*Tetrahedron Asymmetry* Vol 2, No 2, pp 109-110, 1991
Printed in Great Britain

0957-4166/91 $3 00+00
Pergamon Press plc

# ASYMMETRIC 1,4-ADDITIONS TO γ-MENTHYLOXYBUTENOLIDES. (part II)[1]
# ENANTIOSELECTIVE SYNTHESIS OF LIGNAN TYPE COMPOUNDS.

J F G A Jansen, C Jansen and B L Feringa*
Department of Organic Chemistry, University of Groningen,
Nijenborgh 16, 9747 AG, Groningen, The Netherlands

(*Received* 7 *January* 1991)

**Abstract:** Addition of dithianes, derived from alkyl- and aryl-aldehydes, to (5R)-menthyloxy-2[5H]-furanone followed by quenching with substituted benzylhalides or a benzaldehyde gives enantiomerically pure lignan type compounds in good yields

Currently an increasing activity in the stereocontrolled synthesis of lignans is observed[2] due to the interesting biological activity[3] that is associated with many members of this class of compounds Chiral butenolides can serve as excellent starting materials for these syntheses as they have served in the preparation of many chiral building blocks with arrays of methyl- and hydroxy-substituents at vicinal or remote stereogenic centers[4] In particular tandem conjugate additions-alkylations to non-chiral and chiral butenolides have been reported to provide usefull routes to several lignans[5] We have extensively explored menthyloxyfuranone 1 as a chiral synthon due to the excellent stereocontrol exerted by the γ-menthyloxy substituent, the easy way of preparation and the use of cheap d- or l- menthol as chiral auxiliary[6] A very recent report of Pelter, Ward and coworkers[7] on the asymmetric synthesis of a dibenzylbutyrolactone lignan precursor prompts us to report our results in the formation of lignan type compounds

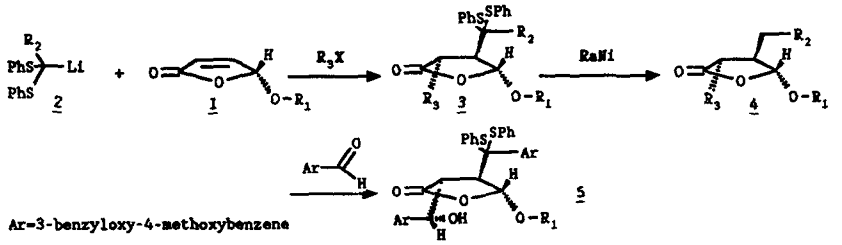

Table products and yields of 1,4-addition/alkylation and desulphurisation

| entry | $R_1$ | $R_2$ | $R_3$ | yield of 4 (%) |
|---|---|---|---|---|
| a | $CH_3$ | $CH_3$ | $PhCH_2$ | 65 |
| b | $CH_3$ | $(CH_3O)_2C_6H_3$ | $PhCH_2$ | 76 |
| c | $CH_3$ | $(CH_3O)_2C_6H_3$ | $(CH_3O)_2C_6H_3CH_2$ | 85 |
| d | Menth | $CH_3$ | H | 71 |
| e | Menth | $CH_3$ | $CH_3$ | 72 |
| f | Menth | Ph | H | 71 |
| g | Menth | Ph | $CH_3$ | 69 |
| h | Menth | $(CH_3O)_2C_6H_3$ | $(CH_3O)_2C_6H_3CH_2$ | 81 |

The addition of the dithianes 2, prepared from several alkyl and aryl aldehydes, to enantiomerically pure butenolide 1 proceeds smoothly if the dithiane is a bis(phenylthio)acetal[8] (entry 4,6, enolate quenched with NH$_4$Cl aq ) and is a poor reaction if the dithiane is a 1,3-dithiane[9] (scheme) Quenching of the resulting lactone enolate anion with a benzylbromide (entry 1-3,8) or methyliodide (entry 5,7) resulted in single diastereoisomers, (NMR,TLC) with the all trans geometry at the lactone ring[10] The trans sterochemical assignment is based on $^1$H-NMR and by analogy with previous results[1,6], for example $J_{H3\,H4}$ = 3 3Hz and $J_{H4\,H5}$ = < 0 2Hz in compound 3e support the C3-C4 and C4-C5 trans configurations Desulphurisation with Raney-Nickel is a nearly quantitative process wich results in the dibenzylsubstituted butyrolactones in enantiomerically pure form in 60-81% yield Similar addition of the lithio derivative of 3-benzyloxy-4-methoxybenzaldehyde bis(phenylthio)acetal to 1 followed by quenching with 3-benzyloxy-4-methoxybenzaldehyde provides 5 as a single diastereoisomer in 50% yield The configuration at the exocyclic stereogenic center as depicted (scheme) was assigned on the basis of extensive COSY and NOESY experiments

In conclusion we describe a short and efficient asymmetric synthesis of chiral lignan type compounds Application of this strategy in the synthesis of Pinoresinol and related lignans is currently under investigation.

Acknowledgement

The investigations were supported by the Netherlands Foundation for Chemical Reseach (SON) with financial aid from the Netherlands Organisation for Scientific Research (NWO)

## References and notes

1 For part I see J F G A Jansen, B L Feringa, Tetrahedron Lett 30, 5481 (1989)

2. R S Ward, Chem Soc. Rev 11, 75 (1982)

3. W D MacRea, G H N Towers, Phytochemistry 23, 1207 (1984)

4 a) J W Scott in "Asymmetric Synthesis", J D Morrison, J W Scott eds, Academic Press, Orlando, vol 4, ch 1, 1984 b) S Kano, S Shibuija, T Ebata, Heterocycles 14, 661 (1980) c) S Takano, J Kudo, M Takahashi, K. Ogasawara, Tetrahedron Lett 27, 2405 (1986) d) S Hanessian, S P Sahoo, M Botta, Tetrahedron Lett 28, 1143, 1147 (1987)

5. For examples, see a) N Rehnberg, G Magnussen, J Org Chem 55, 4340 (1990) b)K. Tomioka, T Ishiguro, Y Itaka, K Koga, Tetrahedron 40, 1303 (1984) c) A Pelter, P Satyanarayana, R S Ward, Tetrahedron Lett 22, 1549 (1981) d) R E Damon R H Schlessinger, J F Bloumt, J Org Chem 41, 3773 (1976)

6 a) B de Lange, B L Feringa, Tetrahedron Lett 29, 1303 (1988) b) B L Feringa, J C de Jong, J Org Chem 53, 1125 (1988) c) B L Feringa, B de Lange, J C de Jong, J Org. Chem. 54, 2471 (1989) d) J F G.A Jansen, B L Feringa, Tetrahedron Asym 1, 719 (1990) e) J C de Jong, J F G A Jansen, B L Feringa, Tetrahedron Lett 31, 3047 (1990)

7 A Pelter, R S Ward, D M Jones P Maddocks, Tetrahedron Asym 1, 857 (1990)

8 Prepared according to B S Ong, Tetrahedron Lett 21, 4225 (1980)

9 Only the aryl-1,3-dithianes add however in a low yield (30%) A succesful addition of the dithianes to $\alpha,\beta$-unsaturated nitriles is known See F Z Basha, J F DeBernadis, S Spanton, J Org. Chem 50, 4160 (1985) For a review on 1,3-dithianes, see D Seebach, Synthesis 1969, 17

10 Based on the coupling constants in the 300 MHz $^1$H-NMR spectra, all compounds showed spectral and analytical data in accordance with the proposed structures