

University of Groningen

ENANTIOSELECTIVE SYNTHESIS OF FURYLALCOHOLS BY CATALYTIC ASYMMETRIC ADDITION OF DIETHYLZINC TO FURANALDEHYDES

VANOEVEREN, A; MENGE, W; FERINGA, BL; Oeveren, Arjan van

Published in:
Tetrahedron Letters

DOI:
[10.1016/S0040-4039\(01\)93913-9](https://doi.org/10.1016/S0040-4039(01)93913-9)

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:
1989

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

Citation for published version (APA):

VANOEVEREN, A., MENGE, W., FERINGA, BL., & Oeveren, A. V. (1989). ENANTIOSELECTIVE SYNTHESIS OF FURYLALCOHOLS BY CATALYTIC ASYMMETRIC ADDITION OF DIETHYLZINC TO FURANALDEHYDES. *Tetrahedron Letters*, 30(46), 6427-6430. [https://doi.org/10.1016/S0040-4039\(01\)93913-9](https://doi.org/10.1016/S0040-4039(01)93913-9)

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.

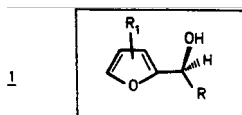
Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

**ENANTIOSELECTIVE SYNTHESIS OF FURYLALCOHOLS BY CATALYTIC
ASYMMETRIC ADDITION OF DIETHYLZINC TO FURANALDEHYDES**

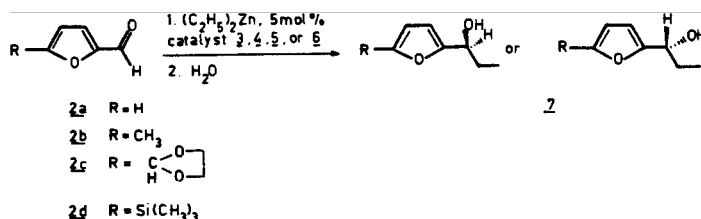
Arjan van Oeveren, Wiro Menge and Ben L. Feringa*
Department of Organic Chemistry, University of Groningen,
Nijenborgh 16, 9747 AG Groningen, The Netherlands

Abstract. Optically active 2-furylcarbinols with up to 97% enantiomeric excess were prepared by highly π -face selective addition of diethylzinc to furan aldehydes catalyzed by aminoalcohol ligands 3 to 6.

Substituted furans have gained importance as versatile multifunctional building blocks in synthesis.¹ For example strategies based on photochemically mediated [2+2] cycloadditions to furans,² and conversions of furans to cyclopentenones³ and chiral butenolides⁴ have been developed. Further application in the synthesis of natural products would be considerably stimulated if homochiral 2-furylcarbinols 1 were readily accessible.

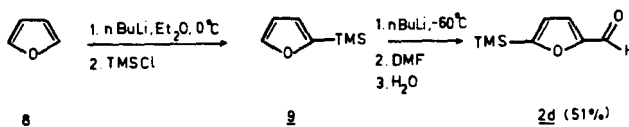


Recently methodology for the preparation of optically active 2-furylcarbinols by kinetic resolution using the Sharpless epoxidation procedure was described.⁵ Herein we describe a catalytic asymmetric synthesis of 5-substituted-2-furylcarbinols 7 by the chiral ligand induced addition of diethylzinc to 5-substituted-2-furan aldehydes 2 (eq. 1).



Following Oguni's report on the enantioselective addition of diethylzinc to benzaldehyde catalyzed by chiral 2-amino-1-alcohols much progress has been made in the asymmetric addition of alkyl- and vinyl groups to aryl- and α, β -unsaturated aldehydes using this procedure.⁷⁻¹¹ In order to find a practical synthetic route to optically active furylcarbinols of high optical purity (e.e. > 90%) we examined furanaldehydes 2a-2d and chiral catalysts 3-

6.^{12,13} 5-Trimethylsilyl-2-furaldehyde (**2d**)^{14,15} was prepared in a new one pot procedure via sequential lithiation of furan (eq. 2).



The catalysts (S)-(+)-diphenyl-(1-methylpyrrolidin-2-yl) methanol (DPMPM) **4**⁸ and N,N-dibutylaminonorephedrine (DBNE) **6**¹⁰ were prepared following literature procedures. (-)-3-Exo dimethylaminoisoborneol (DAIB) **5**⁹ was synthesized from (+)-camphor following a slightly modified procedure as reported⁹ using KOTBu as a base in the first step and MeI as the methylating agent in the final step. When 2-furaldehyde (**2a**) was treated with diethylzinc at +4°C for 16 h using quinine **3** (5 mol %) as a catalyst (R)-2-furyl-1-propanol (**7a**) was obtained in 83% isolated yield and 60% enantiomeric excess (e.e.) after distillation.

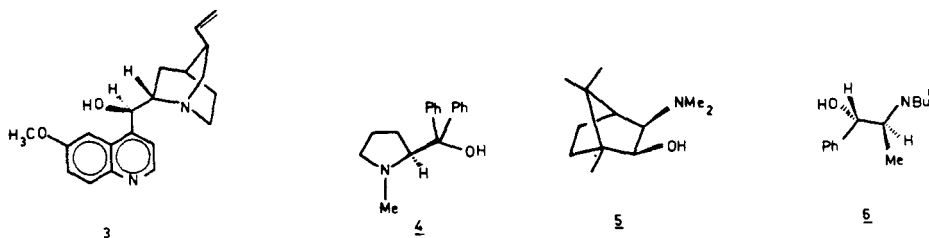


Table Catalytic asymmetric synthesis of furylcarbinols **7a-7d** and **7e**.

Entry	Aldehyde (R ¹)	Solvent ¹	Catalyst	Product	Yield ² (%)	[α] _D ^{22, 578} (c, CHCl ₃) (%)	o.p. ³ (%)	e.e. ³ (%)
1	2a	H	3	7a	83	+11.6 (1.00)	60	57 ⁴
2	2a	H	4	7a	81	-16.5 (0.98)	85	
3	2a	H	5	7a	68	-12.6 (1.02)	65	
4	2a	H	6	7a	82	-17.9 (1.75)	92	
5	2b	CH ₃	3	7b	85	+ 7.5 (1.72)	62.5	62.5
6	2b	CH ₃	5	7b	90.5	-11.6 (0.99)	97	
7	2b	CH ₃	6	7b	88	-10.9 (1.17)	91	91.1 (89) ⁴
8	2c	CHOCH ₂ CH ₂ O	3	7c	96	+ 5.2 (1.07)	51	51
9	2c	CHOCH ₂ CH ₂ O	4	7c	77	- 7.3 (1.07)	72	
10	2c	CHOCH ₂ CH ₂ O	5	7c	56	- 4.7 (1.12)	46	
11	2c	CHOCH ₂ CH ₂ O	6	7c	- ⁵	-		
12	2d	Si (CH ₃) ₃	3	7d	78	+ 5.1 (1.00)	51	51
13	2d	Si (CH ₃) ₃	4	7d	84	- 9.4 (1.04)	94	
14	2d	Si (CH ₃) ₃	5	7d	78	- 9.0 (1.00)	90	89 ³
15	2d	Si (CH ₃) ₃	6	7d	82	- 8.5 (1.00)	85	85
16	2c ⁵		3	7e (R ₁ =CHO)	93	+18.7 (1.03)	51	
17	2c ⁵		6	7e (R ₁ =CHO)	92	-29.9 (0.98)	83	83

1) T = toluene; H = n-hexane; 2) isolated yields of pure furylalcohols after distillation; 3) o.p. = optical purity; e.e. = enantiomeric excess; e.e. based on ¹H MMR via complexation with quinine.¹⁷ 4) e.e. based on ¹⁹F NMR of the (-)-MTPA esters.¹⁶ 5) the dioxolane **7c** was directly converted into **7e** (see text).

A Re-face selective addition takes place and the enantio- and Re-face-selectivities are in accordance with the result of the addition of Et_2Zn to benzaldehyde using quinine.¹¹ Employing **6** as a catalyst the optical yield can be raised to 92% while Si-face addition leads now to (S)-**7a** (table, entry 4).

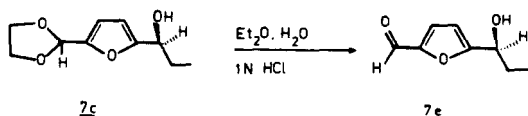
The e.e. of **7a** ($[\alpha]_{578}^{22} -17.9^\circ$ (c 1.75, CHCl_3)) was determined by ^{19}F NMR of the corresponding (-)- α -methoxy- α -(trifluoromethyl)phenylacetic (MTPA) ester¹⁶ and independently by ^1H NMR using complexation with quinine.¹⁷ The use of quinine as a chiral solvating agent in CDCl_3 proved to be an operationally extremely simple way of e.e. determination of furfuralcohols with base line separations in various cases.

Using the same four catalysts **3** - **6** the addition of Et_2Zn was also carried out with substrates **2b** - **2d**. The results are given in the table. It has to be noted that the reaction conditions where identical using the same catalyst for the different furanaldehydes **2a** - **2d**.

It is interesting to see that the substituent in position 5 at the furan ring has little influence on the catalytic asymmetric addition; for the quinine catalyzed reaction e.e.'s of 51-62% are observed (entries 1, 5, 8, 12). When furan aldehydes are used as substrates for the diethylzinc addition additional coordination via the furan oxygen can be envisaged which could influence the stereochemical bias of this reaction.

Comparable enantioselectivities for benzaldehydes^{7,11} and furanaldehyde however indicate that such an effect, if it exists, has only a minor stereochemical consequence. The results with different catalysts show that high e.e.'s (92-97%) are reached by the proper combination of aminoalcohol and furan aldehyde.

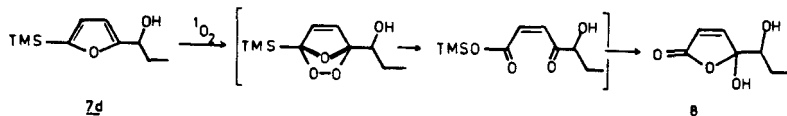
The deprotection of the aldehyde functionality in furylcarbinol **7c** is readily accomplished in situ (eq. 3).



The addition of Et_2Zn to **2c** using catalyst **6** followed by a washing procedure of the ethereal solution of **7c** using aqueous 1N HCl provided **7e** in 92% yield (e.e. = 83%, entry 17). Optically active furanaldehyde **7e** is an interesting starting material for various homochiral furans.

The access to furylalcohols with synthetically useful e.e.'s which contain a 5-trimethylsilyl-substituent allow for an attractive route to chiral butenolides via oxidative methods.

Thus singlet oxygen photooxidation of **7d** resulted in a fast and quantitative addition leading to butenolide **8**.



The initial $^1\text{O}_2$ addition to **7d** is presumably followed by a silatropic shift and cyclization to **8** in accordance with reported experiments with silylfurans.¹⁸ Further studies along these lines are in progress.

References

1. Barton and Ollis: "Comprehensive Organic Chemistry", Vol. 4, Sammes, P.G. (ed.), Pergamon Press, Oxford, 1979, Chap. 18.4; Dean, F.M., Adv. Heterocycl. Chem. 1982, 30, 167; 31, 238; Tanis, S.P.; Herrinton, P.M., J. Org. Chem. 1985, 50, 3988.
2. Schreiber, S.L., Science, 1985, 227, 859.
3. D'Ascoli, R.; D'Auria, M.; Iavarone, C.; Piancatelli, G.; Scettri, A., J. Org. Chem. 1980, 45, 4502; Elliott, J.D.; Hetmanski, M.; Stoodley, R.J.; Palfreyman, M.N., J. Chem. Soc., Perkin I, 1981, 1782.
4. Feringa, B.L.; de Jong, J.C., J. Org. Chem. 1988, 53, 1125; Feringa, B.L.; de Lange, B.; de Jong, J.C., J. Org. Chem. 1989, 54, 2471; de Lange, B.; Feringa, B.L., Tetrahedron Lett. 1988, 29, 5317.
5. Kametani, T.; Tsubuki, M.; Tatsuzaki, Y.; Honda, T., Heterocycles, 1988, 27, 2107; Kobayashi, Y.; Kusakabe, M.; Kitano, Y.; Sato, F., J. Org. Chem. 1988, 53, 1586; Kusakabe, M.; Kitano, Y.; Kobayashi, Y.; Sato, F., J. Org. Chem. 1989, 54, 2085.
6. Oguni, N.; Omi, T., Tetrahedron Lett. 1984, 25, 2823.
7. Itsuno, S.; Fréchet, J.M.J., J. Org. Chem. 1987, 52, 4140; Corey, E.J.; Hannon, F.J., Tetrahedron Lett. 1987, 28, 5233; Corey, E.J.; Hannon, F.J., *ibid.*, 1987, 28, 5237; Oppolzer, W.; Radinov, R.N., Tetrahedron Lett. 1988, 29, 5645; and refs. 8-11.
8. Soai, K.; Ookawa, A.; Kaba, T.; Ogawa, K., J. Am. Chem. Soc. 1987, 109, 7111.
9. Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R., J. Am. Chem. Soc. 1986, 108, 6071.
10. Soai, K.; Yokoyama, S.; Ebihara, K.; Hayasaka, T., J. Chem. Soc., Chem. Commun. 1987, 1690; Soai, K.; Yokoyama, S.; Hayasaka, T.; Ebihara, K., J. Org. Chem. 1988, 53, 4148.
11. Smaardijk, A.A.; Wynberg, H., J. Org. Chem. 1987, 52, 135.
12. 2-(5-Formyl-2-furanyl)-1,3-dioxolane (2c) was prepared from 2-furaldehyde in 40% overall yield following the reported procedure.¹⁴
13. Feringa, B.L.; Hulst, R.; Rikers, R.; Brandsma, L., Synthesis, 1988, 316.
14. All new products were fully characterized by IR, ¹H-NMR, ¹³C-NMR and HRMS; yields given are of isolated pure material.
15. For related lithiations, see: Kuwajima, I.; Urabe, H., Tetrahedron Lett. 1981, 22, 5191; Carpenter, A.J.; Chadwick, D.J., Tetrahedron, 1985, 41, 3803.
16. Dale, J.A.; Dull, D.L.; Mosher, H.S., J. Org. Chem. 1969, 34, 2543.
17. Rosini, C.; Uccello-Baretta, G.; Pini, D.; Abete, C.; Salvadori, P., J. Org. Chem. 1988, 53, 4579.
18. Feringa, B.L., Recl. Trav. Chim. Pays-Bas 1987, 106, 469 and references cited.

(Received in UK 7 September 1989)