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A Novel Imidazolidin-2-one Auxiliary for a Highly Stereoselective Aldol Route to β-Hydroxyesters.

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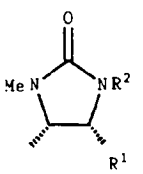
Abstract: Enantiomerically pure *syn*-aldols are obtained from the boron enolate of (4R,5S)-1,5-dimethyl-4-cyclohexyl-3- propanoyl imidazolidin-2-one. Cleavage of the auxiliary affords the homochiral title esters in good yield.

Efficient asymmetric aldol methodology continues to be the subject of much literature.[1] We have recently reported the synthesis of highly crystalline, enantiomerically pure aldols by the utilisation of the (-)-ephedrine-derived N-acylimidazolidin-2-one **(3)**.[2] However, whilst this auxiliary showed excellent selectivity (d.e. ≥ 96% crude; > 99% after recryst.) with aromatic aldehydes, the results with the aliphatic counterparts were disappointing (eg: CH_3CHO d.e. 10%; ^iPrCHO d.e.60%; $cyclo C_6H_{11}CHO$ d.e. 70%).

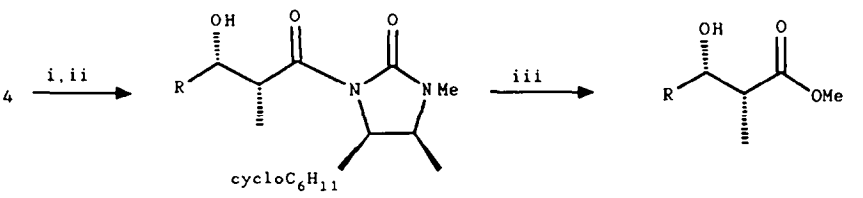


(4R,5S)

1. R^1 = Ph; R^2 = H
2. R^1 = $cyclo C_6H_{11}$; R^2 = H
3. R^1 = Ph; R^2 = $CO.CH_2CH_3$
4. R^1 = $cyclo C_6H_{11}$; R^2 = $CO.CH_2CH_3$

We report here that the solution to this problem lies in simple hydrogenation[3] of the auxiliary **(1)**[4] to its cyclohexyl derivative **(2)** (M.p. 162°C; $[\alpha]_D^{26}$ -1 , c = 0.6, $CHCl_3$).[5] Subsequent N-acylation afforded **(4)** (M.p. 99-100°C; $[\alpha]_D^{26}$ -14.2 , c = 0.16, $CHCl_3$),[5] use of which in appropriate boron-mediated aldol methodology[6] has allowed the highly selective preparation of the homochiral *syn*-esters **(6)** after removal and recovery of the auxiliary[6] **(Scheme)**. In addition, check reactions revealed no loss of selectivity in the case of the aromatic aldehyde substrates. A representative selection of results is shown in **Table.**[7]

SCHEME



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Reagents:

i. Bu_2BOTf, Et_3N, -10°C, CH_2Cl_2

ii. RCHO, -78°C

iii. NaOMe, MeOH, 0°C

	R
a	Me
b	iPr
c	$cycloC_6H_{11}$
d	Ph

Table. Details of aldol products and derived esters.

Aldol product (isol %)	Ratio of major:others[8]	Ester (isol %)	$[\alpha]_D^{25}$ (conc.; solvent)
5a (80)	96:4	6a (70)	-13.4 (0.51; CH_3OH) lit.[9] -13.5 (0.87; CH_3OH)
5b (82)	>99:1	6b (68)	+7.6 (1.21; $CHCl_3$) lit.[10] +7.7 (5.4; $CHCl_3$)
5c (92)	>99:1	6c (78)	-6.17 (1.1; CH_2Cl_2)
5d (75)	98:2	6d (80)	+23.2 (1.5; $CHCl_3$) lit.[9] +23.2 (3.2; $CHCl_3$)

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References and Notes:

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2. Drewes, S.E.; Malissar, D.G.S.; Roos, G.H.P. *Chem. Ber.*, **1991**, in print.
3. Via an adaptation of the method of Blum, J.; Amer, I.; Zoran, A.; Sasson, Y. *Tetrahedron Lett.* **1983**, *24*, 4139-4142 where the reaction is conducted at 5 atmos. H_2 pressure.
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5. Drewes, S.E.; Malissar, D.G.S.; Roos, G.H.P. **1991**, Provisional patent, RSA 91/5087.
6. Representative experimental detail is analogous to that described in ref.2.
7. All new compounds were satisfactorily characterised (C,H,N; ^1H and ^{13}C NMR).
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