

University of Groningen

Asymmetric 1,4-Additions to γ -Menthylxybutenolides. (part II) Enantioselective Synthesis of Lignan Type Compounds.

Jansen, J.F.G.A.; Jansen, C.; Feringa, B.L.

Published in:
Tetrahedron%3A Asymmetry

DOI:
[10.1016/S0957-4166\(00\)80529-7](https://doi.org/10.1016/S0957-4166(00)80529-7)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1991

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Jansen, J. F. G. A., Jansen, C., & Feringa, B. L. (1991). Asymmetric 1,4-Additions to γ -Menthylxybutenolides. (part II) Enantioselective Synthesis of Lignan Type Compounds. *Tetrahedron%3A Asymmetry*, 2(2). DOI: 10.1016/S0957-4166(00)80529-7

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

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 observed² due to the interesting biological activity³ 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 centers⁴. In particular tandem conjugate additions-alkylations to non-chiral and chiral butenolides have been reported to provide usefull routes to several lignans⁵. 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 auxiliary⁶. A very recent report of Pelter, Ward and coworkers⁷ on the asymmetric synthesis of a dibenzylbutyrolactone lignan precursor prompts us to report our results in the formation of lignan type compounds.

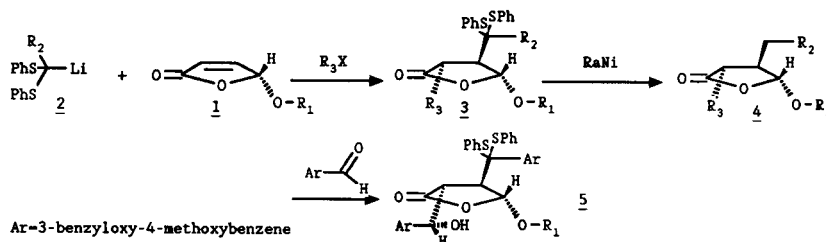


Table: products and yields of 1,4-addition/alkylation and desulphurisation

entry	R ₁	R ₂	R ₃	yield of 4 (%)
a	CH ₃	CH ₃	PhCH ₂	65
b	CH ₃	(CH ₃ O) ₂ C ₆ H ₃	PhCH ₂	76
c	CH ₃	(CH ₃ O) ₂ C ₆ H ₃	(CH ₃ O) ₂ C ₆ H ₃ CH 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 ₃ O) ₂ C ₆ H ₃	(CH ₃ O) ₂ C ₆ H ₃ CH 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)acetal⁸ (entry 4,6; enolate quenched with NH₄Cl aq.) and is a poor reaction if the dithiane is a 1,3-dithiane⁹ (scheme). Quenching of the resulting lactone enolate anion with a benzylbromide (entry 1-3,8) or methyl iodide (entry 5,7) resulted in single diastereoisomers, (NMR,TLC) with the all trans geometry at the lactone ring¹⁰. The trans stereochemical assignment is based on ¹H-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 which 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 Research (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 successful addition of the dithianes to α,β -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 ¹H-NMR spectra; all compounds showed spectral and analytical data in accordance with the proposed structures.