Pergamon

Tetrahedron 55 (1999) 11773–11786

TETRAHEDRON

Direct Synthesis of Pterocarpans *via* Aldol Condensation of Phenylacetates with Benzaldehydes

Theunis G. van Aardt,*[a] Hendrik van Rensburg[a] and Daneel Ferreira*[b]

[a]Department of Chemistry, University of the Orange Free State, P.O.Box 339, Bloemfontein, 9300, South Africa

[b]National Center for Natural Products Research,Thad Cochran Research Center, Research Institute of Pharmaceutical Sciences, School of Pharmacy, The University of Mississippi, MS 38677, USA

Received 21 May 1999; revised 2 August 1999; accepted 5 August 1999

Abstract: Aldol condensation between phenylacetates and benzaldehydes affords 2,3-diaryl-3-hydroxypropanoates which are converted into pterocarpans *via* stepwise deprotection and cyclization in moderate to high yields.

Keywords: Pterocarpans; Aldol condensation; Isoflavonoids.

INTRODUCTION

Over the last few years pterocarpans, the second largest group of natural isoflavonoids,[1] have received considerable interest on account of their medicinal properties. These potent phytoalexins[2] are not only employed as antitoxins[3] but also display antifungal,[4,5] antiviral[3] and antibacterial[6] properties. Recent synthetic endeavours towards pterocarpans comprise Heck arylation,[7,8] the reduction and cyclization of the corresponding 2'-hydroxyisoflavanones,[9] cycloaddition reactions of 2*H*-chromenes with 2-alkoxy-1,4-benzoquinones,[10,11] and 1,3-Michael-Claisen annulation.[12,13] Only two methods, *i.e.* asymmetric dihydroxylation of an isoflav-3-ene and subsequent 'hydrogenative cyclization',[14] and 1,4-benzoquinone cyclo- addition reactions utilizing chiral Ti(IV) complexes,[15,16] permit enantioselective access to this class of compounds. We opted[17] for a direct synthetic approach which is based on aldol condensation between phenylacetates and benzaldehydes with a view to expand the protocol to address the issue of stereocontrol at C-6a and C-11a of the pterocarpan framework.

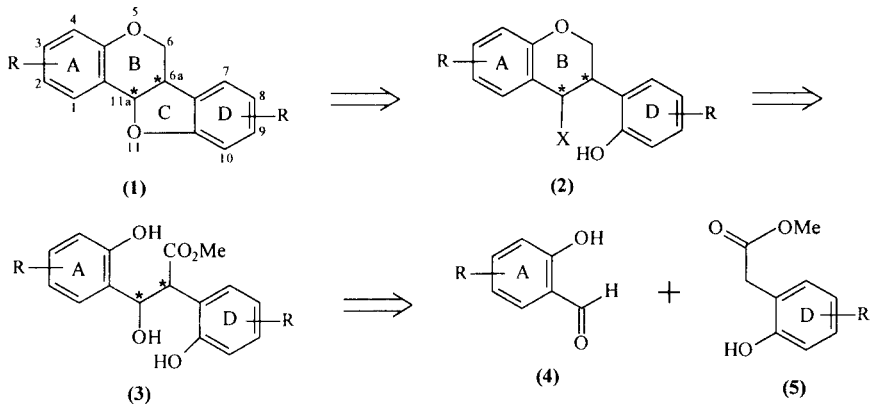
RESULTS AND DISCUSSION

The *retro*-synthetic sequence, **1** ⇒ **2** ⇒ **3** ⇒ **4+5**, indicates the construction of the C_6-C_3-C_6 framework *via* aldol condensation between oxygenated phenylacetates **5** (C_6-C_2 fragment involving the D-ring) and benzaldehydes **4** (C_6-C_1 fragment involving the A-ring) yielding 2,3-diaryl-3-hydroxypropanoates **3**. Subsequent reduction and cyclization would then afford the pterocarpans, *e.g.* **1** (Scheme 1).

* Corresponding authors: E-mail: dferreir@olemiss.edu; vaardti@cem.nw.uovs.ac.za

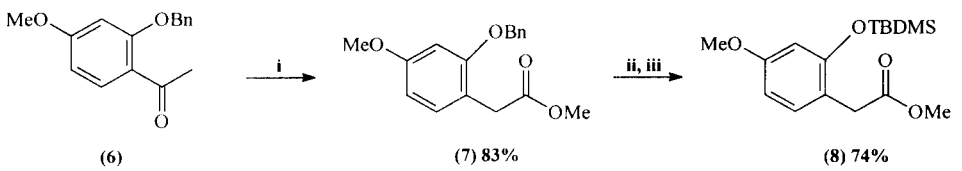
0040-4020/99/$ - see front matter
PII: S0040-4020(99)00679-1

Protection/deprotection of the 2-hydroxyl group in **4** was a prerequisite for the construction of the B-ring of the pterocarpan backbone. Thus, benzaldehydes of type **4** were protected by a methoxymethyl (MOM) group,[18] which is labile in the presence of Lewis acids such as tin tetrachloride ($SnCl_4$).[19]



Scheme 1 *Retro*-synthetic approach towards pterocarpans.

The phenylacetates **8** and **9** were protected as *t*-butyldimethylsilyl ethers (TBDMS), because of their stability towards Lewis acids and potential for deprotection at a later stage.[20] Since 2-hydroxy-4-methoxyphenylacetic acid is not commercially available, the requisite phenylacetate **8** was prepared *via* a thallium(III)nitrate (TTN) oxidative rearrangement[21] of 2-benzyloxy-4-methoxyacetophenone **6**. Debenzylation of compound **7** and silylation gave **8** in good yield (Scheme 2).

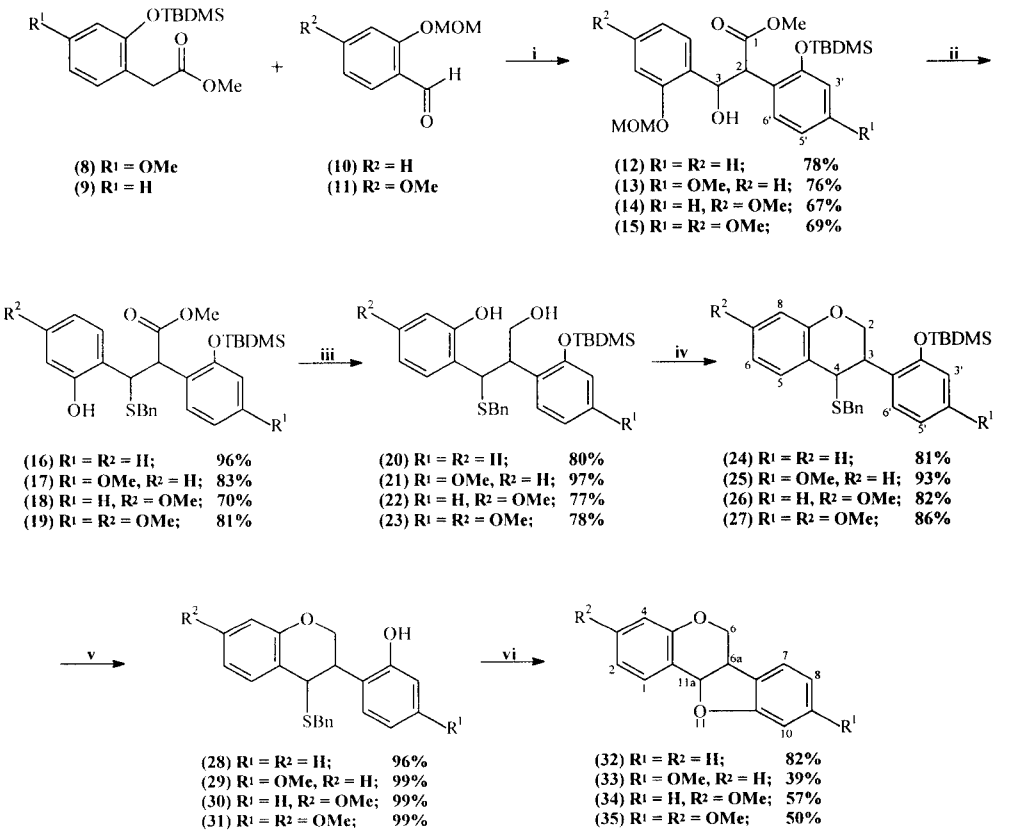


Scheme 2 *Reagents and conditions:* i) TTN, $HClO_4$, MeOH, rt; ii) H_2/Pt, acetone, rt; iii) TBDMSCl, imidazole, DMF, rt.

Owing to the results reported for stereoselective aldol condensation between methyl ketones and aldehydes employing diisopropylethylamine and chiral boron triflates,[22] the amine base was first employed for generation of the enolates. This system did not generate the required enolates, thus the hindered base, lithium diisopropylamide (LDA),[23,24] was selected as the deprotonating agent. The efficiency of this system to produce the *trans*-enolates[25] within 30 minutes at -78 °C was demonstrated by quenching with D_2O. Subsequent condensation between the ester enolates and the benzaldehydes **10** and **11** afforded the 2,3-diaryl-3-hydroxypropanoates **12-15** in moderate to good yields (67-78%) (Scheme 3). Since acid deprotection of the MOM-group[20] led to decomposition, tin tetrachloride ($SnCl_4$), in the presence of benzenemethanethiol (BnSH) as nucleophile, was utilized as a selective deprotecting agent[19] affording the 2,3-diaryl-3-

benzylsulfanylpropanoates **16 -19** in 70-96% yield.

These propanoates were smoothly converted to the corresponding 3-benzylsulfanylpropanol derivatives **20-23** (77-97% yield) by reduction with lithium aluminium hydride ($LiAlH_4$) in diethyl ether at room temperature. Under Mitsunobu cyclization conditions[26] [PPh_3-diethylazodicarboxylate (DEAD)] compounds **20-23** were converted to the isoflavans **24-27** in excellent yields (81-93%). Subsequent cleavage of the silyl ethers using tetrabutylammonium fluoride (TBAF) on silica[27] gave compounds **28-31** which were converted to the 6a,11a-*cis* pterocarpans **32-35** in yields of 39-82% using the thiophilic Lewis acids, dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF)[28,29] or silver trifluoromethanesulfonate (CF_3SO_3Ag).[30]



Scheme 3 *Reagents and conditions*: i) LDA (1.1 eq.), Et_2O, -78°C, then benzaldehydes **10**, **11**, -78 to 0°C; ii) BnSH, $SnCl_4$, CH_2Cl_2, 0°C; iii) $LiAlH_4$, Et_2O, rt; iv) PPh_3, DEAD, rt; v) TBAF(silica), THF, rt; vi) AgOTf or DMTSF, CH_2Cl_2, 0°C.

The low degree of diastereoselectivity in the aldolisation step (Table 1) is in accordance with the results of Roush[31] and Evans *et al.*[32] using lithium as the counter-ion.

Table 1: Diastereoselectivities[a] for the condensation of phenylacetates **8** and **9** with aldehydes **10** and **11**.

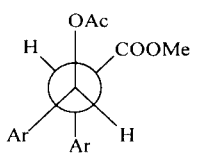
Entry	2,3-diarylpropanoate	*threo* (%)	*erythro* (%)	de (%)	yield (%)
A	**12**	64	36	28	78
B	**13**	61	39	22	76
C	**14**	77	23	55	67
D	**15**	66	34	32	69

[a] Determined by ^{1}H NMR[33]

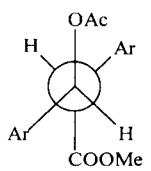
Table 2: ^{1}H NMR data of the *erythro*- and *threo*-2,3-diaryl-3-hydroxypropanoates **12-15** in $CDCl_3$ at 300 MHz. Splitting patterns and J-values (in Hz) are given in parentheses.

	12		13		14		15	
	erythro	*threo*	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*
2-H	4.67 (d; 6.1)	4.54 (d; 10.0)	4.56 (d; 6.5)	4.46 (d; 10.0)	4.66 (d; 7.0)	4.51 (d; 10.0)	4.55 (d; 7.0)	4.45 (d; 10.0)
3-H	5.69 (dd; 5.5, 6.1)	5.74 (dd; 4.9, 10.0)	5.65 (dd; 5.1, 6.5)	5.69 (dd; 5.0, 10.0)	5.59 (dd; 5.1, 7.0)	5.66 (dd; 4.5, 10.0)	5.55 (dd; 5.1, 7.0)	5.64 (dd; 4.5, 10.0)
C_3-O*H*	3.30 (d; 5.5)	3.64 (d; 4.9)	3.27 (d; 5.1)	3.59 (d; 5.0)	3.11 (d; 5.1)	3.50 (d; 4.5)	3.11 (d; 5.1)	3.47 (d; 4.5)
OCH_2OCH_3	5.20, 5.26 (2xd; 6.5)	4.86, 4.98 (2xd; 6.9)	5.20, 5.26 (2xd; 6.5)	4.93, 5.03 (2xd; 6.9)	5.18, 5.21 (2xd; 6.9)	4.85, 4.96 (2xd; 6.9)	5.18, 5.22 (2xd; 6.5)	4.91, 5.02 (2xd; 6.9)
OCH_2OCH_3	3.51 (s)	3.40 (s)	3.51 (s)	3.41 (s)	3.51 (s)	3.39 (s)	3.50 (s)	3.40 (s)
$SiCH_3$	0.19, 0.22 (2xs)	0.20, 0.25 (2xs)	0.18, 0.22 (2xs)	0.20, 0.26 (2xs)	0.20, 0.24 (2xs)	0.21, 0.26 (2xs)	0.20, 0.24 (2xs)	0.23, 0.27 (2xs)
Bu^t	0.99 (s)	1.05 (s)	0.98 (s)	1.05 (s)	1.00 (s)	1.05 (s)	1.00 (s)	1.06 (s)
OCH_3	3.57 (s)	3.71 (s)	3.57, 3.78 (2xs)	3.70, 3.71 (2xs)	3.56, 3.77 (2xs)	3.71, 3.73 (2xs)	3.55, 3.77, 3.78 (3xs)	3.69, 3.70, 3.74 (3xs)
3'-H	7.07 (dd; 1.1, 8.1)	6.94 (dd; 1.1, 8.5)	7.07 (dd; 1.1, 8.5)	6.95 (dd; 1.1, 8.1)	6.69 (d; 2.2)	6.54 (d; 2.3)	6.68 (d; 2.2)	6.55 (d; 2.5)
4'-H	7.19 (ddd; 1.9, 7.1, 8.1)	7.12 (ddd; 1.9, 7.1, 8.5)	7.19 (ddd; 1.9, 7.3, 8.5)	7.12 (ddd; 1.9, 7.0, 8.1)	—	—	—	—
5'-H	6.87 (ddd; 1.1, 7.1, 7.4)	6.91 (ddd; 1.1, 7.1, 7.5)	6.88 (ddd; 1.1, 7.3, 7.5)	6.91 (ddd; 1.1, 7.0, 7.6)	6.44 (dd; 2.2, 8.9)	6.45 (dd; 2.3, 8.5)	6.44 (dd; 2.2, 8.9)	6.45 (dd; 2.5, 8.5)
6'-H	7.06 (dd; 1.9, 7.4)	7.39 (dd; 1.9, 7.5)	7.05 (dd; 1.9, 7.5)	7.37 (dd; 1.9, 7.6)	6.98 (d; 8.9)	7.30 (d; 8.5)	6.99 (d; 8.9)	7.28 (d; 8.5)
3"-H	6.77 (dd; 1.1, 8.1)	6.65 (dd; 1.1, 8.1)	6.35 (d; 2.5)	6.22 (d; 2.2)	6.80 (dd; 1.1, 8.1)	6.66 (dd; 1.1, 8.0)	6.36 (d; 2.5)	6.24 (d; 2.5)
4"-H	7.16 (ddd; 1.9, 7.1, 8.1)	7.01 (ddd; 1.9, 7.5, 8.1)	—	—	7.16 (ddd; 1.9, 7.5, 8.1)	7.01 (ddd; 1.9, 7.5, 8.0)	—	—
5"-H	6.96 (ddd; 1.1, 7.1, 7.5)	6.79 (ddd; 1.1, 7.5, 7.9)	6.55 (dd; 2.5, 8.5)	6.36 (dd; 2.2, 8.9)	6.97 (ddd; 1.1, 7.5, 7.5)	6.79 (ddd; 1.1, 7.5, 8.1)	6.55 (dd; 2.5, 8.5)	6.37 (dd; 2.5, 8.6)
6"-H	7.52 (dd; 1.9, 7.5)	7.30 (dd; 1.9, 7.9)	7.44 (d; 8.5)	7.23 (d; 8.9)	7.55 (dd; 1.9, 7.5)	7.29 (dd; 1.9, 8.1)	7.45 (d; 8.5)	7.24 (d; 8.6)

Acetylation of the two diastereoisomers of **12** led to the anticipated shifting of the carbonyl band toward higher frequency (1730 cm^{-1} to 1740 cm^{-1}), thus implicating the presence of an intramolecular hydrogen bond in the aldol products. The *erythro*-acetate of **12** displayed an increase in the $^3J_{2,3}$- value from 6.1 to 8.0 Hz, while the *threo*-acetate of **12** showed an increase from 10.0 to 11.0 Hz thus correlating with the predicted conformations **36** and **37** (Scheme 4) for the acetates and confirming the intramolecular hydrogen bond in a fashion similar to the observations of Stiles *et al.*[33]



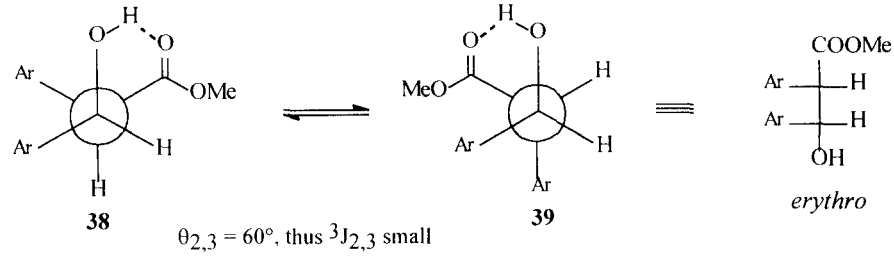
36 (*threo*)



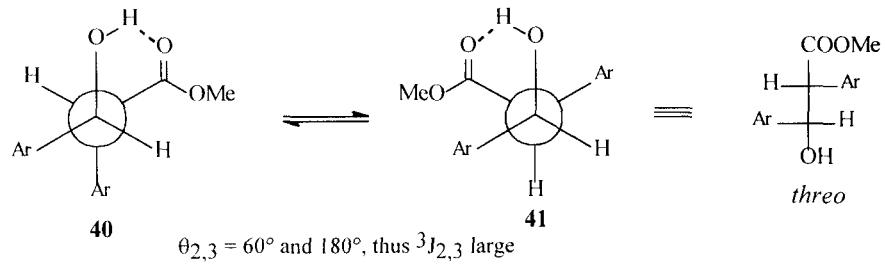
37 (*erythro*)

Scheme 4 Newman projections for the acetylated *erythro*- and *threo*-propanoates **12**. For both conformations $\theta_{2,3} = 180°$, thus $^3J_{2,3}$ large.

Stereochemical assignment of the aldol diastereoisomers was thus effected by comparing the observed ^{1}H NMR coupling constants ($^3J_{2,3}$, Table 2) with the H-C_2-C_3-H dihedral angles of the predicted hydrogen bonded conformations.[33] Structures **38** and **39** (Scheme 5) represent the *erythro* product and display a H-C_2-C_3-H dihedral angle of 60° which is smaller than the corresponding average dihedral angle of the *threo* conformations **40** and **41**, hence leading to "small" (6-7 Hz) and "large" (*ca.* 10.0 Hz) $^3J_{2,3}$ values, respectively.



$\theta_{2,3}$ = 60°, thus $^3J_{2,3}$ small



$\theta_{2,3}$ = 60° and 180°, thus $^3J_{2,3}$ large

Scheme 5 Newman projections for the hydrogen bonded *erythro*- and *threo*-propanoates.

The individual *threo*-($^3J_{2,3}$ = 10.0 Hz) and *erythro*-($^3J_{2,3}$ = 6.1-7.0 Hz) propanoates **12**, **14** and **15** gave mixtures of *threo*- and *erythro*-3-benzylsulfanylpropanoates **16**, **18** and **19**, while both isomers of **13** afforded only the *threo*-3-benzylsulfanylpropanoate **17** (Table 4). A mixed S_N1 / S_N2 mechanism is thus implied, the 2,4-dioxygenated aromatic ring of compounds **14** and **15** leading to a stabilized incipient carbocation hence explaining the low diastereoselectivity of the **14/15** → **18/19** conversion (Table 3).

Table 3: Diastereoselectivities of the BnSH/$SnCl_4$ thiolysis/deprotection of MOM-ethers **12-15**.

Entry	3-benzylthio-propanoate	*threo* (%)	*erythro* (%)	de (%)	total yield (%)
A	**16**	87	13	74	96
B	**17**	100	0	100	83
C	**18**	77	23	54	70
D	**19**	52	48	4	81

Scheme 6 represents the possible conformations of the *cis*- and *trans*-4-benzylsulfanylisoflavans **24-27**. ^{1}H NMR spectra (Table 6) of the isomeric pairs display small coupling constants between H-3 and H-4 ($^3J_{3,4}$ = 3.5-4.0 Hz), as well as between H-3 and H-2_{eq} ($^3J_{2eq,3}$ = 3.0-4.8 Hz). One of the isomers, however, exhibits a

Table 4: ^{1}H NMR data of the *erythro*- and *threo*-3-benzylsulfanyl-2,3-diaryl-3-hydroxypropanoates **16-19** in $CDCl_3$ at 300 MHz. Splitting patterns and J-values (in Hz) are given in parentheses.

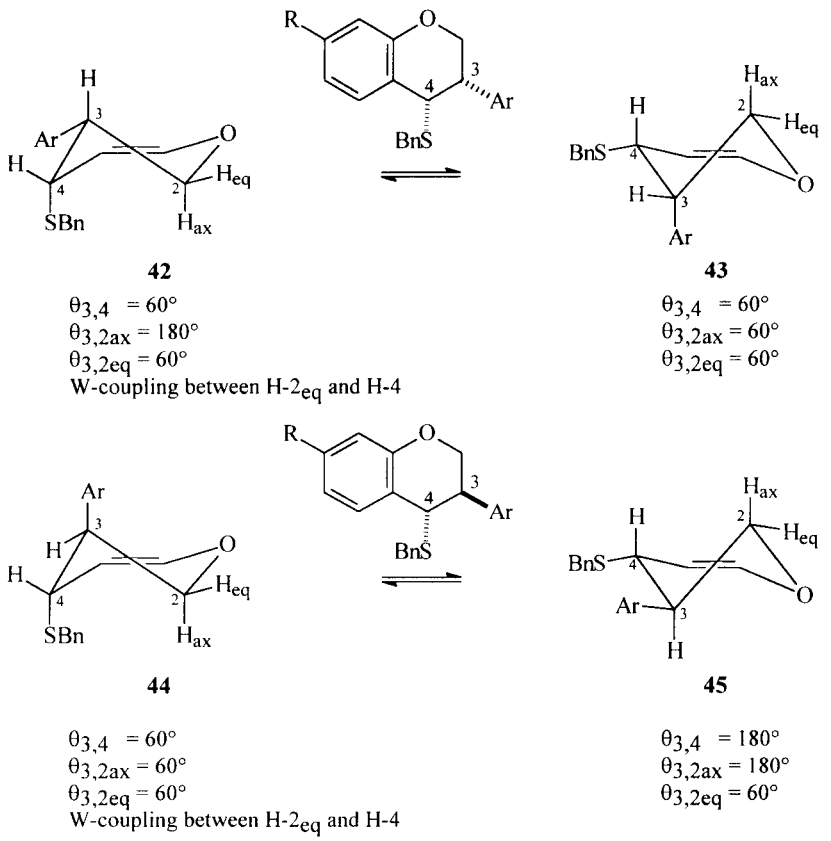
	16		**17**	**18**		**19**	
	erythro	*Threo*	*threo*	*erythro*	*threo*	*erythro*	*Threo*
2-H	4.46-4.63 (m)	4.70 (d; 11.0)	4.70 (d; 11.0)	4.38-4.55 (m)	4.61 (d; 10.9)	4.40-4.51 (m)	4.58 (d; 10.5)
3-H	4.70-4.89 (m)	4.86 (d; 11.0)	4.77 (d; 11.0)	4.66-4.87 (m)	4.81 (d; 10.9)	4.59-4.74 (m)	4.70 (d; 10.5)
ArCH_2S	3.27, 3.39 (2xd; 13.0)	3.55, 3.66 (2xd; 13.0)	3.55, 3.65 (2xd; 12.9)	3.29, 3.42 (2xd; 14.5)	3.53, 3.62 (2xd; 13.0)	3.29, 3.41 (2xd; 13.1)	3.51, 3.61 (2xd; 13.0)
SiCH_3	0.26, 0.34 (2xs)	0.22 (2xs)	0.24 (2xs)	0.26, 0.34 (2xs)	0.22 (2xs)	0.26, 0.34 (2xs)	0.23 (2xs)
Bu^t	1.07 (s)	1.06 (s)	1.06 (s)	1.08 (s)	1.06 (s)	1.06 (s)	1.05 (s)
OCH_3	3.40 (s)	3.70 (s)	3.67, 3.70 (2xs)	3.43, 3.82 (2xs)	3.69, 3.71 (2xs)	3.42, 3.80, 3.82 (3xs)	3.68, 3.69, 3.72 (3xs)
3'-H	6.84-7.05 (m)	6.73-6.82 (m)	6.75 (dd; 1.1, 8.0)	6.55 (d; 2.9)	6.34 (d; 2.9)	6.54 (d; 2.9)	6.34 (d; 2.9)
4'-H	6.84-7.05 (m)	6.99 (ddd; 1.9, 7.2, 8.0)	7.04 (ddd; 1.9, 7.1, 8.0)	—	—	—	—
5'-H	6.84-7.05 (m)	6.61 (ddd; 1.1, 7.2, 7.5)	6.65 (ddd; 1.1, 7.1, 7.2)	6.51 (dd; 2.9, 8.1)	6.16 (dd; 2.9, 8.5)	6.51 (dd; 2.9, 8.9)	6.37 (dd; 2.9, 8.9)
6'-H	7.16-7.32 (m)	6.73-6.82 (m)	6.79-6.86 (m)	7.16-7.31 (m)	6.65 (d; 8.5)	7.19 (d; 8.9)	6.67 (d; 8.9)
3"-H	6.84-7.05 (m)	6.62 (dd; 1.1, 8.0)	6.19 (d; 2.9)	6.86 (dd; 1.1, 8.0)	6.64 (dd; 1.1, 8.0)	6.42 (d; 2.2)	6.20 (d; 2.9)
4"-H	6.84-7.05 (m)	7.02 (ddd; 1.9, 7.2, 8.0)	—	6.94 (ddd; 1.1, 7.1, 7.3)	7.00 (ddd; 1.9, 7.2, 8.0)	—	—
5"-H	6.84-7.05 (m)	6.73-6.82 (m)	6.35 (dd; 2.9, 8.5)	7.02-7.06 (m)	6.80 (ddd; 1.1, 7.1, 7.2)	6.49 (dd; 2.2, 8.5)	6.19 (dd; 2.9, 8.5)
6"-H	7.16-7.32 (m)	7.17-7.36 (m)	7.16-7.31 (m)	7.02-7.06 (m)	7.16-7.32 (m)	7.03-7.07 (m)	7.16-7.31 (m)
Ar*OH*	7.16-7.32 (m)	6.73-6.82 (m)	6.79-6.86 (m)	7.44 (m)	7.06 (m)	7.40-7.47 (m)	7.05-7.10 (m)
ArCH_2S	7.16-7.32 (m)	7.17-7.36 (m)	7.16-7.31 (m)	7.16-7.31 (m)	7.16-7.32 (m)	7.20-7.27 (m)	7.16-7.31 (m)

Table 5: ^{1}H NMR data of the *erythro*- and *threo*-2,3-diaryl-3-hydroxypropanols **20-23** in $CDCl_3$ at 300 MHz. Splitting patterns and J-values (in Hz) are given in parentheses.

	20	**21**	**22**		**23**	
	Threo	*threo*	*erythro*	*threo*	*erythro*	*Threo*
2-H	3.91-4.06 (m)	3.82-4.01 (m)	3.70-3.82 (m)	3.89-4.02 (m)	3.61-3.71 (m)	3.77-3.96 (m)
3-H	4.50 (d; 9.1)	4.47 (d; 9.1)	4.31 (d; 12.0)	4.40 (d; 8.9)	4.29 (d; 11.1)	4.37 (d; 9.0)
1-CH_2	3.91-4.06 (m)	3.82-4.01 (m)	3.47-3.60 (m)	3.89-4.02 (m)	3.47-3.54 (m)	3.77-3.96 (m)
C_1-O*H*	1.79-1.86 (m)	1.80-1.91 (m)	1.61 (m)	1.68-1.74 (m)	1.41-1.54 (m)	1.70-1.79 (m)
ArCH_2S	3.47, 3.60 (2xd; 13.0)	3.46, 3.57 (2xd; 10.9)	3.35, 3.47 (2xd; 13.5)	3.46, 3.59 (2xd; 13.1)	3.35, 3.47 (2xd; 13.5)	3.44, 3.57 (2xd; 13.1)
SiCH_3	0.22, 0.24 (2xs)	0.23, 0.25 (2xs)	0.25, 0.30 (2xs)	0.21, 0.24 (2xs)	0.25, 0.30 (2xs)	0.22, 0.25 (2xs)
Bu^t	1.04 (s)	1.03 (s)	1.01 (s)	1.02 (s)	1.01 (s)	1.02 (s)
OCH_3	—	3.70 (s)	3.84 (s)	3.74 (s)	3.80, 3.84 (2xs)	3.71, 3.75 (2xs)
3'-H	6.77 (dd; 1.1, 8.0)	6.79 (dd; 1.1, 8.1)	6.56 (d; 2.9)	6.36 (d; 2.9)	6.56 (d; 2.5)	6.38 (d; 2.9)
4'-H	7.06 (ddd; 1.9, 7.1, 8.0)	7.08 (ddd; 1.9, 7.1, 8.1)	—	—	—	—
5'-H	6.69 (ddd; 1.1, 7.1, 7.9)	6.71 (ddd; 1.1, 7.1, 7.9)	6.54 (dd; 2.9, 8.1)	6.25 (dd; 2.9, 8.5)	6.49 (dd; 2.5, 8.5)	6.27 (dd; 2.9, 8.1)
6'-H	6.86 (dd; 1.9, 7.9)	6.89 (dd; 1.9, 7.9)	7.09 (d; 8.1)	6.72 (d; 8.5)	6.92 (d; 8.5)	6.74 (d; 8.1)
3"-H	6.70 (dd; 1.1, 7.9)	6.28 (d; 2.5)	6.85 (dd; 1.1, 8.0)	6.71 (dd; 1.1, 8.1)	6.43 (d; 2.9)	6.29 (d; 2.5)
4"-H	7.01 (ddd; 1.9, 7.1, 7.9)	—	7.16 (ddd; 1.9, 7.2, 8.0)	7.03 (ddd; 1.9, 7.1, 8.1)	—	—
5"-H	6.75 (ddd; 1.1, 7.1, 7.5)	6.32 (dd; 2.5, 8.1)	6.91 (ddd; 1.1, 7.2, 7.5)	6.77 (ddd; 1.1, 7.1, 7.1)	6.53 (dd; 2.9, 8.0)	6.34 (dd; 2.5, 8.2)
6"-H	6.96 (dd; 1.9, 7.5)	6.82 (d; 8.1)	7.02 (dd; 1.9, 7.5)	6.94 (dd; 1.9, 7.1)	7.10 (d; 8.0)	6.81 (d; 8.2)
Ar*OH*	6.92-6.94 (m)	6.98-7.05 (m)	7.59-7.61 (m)	7.12-7.15 (m)	7.55-7.65 (m)	7.15-7.32 (m)
ArCH_2S	7.16-7.33 (m)	7.15-7.32 (m)	7.07-7.12 (2H, m) 7.24-7.31 (3H, m)	7.15-7.33 (m)	7.07-7.12 (2H, m) 7.20-7.31 (3H m)	7.15-7.32 (m)

large coupling between H-3 and H-2_{ax} ($^3J_{2ax,3}$ = 11.5-11.8 Hz) and the other a small coupling ($^3J_{2ax,3}$ = 3.0-3.1 Hz). The small coupling between H-3 and H-4 eliminates **45** leaving **44** with its *trans*-diaxial benzylsulfanyl and phenyl groups as the preferred conformation[34] with a dihedral angle of *ca.* 60° between H-3 and both H-2_{eq}

and H-2_{ax}. Both pairs of spectra also display W-coupling between H-4 and H-2_{eq} ($^4J_{2eq,4}$ = 1-2 Hz) which is only permitted for conformations **42** and **44**. This data facilitated identification of the *trans*-isomers and thus differentiation of the two isomers which could be extrapolated to determine the configuration of structures **16-23** (Tables 4 and 5) and **28-31** (Table 7).



Scheme 6 Possible conformations for *cis*- and *trans*-isoflavans.

The reactivity of the diastereomeric compounds **16, 18** and **19** was the same in all instances and the **6a,11a**-*cis* pterocarpans **32**, **34** and **35** could be generated from both the 3,4-*cis*- and *trans*-benzylsulfanylisoflavans, excluding *trans*-**28** which was not isolated, in comparable yields. This presumably reflects a thermodynamically controlled S_N1 cyclization mechanism. We cannot, however, explain the low yield of formation of the pterocarpan **33**.

We have thus developed a novel synthetic route towards pterocarpans. This protocol should contribute substantially towards the chemistry of pterocarpans and has the potential to address the stereoselective synthesis of these compounds, a process which is currently being pursued and will be reported elsewhere.

Table 6: ^{1}H NMR data of the *cis*- and *trans*-4-benzylsulfanylisoflavans **24 - 27** in $CDCl_3$ at 300 MHz. Splitting patterns and J-values (in Hz) are given in parentheses.

	24	**25**	**26**		**27**	
	Cis	*cis*	*cis*	*trans*	*cis*	*trans*
2-H_{eq}	4.41 (ddd; 2.0, 3.0, 10.5)	4.38 (ddd; 2.1, 3.1, 10.1)	4.39 (ddd; 2.0, 3.0, 10.1)	4.26 (ddd; 1.1, 4.5, 10.9)	4.34 (ddd; 2.0, 3.0, 10.1)	4.24 (ddd; 1.1, 4.8, 10.9)
2-H_{ax}	4.77 (dd; 10.1, 11.5)	4.74 (dd; 10.1, 11.8)	4.75 (dd; 10.1, 11.8)	4.57 (dd; 3.0, 10.9)	4.71 (dd; 10.1, 11.9)	4.56 (dd; 3.1, 10.9)
3-H	3.93 (ddd; 3.0, 3.5, 11.5)	3.86 (ddd; 3.1, 3.9, 11.8)	3.90 (ddd; 3.0, 3.8, 11.8)	3.87 (ddd; 3.0, 4.0, 4.5)	3.82 (ddd; 3.0, 3.9, 11.9)	3.77 (ddd; 3.1, 3.9, 4.8)
4-H	4.24 (dd; 2.0, 3.5)	4.19 (dd; 2.1, 3.9)	4.20 (dd; 2.0, 3.8)	4.08 (d; 4.0)	4.14 (dd; 2.0, 3.9)	4.05 (d; 3.9)
SiCH_3	0.21, 0.34 (2xs)	0.23, 0.36 (2xs)	0.21, 0.34 (2xs)	0.34, 0.35 (2xs)	0.22, 0.34 (2xs)	0.35, 0.36 (2xs)
Bu^t	0.89 (s)	0.88 (s)	0.88 (s)	1.07 (s)	0.88 (s)	1.07 (s)
OCH_3	—	3.85 (s)	3.76 (s)	3.78 (s)	3.76, 3.84 (2xs)	3.76, 3.78 (2xs)
ArCH_2S	2.71, 3.01 (2xd; 13.1)	2.79, 3.10 (2xd; 13.1)	2.67, 2.96 (2xd; 13.1)	3.69, 3.80 (2xd; 12.9)	2.75, 3.05 (2xd; 13.1)	3.70, 3.80 (2xd; 13.0)
5-H	7.05-7.16 (m)	7.08-7.35 (m)	6.80 (d; 8.2)	7.20-7.28 (m)	6.78 (d; 9.0)	7.20-7.30 (m)
6-H	7.05-7.16 (m)	6.79-6.91 (m)	6.43 (dd; 2.9, 8.2)	6.53 (dd; 2.8, 8.8)	6.42 (dd; 2.5, 9.0)	6.53 (dd; 2.8, 8.5)
7-H	7.05-7.16 (m)	6.79-6.91 (m)	—	—	—	—
8-H	6.79-6.85 (m)	6.79-6.91 (m)	6.35 (d; 2.9)	6.37 (d; 2.8)	6.34 (d; 2.5)	6.38 (d; 2.8)
3'-H	6.88-6.95 (m)	6.52 (d; 2.9)	6.91 (dd; 1.1, 8.0)	6.76-6.90 (m)	6.50 (d; 2.8)	6.46 (d; 2.5)
4'-H	7.05-7.16 (m)	—	7.11-7.18 (m)	7.13 (ddd; 2.2, 6.2, 8.0)	—	—
5'-H	6.79-6.85 (m)	6.65 (dd; 2.9, 8.5)	7.06 (ddd; 1.1, 7.2, 7.5)	6.76-6.90 (m)	6.62 (dd; 2.8, 8.5)	6.36 (dd; 2.5, 8.5)
6'-H	6.88-6.95 (m)	7.14 (d; 8.5)	7.11-7.18 (m)	6.76-6.90 (m)	7.11 (d; 8.5)	6.74 (d; 8.5)
ArCH_2S	7.20-7.32 (m)	7.08-7.35 (m)	7.18-7.32 (m)	7.20-7.28 (m)	7.14-7.32 (m)	7.20-7.30 (m)

Table 7: ^{1}H NMR data of the *cis*- and *trans*-2'-hydroxy-4-benzylsulfanylisoflavans **28 - 31** in $CDCl_3$ at 300 MHz. Splitting patterns and J-values (in Hz) are given in parentheses.

	28	**29**	**30**		**31**	
	Cis	*cis*	*cis*	*trans*	*cis*	*trans*
2-H_{eq}	4.44 (ddd; 2.0, 3.0, 10.5)	4.39 (ddd; 2.1, 2.9, 10.5)	4.41 (ddd; 2.0, 3.0, 10.1)	4.40 (ddd; 1.1, 5.1, 11.0)	4.37 (ddd; 2.0, 3.0, 10.5)	4.35 (ddd; 1.1, 5.5, 10.9)
2-H_{ax}	4.76 (dd; 10.5, 11.8)	4.72 (dd; 10.5, 11.5)	4.75 (dd; 10.1, 11.5)	4.61 (dd; 3.1, 11.0)	4.72 (dd; 10.5, 11.5)	4.57 (dd; 3.0, 10.9)
3-H	3.96 (ddd; 3.0, 4.0, 11.8)	3.85 (ddd; 2.9, 4.9, 11.5)	3.92 (ddd; 3.0, 4.0, 11.5)	3.74 (ddd; 3.1, 5.1, 5.1)	3.82 (ddd; 3.0, 4.0, 11.5)	3.65 (ddd; 3.0, 5.0, 5.5)
4-H	4.27 (dd; 2.0, 4.0)	4.19 (dd; 2.1, 4.9)	4.22 (dd; 2.0, 4.0)	4.14 (d; 5.1)	4.16 (dd; 2.0, 4.0)	4.06 (d; 5.0)
OCH_3	—	3.84 (s)	3.76 (s)	3.78 (s)	3.76, 3.84 (2xs)	3.76, 3.78 (2xs)
ArCH_2S	2.85, 3.08 (2xd; 13.0)	2.92, 3.17 (2xd; 13.0)	2.81, 3.05 (2xd, 13.1)	3.73, 3.84 (2xd; 13.0)	2.90, 3.14 (2xd; 13.0)	3.73, 3.82 (2xd; 13.1)
5-H	7.11-7.16 (m)	7.08-7.19 (m)	6.88 (d; 8.5)	7.21 (d; 8.5)	6.86 (d; 8.5)	7.21 (d; 8.5)
6-H	6.80-6.89 (m)	6.79-6.86 (m)	6.46 (dd; 2.8, 8.5)	6.50 (dd; 2.5, 8.5)	6.46 (dd; 2.5, 8.5)	6.50 (dd; 2.5, 8.5)
7-H	6.80-6.89 (m)	6.79-6.86 (m)	—	—	—	—
8-H	6.96-7.00 (m)	6.92-6.97 (m)	6.36 (d; 2.8)	6.39 (d; 2.5)	6.35 (d; 2.5)	6.40 (d; 2.5)
3'-H	6.80-6.89 (m)	6.46 (d; 2.5)	6.86 (dd; 1.0, 7.9)	6.81 (dd; 1.1, 7.8)	6.46 (d; 2.5)	6.40 (d; 2.5)
4'-H	7.11-7.16 (m)	—	7.10-7.14 (m)	7.14 (ddd; 1.9, 7.2, 7.8)	—	—
5'-H	7.03-7.10 (m)	6.61 (dd; 2.5, 8.5)	7.05 (ddd; 1.0, 7.2, 7.5)	6.86 (ddd; 1.1, 7.2, 7.8)	6.60 (dd; 2.5, 8.5)	6.41 (dd; 2.5, 9.0)
6'-H	7.11-7.16 (m)	7.08-7.19 (m)	7.10-7.14 (m)	7.07 (dd, 1.9, 7.8)	7.13 (d; 8.5)	6.96 (d; 9.0)
ArCH_2S	7.20-7.33 (m)	7.08-7.34 (m)	7.19-7.32 (m)	7.21-7.31 (m)	7.14-7.33 (m)	7.20-7.31 (m)
Ar-O*H*	5.37-5.51 (m)	5.38-5.44 (m)	5.16 (m)	5.16 (m)	5.48-5.60 (m)	5.35-5.41 (m)

EXPERIMENTAL

^{1}H NMR spectra were recorded at ambient temperature on a Bruker AM-300 spectrometer for solutions in $CDCl_3$ and C_6D_6 with the solvent as internal standard. Infrared spectra were recorded in $CHCl_3$ on a Hitachi infrared model 270-50 spectrophotometer. High and low resolution EI-mass spectra were obtained on a VG 70-70E mass spectrometer. M.p.s. (crystals from Me_2CO) were measured on a Reichert hot-stage apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on DC-Alufolien Kieselgel 60 F_{254} (0.25 mm)

plates with visualisation by UV light and/or HCHO-H_2SO_4 spray. Preparative plates (PLC), Kieselgel PF_{254} (1.0 mm), were air-dried and used without prior activation. Flash column chromatography (FCC) was performed on Merck Kieselgel 60 (230-400 mesh) under a positive pressure by means of compressed N_2.

2-Benzyloxy-4-methoxyacetophenone 6

To a suspension of NaH (2 eq., 80%, 462.1 mg) in dry DMF (50 ml) at 0°C, 2-hydroxy-4-methoxyacetophenone (2.00 g) was added in small portions over 20 min. After 5 min. benzyl chloride (4 eq., 5.5 ml) was added dropwise. The reaction was stirred at 25°C for 3 h and the excess NaH was destroyed with ice. The mixture was extracted with EtOAc (3x50 ml), the combined EtOAc extract was washed with water (3x50 ml), dried (Na_2SO_4), evaporated to dryness and purifiedby FCC in benzene to give **6** as a yellow oil; 2.68 g, R_f 0.24 (TLC/benzene), (87%); ^{1}H NMR ($CDCl_3$) δ 2.58 (COCH_3, s), 3.86 (OCH_3, s), 5.16 (OCH_2Ar, s), 6.54 (3-H, d, J = 2.1 Hz), 6.56 (5-H, dd, J = 2.1, 8.1 Hz), 7.35-7.49 (5xAr-H, m), 7.87 (6-H, d, J = 8.1 Hz).

Methyl 2-benzyloxy-4-methoxyphenylacetate 7

2-Benzyloxy-4-methoxyacetophenone **6** (1.66 g) in MeOH (5 ml) was added dropwise to a solution of TTN (1 eq., 2.88 g) and 60% perchloric acid (6 ml) in MeOH (30 ml). After stirring at r.t. for 5 h the MeOH was decanted, water (50 ml) was added and the mixture extracted with $CHCl_3$ (3x100 ml). The combined chloroform extract was washed with water (2x100 ml), dried (Na_2SO_4), evaporated and purified by FCC in benzene-Me_2CO (9:1) to give **7** as yellow oil 1.54 g, R_f 0.72 (TLC/benzene-Me_2CO 9:1), (83%); ^{1}H NMR ($CDCl_3$) δ 3.64 (ArCH_2, s), 3.66 (COOCH_3, s), 3.80 (OCH_3, s), 5.08 (OCH_2Ar, s), 6.50 (5-H, dd, J = 2.2, 8.1 Hz), 6.54 (3-H, d, J = 2.2 Hz), 7.14 (6-H, d, J = 8.1 Hz), 7.30-7.45 (5xAr-H, m).

2-*t*-Butyldimethylsilyloxyphenylacetates 8 and 9

Methyl 2-benzyloxy-4-methoxyphenylacetate **7** (1.54 g) in Me_2CO (20 ml) was treated with 15% Pd/C (310 mg) and stirred under H_2 for 5 h. After filtering through celite® the Me_2CO was evaporated and the product purified by FCC in benzene-Me_2CO (9:1) to give methyl 2-hydroxy-4-methoxyphenylacetate as a light yellow oil; 877 mg, R_f = 0.42 (TLC/benzene-Me_2CO 9:1), (83%); ^{1}H NMR ($CDCl_3$) δ 3.64 (ArCH_2, s), 3.76 (COOCH_3, s), 3.77 (OCH_3, s), 6.46 (5-H, dd, J = 2.2, 8.0 Hz), 6.51 (3-H, d, J = 2.2 Hz), 7.00 (6-H, d, J = 8.0 Hz), 7.64 (OH, s).

A solution of the 2-hydroxyphenylacetate (6 mmol) in dry DMF (10 ml) was treated with imidazole (15 mmol) and TBDMSCl (9 mmol) and stirred at 25°C for 16 h. Et_2O (50 ml) was added and the mixture was washed with water (50 ml), brine (2x50 ml) and again with water (50 ml), dried (Na_2SO_4), evaporated and separated by PLC.

Methyl 2-*t*-butyldimethylsilyloxy-4-methoxyphenylacetate 8; 1.67 g, (90%); R_f 0.71 (benzene-Me_2CO 9:1) as a colourless oil; ^{1}H NMR ($CDCl_3$) δ 0.26 [Si(CH_3)$_2$,s], 1.01 (Bu^t, s), 3.57 (ArCH_2, s), 3.69 (COOCH_3, s), 3.79 (OCH_3, s), 6.42 (3-H, d, J = 2.2 Hz), 6.50 (5-H, dd, J = 2.2, 8.1 Hz), 7.11 (6-H, d, J = 8.1 Hz).

Methyl 2-*t*-butyldimethylsilyloxyphenylacetate 9; 1.68g, (100%); R_f 0.80 (benzene-Me_2CO 9:1) as a light yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.26 [SiCH_3)$_2$, s], 1.02 (Bu^t, s), 3.64 (ArCH_2, s), 3.69 (COOCH_3, s), 6.83 (3-H, dd, J = 1.1, 7.9 Hz), 6.93 (5-H, ddd, J = 1.1, 7.5, 7.5 Hz), 7.14-7.23 (2xAr-H, m).

2-*O*-Methoxymethylbenzaldehydes 10 and 11.

2-Hydroxybenzaldehyde (8 mmol) was added to a suspension of NaH (9.6 mmol) in dry THF (50 ml) at 0°C. After 5 min chloromethyl methyl ether (8.8 mmol) was added dropwise. The excess NaH was destroyed

with ice, once the starting material was consumed (TLC). The mixture was extracted with EtOAc (3x50 ml) and the combined organic layer was washed with water (2x100 ml), dried (Na_2SO_4), evaporated and separated by FCC.

2-*O*-Methoxymethylbenzaldehyde 10; 1.43 g, (90%); R_f 0.66 (TLC/benzene-Me_2CO 9:1) as a dark orange oil; ^1H NMR ($CDCl_3$) δ 3.55 (OCH_2OCH_3, s), 5.33 (OCH_2OCH_3, s), 7.11 (5-H, ddd, J = 1.0, 7.0, 8.0 Hz), 7.24 (3-H, dd, J = 1.0, 8.5 Hz), 7.56 (4-H, ddd, J = 1.9, 7.0, 8.5 Hz), 7.87 (6-H, dd, J = 1.9, 8.0 Hz), 10.53 (CHO, s).

2-*O*-Methoxymethyl-4-methoxybenzaldehyde 11; 1.77g, (94%); R_f 0.60 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 3.55 (OCH_2OCH_3, s), 3.89 (OCH_3, s), 5.30 (OCH_2OCH_3, s), 6.63 (5-H, dd, J = 2.2, 8.9 Hz), 6.73 (3-H, d, J = 2.2 Hz), 7.84 (6-H, d, J = 8.9 Hz), 10.35 (CHO, s).

Aldol condensation of phenylacetates 8 and 9 with benzaldehydes 10 and 11.

Diisopropylamine (1.1 mmol) in dry Et_2O (1ml) at 0°C was treated with *n*-BuLi (1.1 mmol). The LDA mixture was cooled to -78°C and the propanoates (1 mmol) in Et_2O (1 ml) were added. After stirring for 30 min the aldehydes in Et_2O (1 ml) were added. The mixture was stirred at -78°C for 1 h and then heated to 0°C. After a further 2 h, phosphate buffer (pH 7.0) (30 ml) was added and the mixture was extracted with EtOAc (3x50 ml). The combined EtOAc layer was washed with water (2x100 ml), dried (Na_2SO_4), evaporated and separated by PLC affording the desired aldol products **12-15**.

***Erythro-* and *threo*-methyl 2-(2''-*t*-butyldimethylsilyloxyphenyl)-3-hydroxy-3-(2'-O-methoxymethylphenyl)propanoates (12)** (Table 1, Entry A); 348mg, (78%); de, 28%;

erythro : R_f 0.69 (benzene-Me_2CO 9:1) as a light yellow oil; ^1H NMR ($CDCl_3$), Table 2 .

threo: R_f 0.53 (benzene-Me_2CO 9:1) as yellow needles (m.p. 113°); ^1H NMR ($CDCl_3$),Table 2 ; IR ($CHCl_3$) 2940, 1734(CO), 1494, 1268 cm^{-1}; EI-MS found ($M+H^+$), 447.2201; $C_{24}H_{35}O_6Si$ ($M+H^+$) requires 447.2203.

***Erythro-* and *threo*-methyl 2-(2''-*t*-butyldimethylsilyloxy-4''-methoxyphenyl)-3-hydroxy-3-(2'-O-methoxymethylphenyl)propanoates 13** (Table 1, Entry B); 362mg, (76%); de, 22%;

erythro : R_f 0.42 (benzene-Me_2C 95:5) as a light yellow oil; ^1H NMR ($CDCl_3$), Table 2 ***.threo***: R_f 0.30 (benzene-Me_2CO 95:5) as yellow needles (m.p. 91°); ^1H NMR ($CDCl_3$), Table 2 ; IR ($CHCl_3$) 3008, 1738(CO), 1496, 1270 cm^{-1}; EI-MS found ($M+H^+$), 477.2261; $C_{25}H_{37}O_7Si$ ($M+H^+$) requires 477.2260.

***Erythro-* and *threo*-methyl 2-(2''-*t*-butyldimethylsilyloxyphenyl)-3-hydroxy-3-(2'-O-methoxymethyl-4'-methoxyphenyl)propanoates 14** (Table 1, Entry C); 319mg, (67%); de, 55%;

erythro : R_f 0.63 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 2.

threo: R_f 0.50 (benzene-Me_2CO 9:1) as white needles (m.p. 85°); ^1H NMR ($CDCl_3$, Table 2 ;IR ($CHCl_3$) 2936, 1734(CO), 1494, 1260 cm^{-1}; EI-MS found ($M+H^+$), 477.2258; $C_{25}H_{37}O_7Si$ ($M+H^+$) requires 477.2260.

***Erythro-* and *threo*-methyl 2-(2''-*t*-butyldimethylsilyloxy-4''-methoxyphenyl)-3-hydroxy-3-(2'-*O*-methoxymethyl-4'-methoxyphenyl)propanoates 15** (Table 1, Entry D); 349mg, (69%); de, 32%;

erythro : R_f 0.33 (benzene-Me_2CO 95:5) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table *2* . ***threo***: R_f 0.24 (benzene-Me_2CO 95:5) as yellow needles (m.p. 64°); ^1H NMR ($CDCl_3$) ,Table 2 ; IR ($CHCl_3$) 2940, 1736(CO), 1494, 1265 cm^{-1}; EI-MS found ($M+H^+$), 507.2366; $C_{26}H_{39}O_8Si$ ($M+H^+$) requires 507.2366.

Cleavage of the 2'-MOM derivatives.

The separated *threo*- and *erythro*-3-(2'-*O*-Methoxymethylphenyl)propanoates **12-15** (0.4 mmol) in dry

DCM (5 ml) at -15°C were treated with BnSH (1.6 mmol) followed by $SnCl_4$ (0.6 mmol) under N_2 The reaction was stirred at -15°C for 15 min and then at 5°C for a further 15 min. Water (20ml) was added and the mixture was extracted with EtOAc (3x25 ml). The combined EtOAc layer was washed with water (3x50 ml), dried (Na_2SO_4), evaporated and separated by PLC yielding the 3-benzylsulfanylpropanoates **16-19**. Each time both isomers gave within experimental deviation the same yield.

***Erythro-* and *threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxyphenyl)-3-(2'-hydroxy-phenyl)propanoates 16** (Table 2, Entry A); 195mg, (96%); de, 74%;

erythro: R_f 0.77 (benzene-Me_2CO 9:1) as dark orange oil; ^1H NMR ($CDCl_3$, Table 4.***threo*** : R_f 0.76 (benzene-Me_2CO 9:1) as light yellow plates (m.p. 108°); ^1H NMR ($CDCl_3$, Table 4 ;EI-MS found ($M+H^+$), 509.2183; $C_{29}H_{37}O_4SiS$ ($M+H^+$) requires 509.2182

***Threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxy-4''-methoxyphenyl)-3-(2'-hydroxy-phenyl)propanoates 17** (Table 2, Entry B); 178mg, (83%); de, 100%; R_f 0.23 (benzene) as white needles (m.p. 129°); ^1H NMR ($CDCl_3$) ,Table 4 ; EI-MS found ($M+H^+$), 539,2287; $C_{30}H_{39}O_5SiS$ ($M+H^+$) requires 539.2287.

***Erythro-* and *threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxyphenyl)-3-(2'-hydroxy-4'-methoxyphenyl)propanoates 18** (Table 2, Entry C); 150mg, (70%); de, 54%;

erythro: R_f 0.30 (benzene-Me_2CO 9:1) as a light yellow oil; ^1H NMR ($CDCl_3$) , Table 4 .***threo*** : R_f 0.35 (benzene) as white needles (m.p. 140°); ^1H NMR ($CDCl_3$, Table 4; EI-MS found ($M+H^+$), 539.2288; $C_{30}H_{39}O_5SiS$ ($M+H^+$) requires 539.2287.

***Erythro-* and *threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxy-4''-methoxyphenyl)-3-(2'-hydroxy-4'-methoxyphenyl)propanoates 19** (Table 2, Entry D); 184 mg, (81%); de, 4%;

erythro : R_f 0.27 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$) , Table 4.

threo : R_f 0.25 (benzene) as white needles (m.p. 160°); ^1H NMR ($CDCl_3$) , Table 4; EI-MS found ($M+H^+$), 569.2393; $C_{31}H_{41}O_6SiS$ ($M+H^+$) requires 569.2393.

Reduction of the benzylsulfanylpropanoates 16-19.

Benzylthiopropanoates **16-19** (0.4 mmol) in dry Et_2O (5 ml) at 10°C were treated with an excess of $LiAlH_4$ for 10 min. The $LiAlH_4$ was destroyed by the addition of moist Et_2O (20 ml) followed by *aq*. NH_4Cl (20 ml). The mixture was extracted with EtOAc (3x20 ml) and the combined organic layers washed with saturated $NaHCO_3$ (20 ml) and water (2x20ml), dried (Na_2SO_4), evaporated and separated by PLC.

***Threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxyphenyl)-3-(2'-hydroxy-phenyl)-propan-1-ol 20**; 153mg, (80%); R_f 0.44 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 5; EI-MS found ($M+H^+$), 481.2230; $C_{28}H_{37}O_3SiS$ ($M+H^+$) requires 481.2233.

***Threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxy-4''-methoxyphenyl)-3-(2'-hydroxy-phenyl)propan-1-ol 21**; 198mg, (97%); R_f 0.52 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 5; EI-MS found ($M+H^+$), 511.2338; $C_{29}H_{39}O_4SiS$ ($M+H^+$) requires 511.2338.

***Erythro-* and *threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxyphenyl)-3-(2'-hydroxy-4'-methoxyphenyl)propan-1-ol 22**; 157mg, (77%);

erythro: R_f 0.54 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$), Table 5.

threo: R_f 0.54 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) , Table 5; EI-MS found ($M+H^+$), 511.2336; $C_{29}H_{39}O_4SiS$ ($M+H^+$) requires 511.2338.

***Erythro-* and *threo*-methyl 3-benzylsulfanyl-2-(2''-*t*-butyldimethylsilyloxy-4''-methoxy-phenyl)-3-(2'-hydroxy-4'-methoxyphenyl)propan-1-ol 23**; 168mg, (78%);

erythro: R_f 0.47 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 5.

threo: R_f 0.47 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$, Table 5; EI-MS found ($M+H^+$), 541.2443; $C_{30}H_{41}O_5SiS$ ($M+H^+$) requires 541.2444.

Synthesis of 4-benzylsulfanylisoflavans 24 - 27

Benzylsulfanylpropanols **20-23** (0.2 mmol) in dry THF (2 ml) were treated with a solution of TPP-DEAD complex [TPP (2 mmol) and DEAD (1 mmol) in dry THF 1 ml] at 25°C for 4 h. After evaporation of the THF the mixture was redissolved in DCM and separated by PLC affording isoflavans **24-27**.

***Cis*-4-benzylsulfanyl-2'-*t*-butyldimethylsilyloxyisoflavan 24**; 75 mg, (81%); R_f 0.78 (benzene) as white needles (m.p. 117°); ^1H NMR ($CDCl_3$) ,Table 6; EI-MS found ($M+H^+$), 463.2127; $C_{28}H_{35}O_2SiS$ ($M+H^+$) requires 463.2127.

***Cis*-4-benzylsulfanyl-2'-*t*-butyldimethylsilyloxy-4'-methoxyisoflavan 25**; 91 mg, (93%); R_f 0.79 (benzene) as white needles (m.p. 92°); ^1H NMR ($CDCl_3$) , Table 6; EI-MS found ($M+H^+$), 493.2234; $C_{29}H_{37}O_3SiS$ ($M+H^+$) requires 493.2233.

***Cis*- and *trans*-4-benzylsulfanyl-2'-*t*-butyldimethylsilyloxy-7-methoxyisoflavans 26**; 80mg, (82%);

cis : R_f 0.79 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$), Table 6.

trans : R_f 0.79 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$) , Table 6; EI-MS found ($M+H^+$), 493.2233; $C_{29}H_{37}O_3SiS$ ($M+H^+$) requires 493.2233.

***Cis*- and *trans*-4-benzylsulfanyl-2'-*t*-butyldimethylsilyloxy-4',7-dimethoxyisoflavans 27**; 89mg, (86%);

cis : R_f 0.68 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$), Table 6.

trans : R_f 0.68 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$) , Table 6; EI-MS found ($M+H^+$), 523.2340; $C_{30}H_{39}O_4SiS$ ($M+H^+$) requires 523.2338.

Cleavage of the 2'-TBDMS ethers 24-27.

2'-*t*-Butyldimethylsilyloxyisoflavans **24-27** (0.2 mmol) in dry THF (5 ml) at 25°C were treated with TBAF suspended on silica (0.4 mmol) for 15 min. After the addition of moist THF (5 ml) the solvent was evaporated and the products separated by PLC affording isoflavans **28-31**.

***cis*-4-Benzylsulfanyl-2'-hydroxyisoflavan 28**; 66mg, (96%); R_f 0.35 (benzene) as a light yellow oil; ^1H NMR ($CDCl_3$) , Table 7; EI-MS found ($M+H^+$), 349.1260; $C_{22}H_{21}O_2S$ ($M+H^+$) requires 349.1262.

***cis*-4-Benzylsulfanyl-2'-hydroxy-4'-methoxyisoflavan 29**; 74 mg, (99%); R_f 0.24 (benzene) as a light yellow oil; ^1H NMR ($CDCl_3$) ,Table 7; EI-MS found ($M+H^+$), 379.1368; $C_{23}H_{23}O_3S$ ($M+H^+$) requires 379.1368.

***cis*- and *trans*-4-Benzylsulfanyl-2'-hydroxy-7-methoxyisoflavans 30**; 74 mg, (99%);

cis : R_f 0.41 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 7.

trans : R_f 0.41 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 7; EI-MS found ($M+H^+$), 379.1368; $C_{23}H_{23}O_3S$ ($M+H^+$) requires 379.1368.

***Cis*- and *trans*-4-benzylsulfanyl-2'-hydroxy-4',7-dimethoxyisoflavans 31**; 80 mg, (99%);

cis : R_f 0.55 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) , Table 7.

trans : R_f 0.55 (benzene-Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) ,Table 7; EI-MS found ($M+H^+$),

409.1473; $C_{24}H_{25}O_4S$ ($M+H^+$) requires 409.1474.

Synthesis of pterocarpans 32-35.

Cyclisation with DMTSF:

2-Hydroxyisoflavan **29** (0.1 mmol) was dissolved in dry DCM (2 ml) and treated with DMTSF (0.15 mmol) at -10°C for 1 hour. After the starting material was consumed (TLC) moist DCM (2 ml) was added, the solvent evaporated and the mixture was separated by PLC to yield the desired pterocarpans **32-35**.

(±)-6a,11a-*cis*-9-Methoxypterocarpan 33; 9 mg, (39%); R_f 0.53 (benzene) as white plates (m.p. 112°); ^1H NMR (C_6D_6) δ 3.15 (6a-H, ddd, J = 5.1, 7.1, 11.0 Hz), 3.35 (OCH_3, s), 3.55 (6-H_{ax}, dd, J = 11.0, 11.0 Hz), 4.00 (6-H_{eq}, dd, J = 5.1, 11.0 Hz), 5.30 (11a-H, d, J = 7.1 Hz), 6.51 (8-H, dd, J = 2.1, 8.1 Hz), 6.65 (10-H, d, J = 2.1 Hz), 6.83 (7-H, d, J = 8.1 Hz), 6.95 (2-/3-H, ddd, J = 2.5, 6.0, 7.5 Hz), 7.07-7.15 (2-/3-;4-H, m), 7.60-7.64 (1-H, m); ^{13}C NMR ($CDCl_3$) δ 40.15 (C-6a), 55.92 (OCH$_3$), 66.98 (C-6), 78.89 (C-11a), 97.31, 106.88, 117.85, 119.46, 120.50, 122.12, 125.19, 130.48, 131.47, 155.90, 161.05, 161.56; EI-MS found ($M+H^+$), 255.1021; $C_{16}H_{15}O_3$ ($M+H^+$) requires 255.1021.

Cyclisation with AgOTf :

2'-Hydroxyisoflavans **28**, **30**, **31** (0.1 mmol) were separately dissolved in dry DCM (2 ml) and treated with an excess of AgOTf. When no starting material could be detected on TLC, moist Me_2CO (2 ml) was added, the solvent evaporated and the mixture was separated by PLC.

(±) 6a,11a-*cis*-Pterocarpan 32; temp., 25°C; time, 16 h; 18 mg, (82%); R_f 0.75 (benzene) as white plates (m.p. 102°); ^1H NMR (C_6D_6) δ 3.13 (6a-H, ddd, J = 5.0, 7.1, 11.0 Hz), 3.50 (6-H_{ax}, dd, J = 11.0, 11.0 Hz), 3.96 (6-H_{eq}, ddd, J = 0.8, 5.0, 11.0 Hz), 5.23 (11a-H, d, J = 7.1 Hz), 6.82 (2-/3-H, ddd, J = 1.0, 7.0, 7.0 Hz), 6.90-6.97 (3xAr-H, m), 7.04-7.14 (3xAr-H, m), 7.57-7.62 (1xAr-H, m); ^{13}C NMR ($CDCl_3$) δ 40.74 (C-6a), 66.74 (C-6), 78.01 (C-11a), 110.62, 117.85, 120.40, 121.37, 122.16, 125.15, 127.46, 129.64, 130.48, 131.52, 155.87, 159.68; EI-MS found ($M+H^+$), 225.0918; $C_{15}H_{13}O_2$ ($M+H^+$) requires 225.0916.

(±)-6a,11a-*cis*-3-Methoxypterocarpan 34; temp., 25°C; time, 2 h; 14mg, (57%); R_f 0.65 (benzene) as white needles (m.p. 90°); ^1H NMR (C_6D_6) δ 3.14 (6a-H, ddd, J = 5.0, 7.0, 11.0 Hz), 3.31 (OCH_3, s), 3.58 (6-H_{ax}, dd, J = 11.0, 11.0 Hz), 3.99 (6-H_{eq}, dd, J = 5.0, 11.0 Hz), 5.28 (11a-H, d, J = 7.0 Hz), 6.68-6.72 (2-H; 4-H, m), 6.81-6.87 (8-H, m), 6.92-6.98 (7-H; 10-H, m), 7.05-7.12 (9-H, m), 7.49-7.52 (1-H, m); ^{13}C NMR ($CDCl_3$) δ 40.54 (C-6a), 55.79 (OCH$_3$), 66.76 (C-6), 78.11 (C-11a), 102.03, 109.63, 110.62, 112.66, 121.27, 125.12, 127.54, 129.61, 132.31, 156.99, 159.77, 161.45; EI-MS found ($M+H^+$), 255.1022; $C_{16}H_{15}O_3$ ($M+H^+$) requires 255.1021.

(±)-6a,11a-*cis*-Homopterocarpin 35; temp.,0°C; time, 7 min; 14 mg, (50%); R_f 0.48 (benzene) as white needles (m.p. 125°) (lit.,[35] m.p. 123-125°); ^1H NMR (C_6D_6) δ 3.15 (6a-H, ddd, J = 5.0, 7.0, 10.9 Hz), 3.33, 3.35 (2xOCH_3, 2 x s), 3.63 (6-H_{ax}, dd, J = 10.9, 10.9 Hz), 4.03 (6-H_{eq}, dd, J = 5.0, 10.9 Hz), 5.35 (11a-H, d, J = 7.0 Hz), 6.54 (8-H, dd, J = 2.1, 8.0 Hz), 6.68 (10-H, d, J = 2.1 Hz), 6.71 (4-H, d, J = 2.2 Hz), 6.71 (2-H, dd, J = 2.2, 9.0 Hz), 6.86 (7-H, d, J = 8.0 Hz), 7.52 (1-H, d, J = 9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 39.94 (C-6a), 55.79 (3-OCH$_3$), 55.91 (9-OCH$_3$), 67.00 (C-6), 78.99 (C-11a), 97.30, 102.02, 106.75, 109.58, 112.75, 119.53, 125.15, 132.24, 157.02, 161.12, 161.43, 161.53; EI-MS calcd for $C_{17}H_{17}O_4$ ($M+H^+$) 285.1127; found 285.1127.

ACKNOWLEDGEMENTS

Financial support by the Foundation for Research Development, Pretoria and the 'Sentrale Navorsingsfonds' of the UOFS is acknowledged. We thank Dr J Coetzee for the ^{13}C NMR spectra.

REFERENCES

1. Dewick, P.M. in *The Flavonoids, Advances in Research since* 1986, ed. Harborne, J.B., Chapman & Hall, London, **1994**, pp. 166-178.
2. Mansfield, J.W. in *Phytoalexins,* ed. Bailey, J.A., Mansfield, J.W., Blackie & Son Ltd., Glasgow and London, **1982**, pp. 289-312.
3. Nakagawa, M.; Nakanishi, K. Darko,L.L,; Vick,J.A., *Tetrahedron Lett.*, **1982**, *23*, 3855-3858.
4. Máximo, P.; Lourenço, A. *Phytochemistry*, **1998**, *48*, 359-362.
5. Perrin, D. R. *Tetrahedron Lett.*, **1964**, *1*, 29-35.
6. Ingham, J. L. in *Progress in the Chemistry of Organic Natural Products*, ed. Herz, W., Grisebach, H., Kirby, G. W., Springer-Verlag, New York, **1983**, *43*, pp. 1-266.
7. Ishiguro, M.; Tatsuoka, T.; Nakatsuka, N. *Tetrahedron Lett.*, **1982**, *23*, 3859-3862.
8. Narkhede, D.D.; Iyer, P.R.; Iyer, C.S.R. *Tetrahedron*, **1990**, *46*, 2031-2034.
9 Krishna Prasad, A.V.; Kapil, R.S.; Popli, S.P. *J. Chem. Soc., Perkin Trans I*, **1986**, 1561-1563.
10. Engler, T.A.; Reddy, J.P.; Combrink, K.D.; Vander Velde, D. *J. Org. Chem.*, **1990**, *55*, 1248-1254.
11. Subburaj, K.; Murugesh, M.G.; Trivedi, G.K. *J. Chem. Soc., Perkin Trans I*, **1997**, 1875-1878.
12. Ozaki, Y.; Mochida, K.; Kim, S.-W. *J. Chem. Soc., Chem. Commun.*, **1988**, 374-375.
13. Ozaki, Y.; Mochida, K.; Kim, S.-W. *J. Chem. Soc., Perkin Trans I*, **1989**, 1219-1224.
14. Pinard, E.; Gaudry, M.; Hénot, F.; Thellend, A. *Tetrahedron Lett.*, **1998**, *39*, 2739-2742.
15. Engler, T.A.; Letavic, M.A.; Reddy, J.P. *J. Am. Chem. Soc.*, **1991**, *113*, 5068-5070.
16. Engler, T.A.; Letavic, M.A.; Iyengar, R.; La Tessa, K.O.; Reddy, J.P. *J. Org. Chem.*, **1999**, *64*, 2391-2405.
17. Van Aardt, T.G.; Van Heerden, P.S.; Ferreira, D. *Tetrahedron Lett.*, **1998**, 39, 3881-3884.
18. Auerbach, J.; Weinreb, S.M. *J. Chem. Soc., Chem. Commun.*, **1974**, 298-299.
19. Van Rensburg, H.; Van Heerden, P.S.; Bezuidenhoudt, B.C.B.; Ferreira, D. *J. Chem. Soc., Chem. Commun.*, **1996**, 2747-2748.
20. Greene, T.W. in *Protective Groups in Organic Synthesis*, John Wiley & Sons, New York, **1981**,100-101.
21. M°Killop, A.; Swann, B.P.; Taylor, E.C. *J. Am. Chem. Soc.*, **1973**, *95*, 3340-3343.
22. Paterson, I.; Goodman, J.M. *Tetrahedron Lett.*, **1989**, *30*, 997-1000.
23. Meyers, A.I.; Reider, P.J. *J. Am. Chem. Soc.*, **1979**, *101*, 2501-2502.
24. Pirrung, M.C.; Heathcock, C.H. *J.Org. Chem.*, **1980**, *45*, 1727-1728.
25. Heathcock, C.H.; Buse, C.T.; Kleschick, W.A.; Pirrung, M.C.; Sohn, J.E.; Lampe, J. *J. Org. Chem.*, **1980**, *45*, 1066-1081.
26. Mitsunobu. O. *Synthesis*, **1981**, 1-28.
27. Clark, J.H. *J. Chem. Soc., Chem. Commun.*, **1978**, 789-791.
28. Trost, B.M.; Murayama, E. *J. Am. Chem. Soc.*, **1981**, *103*, 6529-6530.
29. Trost, B.M.; Sato, T. *J. Am. Chem. Soc.*, **1985**, *107*, 719-721.
30. Williams, R.M.; Armstrong, R.W.; Dung, J-S. *J. Am. Chem. Soc.*, **1984**, *106*, 5748-5750.
31. Roush, W.R. *J. Org. Chem.*, **1991**, *56*, 4151-4157.
32. Evans, D.A.; Nelson, J.V.; Vogel, E.; Taber, T.R. *J. Am. Chem. Soc.*, **1981**, *103*, 3099-3111.
33. Stiles, M.; Winkler, R.R.; Chang, Y-L.; Traynor, L. *J. Am. Chem. Soc.*, **1964**, *86*, 3337-3342.
34. Tobiason,F.L.; Hemingway, R.W. *Tetrahedron Lett.*, 1994, *35*, 2137.
35. Suginome, H.; Iwadare, T. *Experientia*, **1962**, *18*, 163-164.