHOH$), 275 (3.19, $M^+ - Me$).

(*Z*) 7-O-*Acetyl*-4,6-O-*isopropylidene*-7-C-*phenyl*-D-gluco-*hept*-2-*enono*-δ-*lactone* **59**.—A solution of the alcohol **58** (325 mg, 1.12 mmol) in dry dichloromethane (20 cm^3) was stirred at room temperature. Pyridine (0.18 cm^3), acetic anhydride (0.21

cm^3) and a catalytic amount of DMAP were added to the solution. The solution was stirred at room temperature for 3 h. The solution was then filtered through a bed of silica gel topped with Celite. Evaporation of the filtrate *in vacuo* gave the *acetate* **59** as a white solid. Purification by flash chromatography [ethyl acetate–hexane (1 : 1 v/v)] gave the *title compound* **59** as white crystals (357 mg, 96%). Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 190—191 °C; R_f 0.18 [ethyl acetate–hexane (1 : 1 v/v)]; (Found: C, 64.7; H, 5.9. $C_{18}H_{20}O_6$ requires C, 65.05; H, 6.1%); $[\alpha]_D^{24}$ + 45 (*c* 0.3 in MeOH); ν_{max}/cm^{-1} 1725 (ester) and 1739 (α,β-unsaturated δ-lactone); δ_H 1.30 (3 H, s, Me), 1.32 (3 H, s, Me), 2.04 (3 H, s, Ac), 4.27 (1 H, d, *J* 9.3, 6-H), 4.35–4.37 (2 H, m, 4-H and 5-H), 5.99 (1 H, d, *J* 9.3, 7-H), 6.27 (1 H, d, *J* 9.6, 2-H), 6.88 (1 H, dd, *J* 5.8 and 9.6, 3-H), 7.29–7.37 (5 H, m, Ph); *m/z* (EI) 318 (5.18%, $MH^+ - Me$).

(+)-*Diacetylgoniofufurone* **60**.—A solution of (+)-goniofufurone **21b** (132 mg, 0.53 mmol) in dry dichloromethane (10 cm^3) was stirred at room temperature. Pyridine (1.0 cm^3), acetic anhydride (1.0 cm^3) and a catalytic amount of DMAP were added to the solution. The solution was stirred at room temperature for 48 h. The solution was then filtered through a bed of silica gel topped with Celite. Evaporation of the filtrate *in vacuo* gave **60** as a white solid. Purification by flash chromatography [diethyl ether–hexane (2 : 1 v/v)] gave the *title compound* **60** as white crystals (157 mg, 89%). Recrystallization from ethyl acetate–hexane gave colorless needles, m.p. 184—185 °C (lit.,[19] m.p. 130—132 °C); R_f 0.25 [diethyl ether–hexane (2 : 1 v/v)]; (Found: C, 61.3; H, 5.3. $C_{17}H_{18}O_7$ requires C, 61.1; H, 5.4%); $[\alpha]_D^{24}$ + 22 (*c* 0.5 in $CHCl_3$); ν_{max}/cm^{-1} 1746 (ester) and 1793 (γ-lactone); δ_H 2.85 (1 H, dd, *J* 1.2 and 19.0, 3-H_b), 2.70 (1 H, dd, *J* 5.7 and 19.0, 3-H_a), 4.46 (1 H, dd, *J* 3.1 and 9.5, 7-H), 4.87 (1 H, d, *J* 4.0, 5-H), 4.98 (1 H, ddd, *J* 1.2, 4.0 and 5.7, 4-H), 5.74 (1 H, d, *J* 2.8, 6-H), 5.84 (1 H, d, *J* 9.5, 8-H), 7.27–7.41 (5 H, m, Ph); *m/z* (EI) 149 (27.89%, $PhCHOAc^+$), 185 (100, $M^+ - PhCHOAc$), 334 (0.20, M^+).

(+)-*Triacetylgoniotriol* **61**.—A solution of the triol **16** (185 mg, 0.74 mmol) in dry dichloromethane (50 cm^3) was stirred at room temperature. Pyridine (0.36 cm^3), acetic anhydride (0.42 cm^3) and a catalytic amount of DMAP were added to the solution. The solution was stirred at room temperature for 21 h and then filtered through a bed of silica gel topped with Celite. Evaporation of the filtrate *in vacuo* gave a white solid. Purification by flash chromatography [diethyl ether–hexane (2 : 1 v/v)] gave the *title compound* **61** as a white solid (236 mg, 85%), m.p. 95—97 °C (lit.,[3] m.p. 90—93 °C); R_f 0.28 [diethyl ether–hexane (2 : 1 v/v)]; (Found: C, 60.5; H, 5.3. $C_{19}H_{20}O_8$ requires C, 60.6; H, 5.4%); $[\alpha]_D^{24}$ + 121 (*c* 0.8 in MeOH); ν_{max}/cm^{-1} 1743 (ester and α,β-unsaturated δ-lactone); δ_H 2.02 (3 H, s, Ac), 2.07 (3 H, s, Ac), 2.11 (3 H, s, Ac), 4.53 (1 H, dd, *J* 2.9 and 6.9, 5-H), 5.28 (1 H, dd, *J* 3.0 and 5.7, 4-H), 5.74 (1 H, dd, *J* 4.8 and 6.9, 6-H), 5.96 (1 H, d, *J* 4.8, 7-H), 6.17 (1 H, d, *J* 9.8, 2-H), 6.93 (1 H, dd, *J* 5.4 and 9.8, 3-H), 7.34–7.44 (5 H, m, Ph); *m/z* (EI) 126 (21.09%, MH^+ – PhCHOAc – OAc – Ac), 149 (7.68, $PhCHOAc^+$), 168 (21.03, M^+ – PhCHOAc – OAc), 228 (2.87, MH^+ – PhCHOAc).

5. References

1. K. Jewers, J. B. Davis, J. Dougan, A. H. Manchanda, G. Blunden, A. Kyi and S. Wetchapinan, *Phytochemistry*, 1972, **11**, 2025–2030.
2. Y. C. Wu, C. Y. Duh, F. R. Chang, G. Y. Chang, S. K. Wang, J. J. Chang, D. R. McPhail, A. T. McPhail and K. H. Lee, *J. Nat. Prod.*, 1991, **54**, 1077–1081.
3. S. K. Talapatra, D. Basu, T. Deb, S. Goswami and B. Talapatra, *Indian J. Chem.*, 1985, **24B**, 29–34.
4. T. W. Sam, C. S. Yeu, S. Matsjeh, E. K. Gan, D. Razak and A. L. Mohamed, *Tetrahedron Lett.*, 1987, **28**, 2541–2544.
5. A. Pelter, R. I. H. Al-Bayati, M. T. Ayoub, W. Lewis, P. Pardasani and R. Hansel, *J. Chem. Soc., Perkin Trans. 1*, 1987, 717–742.
6. J. R. Hlubucek and A. V. Robertson, *Aust. J. Chem.*, 1967, **20**, 2199–2206.
7. B. O'Connor and G. Just, *Tetrahedron Lett.*, 1986, **27**, 5201–5202.
8. F. Gillard, D. Heissler and J. J. Riehl, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2291–2295.
9. J. W. Loder and R. M. Nearn, *Heterocycles*, 1977, **7**, 113–118.
10. A. L. El-Zayat, N. R. Ferrigni, T. G. McCloud, A. T. McKenzie, S. R. Byrn, J. M. Cassady, C. J. Chang and J. L. McLaughlin, *Tetrahedron Lett.*, 1985, **26**, 955–956.
11. J. P. Gesson, J. C. Jacquesy and M. Mondon, *Tetrahedron Lett.*, 1987, **28**, 3945–3948.
12. J. G. Gillhouley and T. K. M. Shing, *J. Chem. Soc., Chem. Commun.*, 1988, 976–977.
13. J. P. Gesson, J. C. Jacquesy and M. Mondon, *Tetrahedron Lett.*, 1987, **28**, 3949–3952.
14. Y. Ueno, K. I. Tadano, S. Ogawa, J. L. McLaughlin, A. Alkofahi, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2328–2337.
15. A. Alkofahi, W. W. Ma, A. T. Mckennzie, S. R. Byrn and J. L. Mclaughlin, *J. Nat. Prod.*, 1989, **52**, 1371–1373.

16. T. K. M. Shing, Z. H. Zhou and T. C. W. Mak, *J. Chem. Soc., Perkin Trans. 1*, 1992, 1907–1910.

17. X. P. Fang, J. E. Anderson, C. J. Chang and J. L. McLaughlin, *J. Nat. Prod.*, 1991, **54**, 1034–1043.

18. M. Tsubuki, K. Kanai and T. Honda, *J. Chem. Soc., Chem. Commun.*, 1992, 1640–1641.

19. X. P. Fang, J. E. Anderson, C. J. Chang, P. E. Fanwick and J. L. McLaughlin, *J. Chem. Soc., Perkin Trans 1*, 1990, 1655–1661.

20. T. K. M. Shing, H. C. Tsui and Z. H. Zhou, *J. Chem. Soc., Chem. Commun.*, 1992, 810.

21. T. K. M. Shing and H. C. Tsui, *J. Chem. Soc., Chem. Commun.*, 1992, 432.

22. T. K. M. Shing, H. C. Tsui and Z. H. Zhou, *Tetrahedron Lett.*, 1993, 691–692.

23. T. Gracza and V. Jager, *Synlett.*, 1992, 191–192.

24. P. J. Murphy, *J. Chem. Soc., Chem. Commun.*, 1992, 1096–1097.

25. K. R. C. Prakash and S. P. Rao, *Tetrahedron*, 1993, **49**, 1505–1510.

26. T. K. M. Shing, H. C. Tsui and Z. H. Zhou, *Tetrahedron*, 1992, **48**, 8659–8666.

27. K. R. C. Prakash and S. P. Rao, *Synlett*, 1993, 123–124.

28. X. P. Fang, J. E. Anderson, C. J. Chang and J. L. McLaughlin, *Tetrahedron*, 1991, **47**, 9751–9758.

29. X. P. Fang, J. E. Anderson, X. X. Qiu, J. F. Kozlowski, C. J. Chang and J. L. McLaughlin, *Tetrahedron*, 1993, **49**, 1563–1570.

30. J. G. Gillhouley, M. Sc., University of Manchester, 1987.

31. J. P. Gesson, J. C. Jacquesy and M. Mondon, *Tetrahedron*, 1989, **45**, 2627–2640.

32. T. K. M. Shing, H. C. Tsui, Z. H. Zhou and T. C. W. Mak, *J. Chem. Soc., Perkin Trans 1*, 1992, 887–893.

33. J. S. Brimacombe and L. C. N. Tucker, *Carbohydr. Res.*, 1966, **2**, 341–348.

34. J. G. Buchanan, M. E. Chacon-Fuertes, A. R. Edgar, S. J. Moorhouse, D. I. Rawson and R. H. Wightman, *Tetrahedron Lett.*, 1980, **21**, 1793–1796.

35. G. Aslani-Shotorbani, J. G. Buchanan, A. R. Edgar, D. Henderson and P. Shahidi, *Tetrahedron Lett.*, 1980, **21**, 1791–1792.

36. T. K. M. Shing, in '*Comprehensive Organic Synthesis*', ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, Vol.7, p.703.

37. D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, 1952, **74**, 5828–5835.

38. W. C. Still and J. A. Schneider, *Tetrahedron Lett.*, 1980, 1035.

39. A. L. Gemal and J. L. Luche, *J. Am. Chem. Soc.*, 1981, **103**, 5454–5459.

40. T. Oishi and T. Nakata, *Synthesis*, 1990, 635–645.

41. S. I. Kiyooka, H. Kuroda and Y. Shimasaki, *Tetrahedron Lett.*, 1986, **27**, 3009–3012.

42. S. Valverde, M. M. Lomas, B. Herradon and S. G. Ochoa, *Tetrahedron*, 1987, **43**, 1895–1901.

43. J. M. J. Tronchet and B. Gentile, *Helv. Chim. Acta.*, 1979, **62**, 2091–2098.

44. B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, 1989, **89**, 863–927.

45. R. M. Silverstein, G. C. Bassler and T. C. Morrill, '*Spectrometric Identification of Organic Compounds*', 4th ed., John Wiley & Sons., 1981, Chapters 4 and 5.

46. K. M. Sun, R. D. Dawe and B. F. Reid, *Carbohydr. Res.*, 1987, **171**, 35–47.

47. J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734–736.

48. J. S. Brimacombe and L. C. N. Tucker, *Carbohydr. Res.*, 1965, **1**, 332–333.

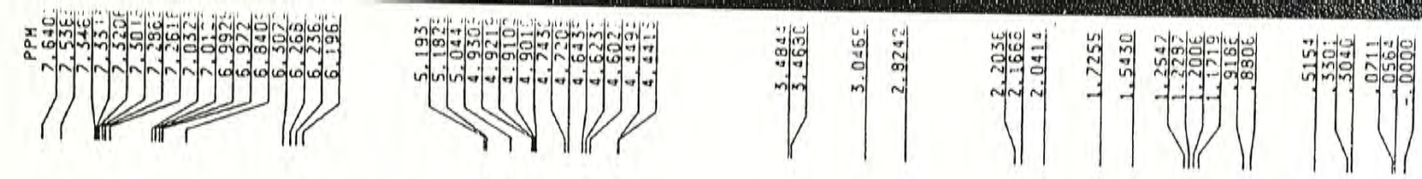
49. S. H. Pine, J. B. Hendrickson, D. J. Cram and G. S. Hammond, '*Organic Chemistry*', 4th ed., McGraw-Hill, 1980, p.449-459.

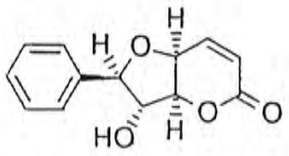
50. T. W. Greene, '*Protective Groups in Organic Synthesis*', 1st ed., John Wiley & Sons, 1981, p.56.

51. Vogel's, '*Textbook of Practical Organic Chemistry*', 5th ed., ELBS, 1989, p.572.

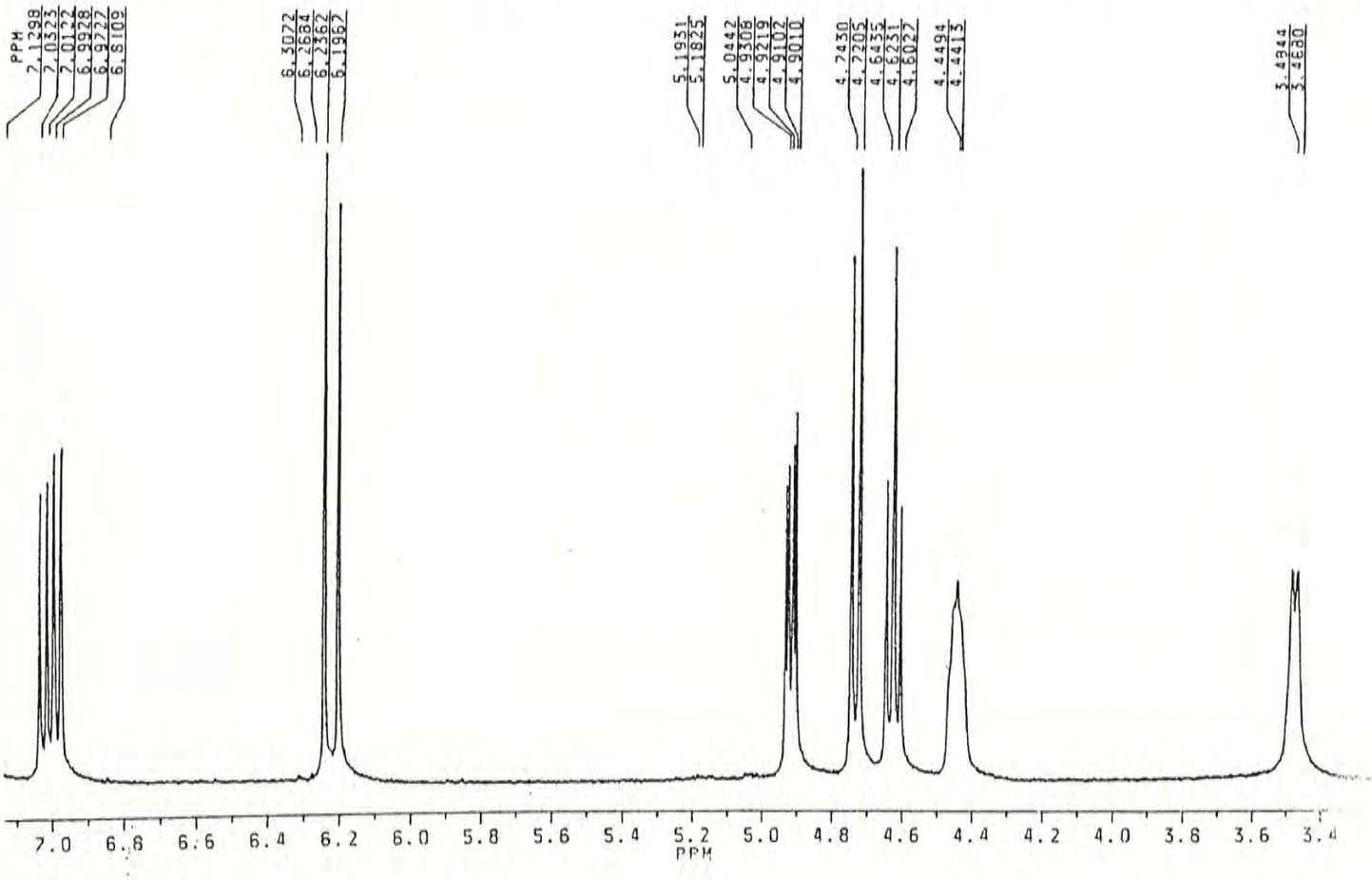
52. W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923–2925.

6. List of Spectra

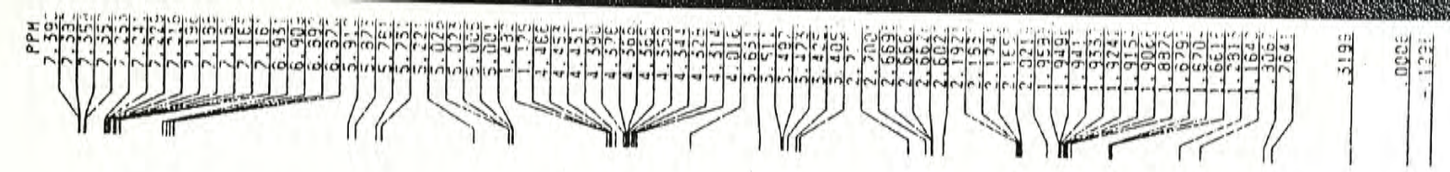


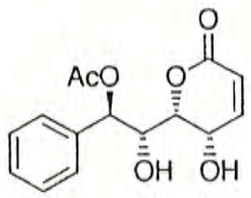


(+)-Altholactone 14

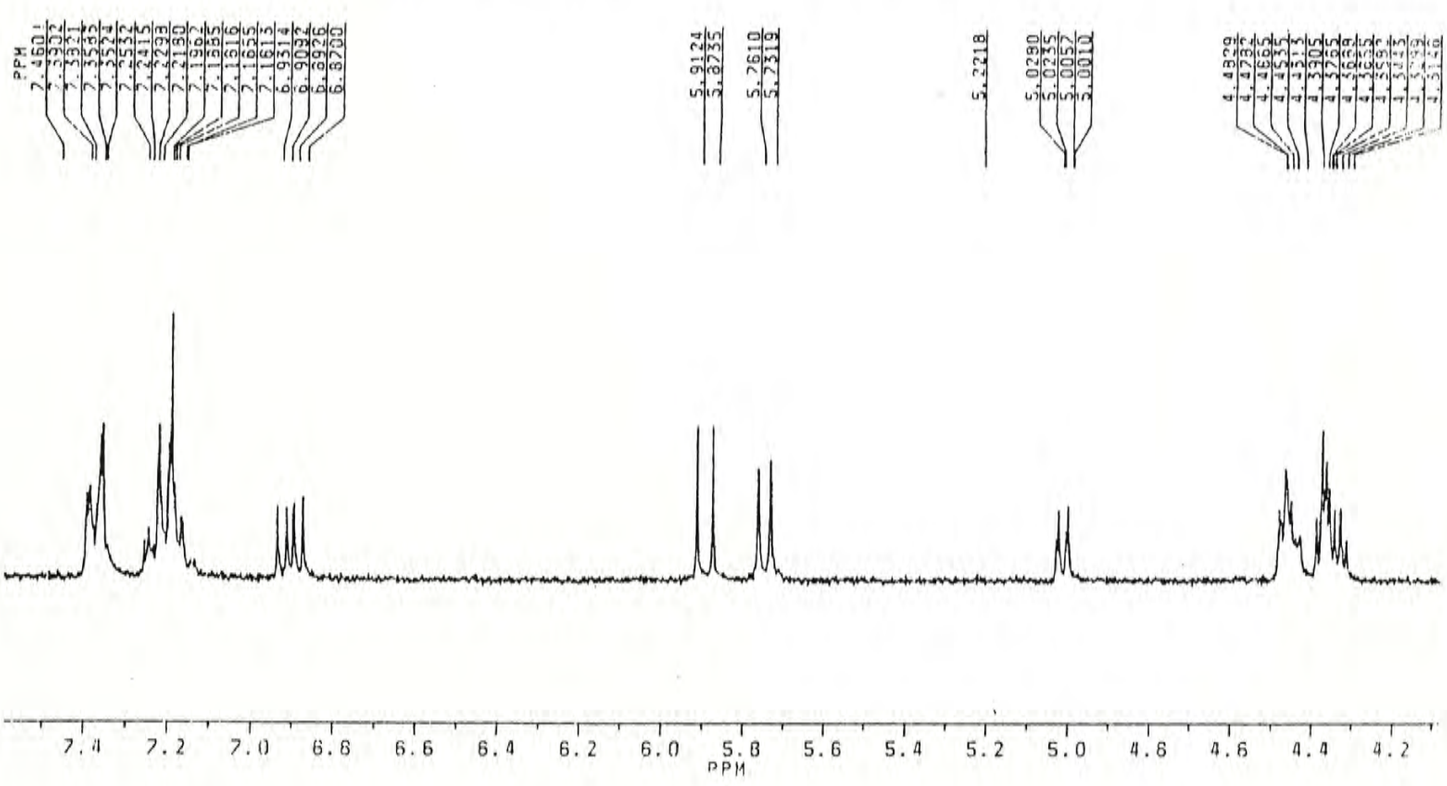


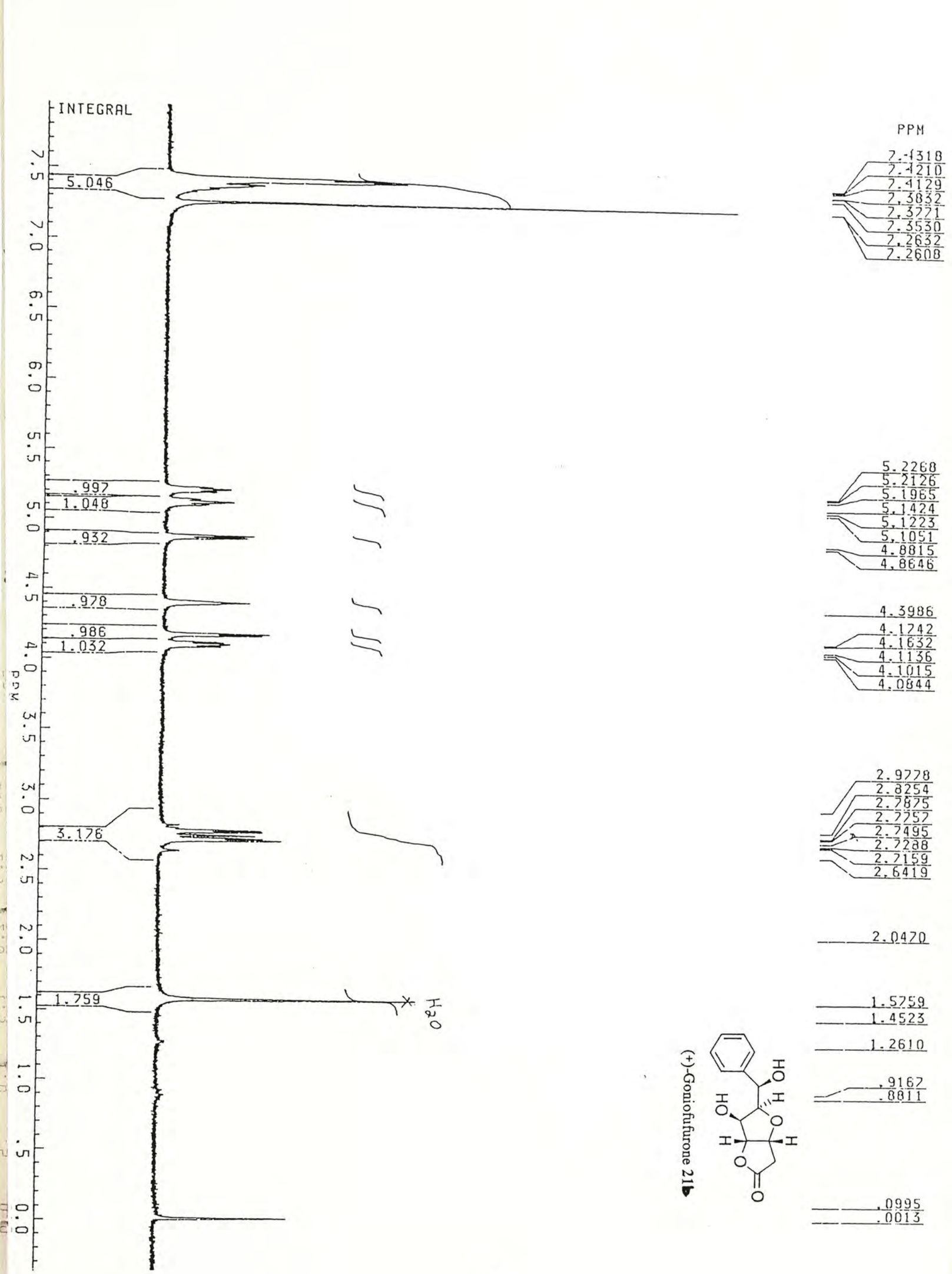

HO
O
OH
OH
(+)-Goniotriol 16
INTEGRAL
PPM



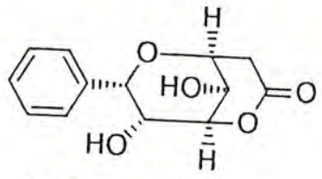


(+)-7-Acetylgoniotriol **20**

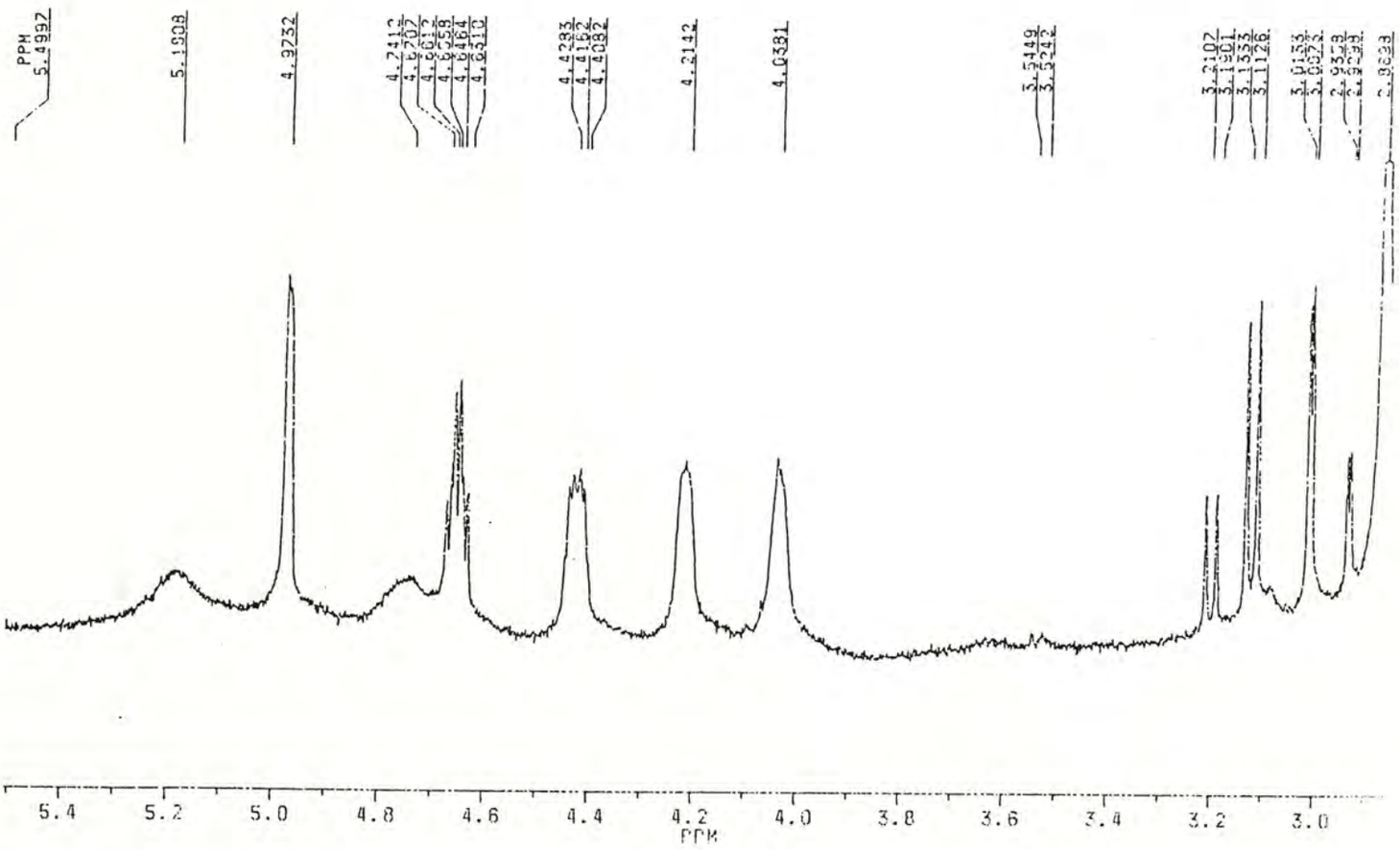


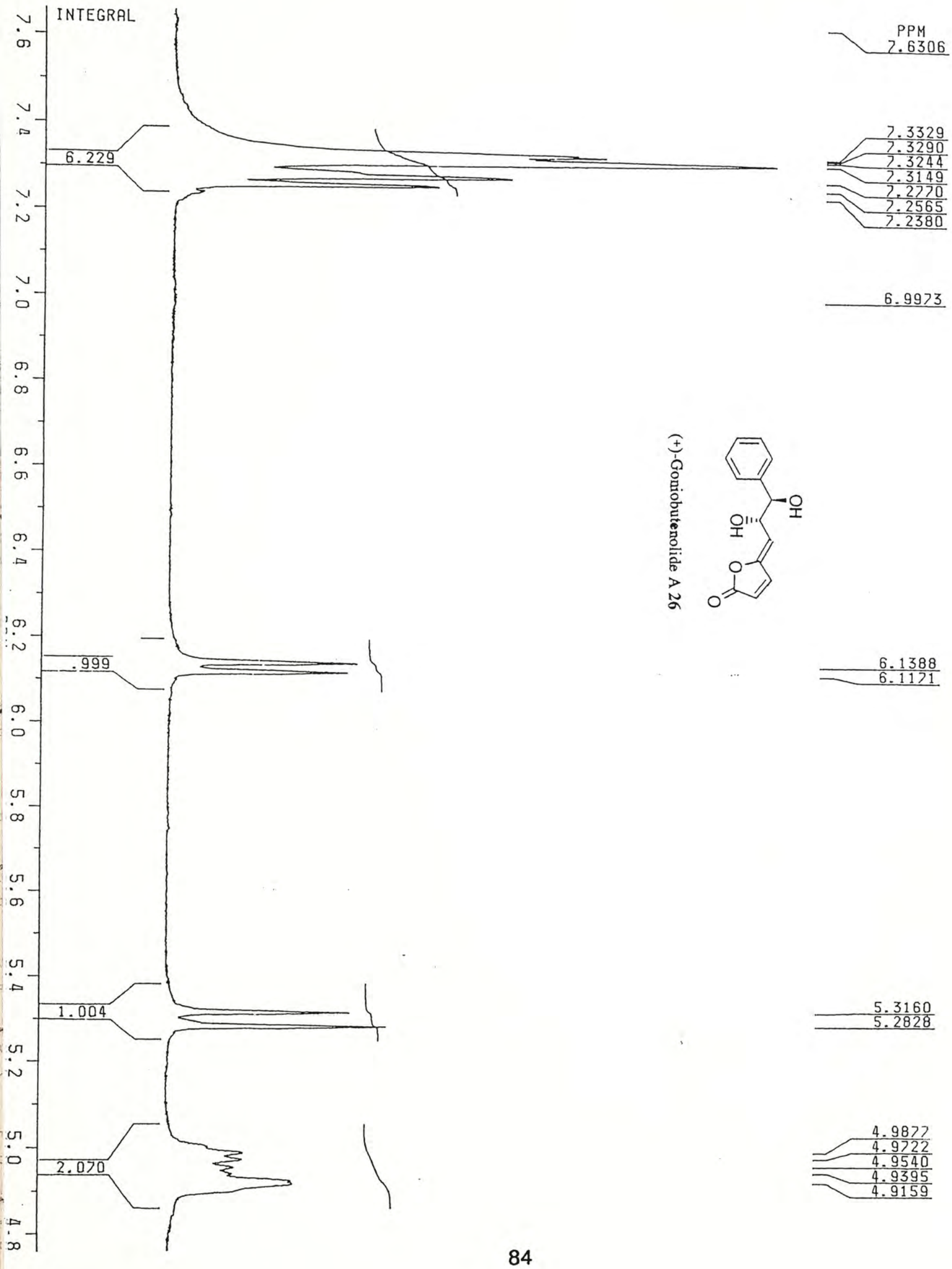


(+)-Goniofufurone **21b**

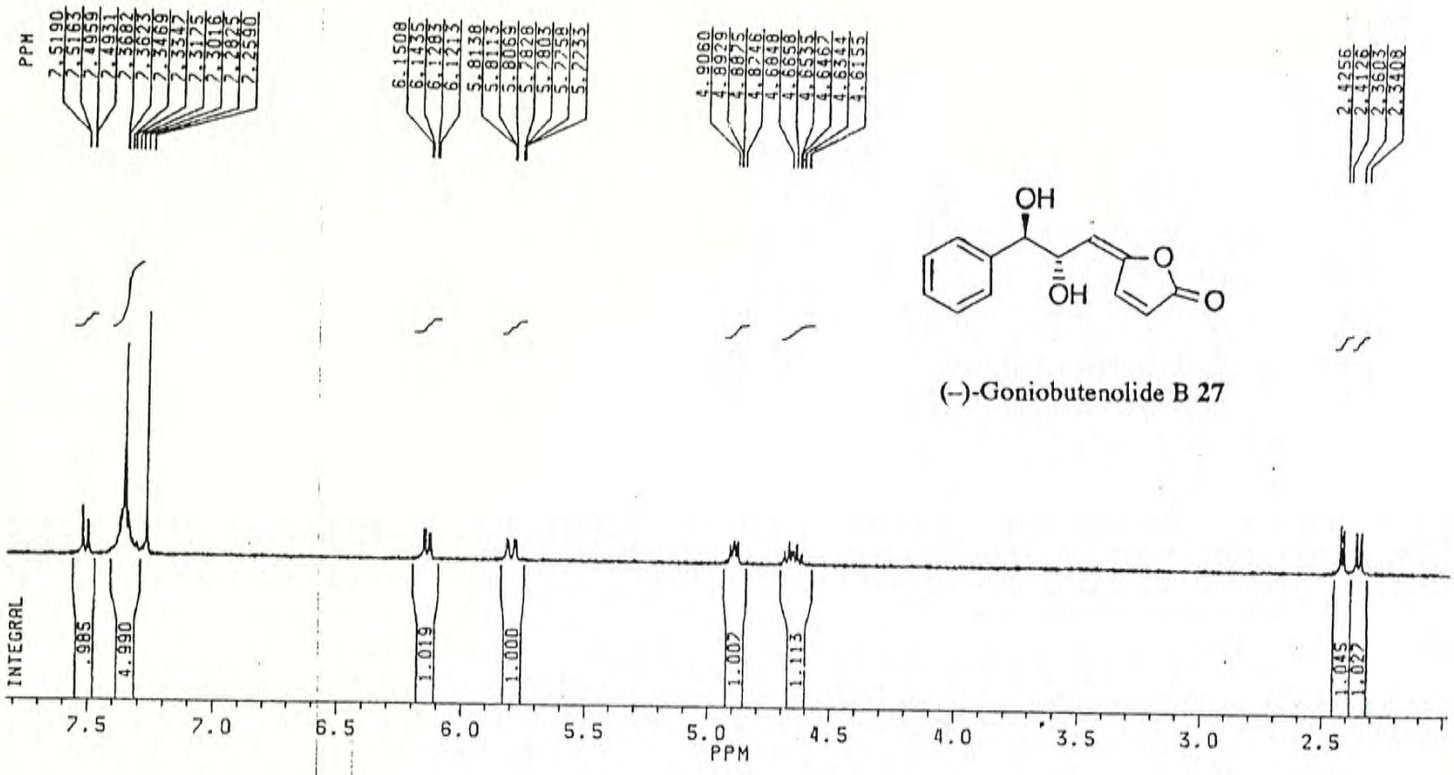


(+)-Goniopypyrone 22





(+)-Goniobutenolide A 26



(–)-Goniobutenolide B **27**