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A Novel DMAP-Promoted Oxazolidinethione Deacylation. Application for the Direct Conversion of the Initial Chiral Thioimide Aldols to Various Ester Protecting Groups.

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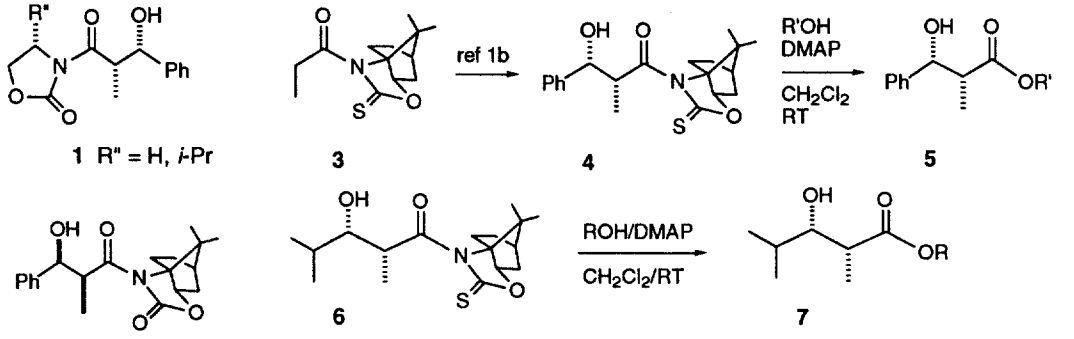
Abstract: DMAP (4-(dimethylamino)pyridine) promoted nucleophilic cleavage of the initial chiral thioimide aldols can be directed to form various ester protecting groups without causing racemization of the newly created stereocenters.

Keywords: Aldols; Asymmetric induction; Catalysts; Enolates

Chiral oxazolidinone[1a] and oxazolidinethione[1b,c] heterocycles have proven to be versatile auxiliaries for the construction of enantiopure aldols. Traditionally, basic reagents (KOH/MeOH,[1a] K_2CO_3/MeOH[1c]) mediated nucleophilic cleavage of imides have been the conditions of choice for removing the chiral auxiliary from substances. However, progress in nucleophilic catalyst promoted nucleophilic cleavage of chiral imide aldols with oxygen nucleophiles like H_2O, ROH, and phenol remains far less developed. In conjunction with a recent study of the asymmetric aldol reactions of camphor-based chiral thioimide enolates,[1b] we wish to report DMAP promoted nucleophilic cleavage of chiral thioimide aldol adducts can be directed to form either chiral acid or various chiral ester protecting groups without causing racemization of the newly created stereocenters.

Initial work centered on the methanolysis (MeOH) and hydrolysis (H_2O) of the imide aldols **1**[1a] and **2**[1b] (Scheme 1). Due to the well-documented excellent shelf lives of *N*-acyloxazolidinones,[2] we were not surprised to discover that DMAP did not effect oxazolidinone auxiliary removal from carboximides **1** and **2**.

Scheme 1



a) R = Me (87%); b) R = H (83%); c) R = CH_2=$CHCH_2$ (93%); d) R = $PhCH_2$ (88%); e) R = Ph (89%); f) R = $BrCH_2CH_2$ (92%); g) R = $Me_3SiCH_2CH_2$ (90%)

Believing a more polarizable heterocycle might facilitate nucleophilic attack, we turned to carboxthioimide derived aldol adducts. To estabilish the feasibility of DMAP as nucleophilic catalyst to effect oxazolidinethione

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"deacylation", we explored the transesterifiaction and hydrolysis of the aldols **4** and **6** derived from *N*-propionyloxazolidinethione **3** (cf. Scheme 1). Treatment of **4** with 1.5 equiv of MeOH and 20 mol % DMAP in CH_2Cl_2 at ambient temperature produced the methyl ester in 90% yield (Table, entry 1). The NMR spectrum of the crude product showed it to be a single compound, free of the diastereomer at C-2. Similarly, DMAP-promoted hydrolysis of **4** afforded the acid. The utility of allyl and benzyl esters as useful carboxy-protecting groups led to our examination of allyl and benzyl alcohols, which participated equally well, giving the corresponding esters in excellent yield (entries 3,4). Switching the nucleophile from alcohol to phenol had little effect. The same conditions effected transesterification of **4** to give phenyl ester in 95% yield. The broad scope of the reaction is illustrated by the tolerance of β-substituents on ethanol. Thus a labile alcohol, 2-bromoethanol, also proved to be a satisfactory nucleophile under our standard conditions in the presence of the DMAP catalyst (entry 6). 2-(Trimethylsilyl)ethanol gave similar result albeit in somewhat slower reaction.

Table. DMAP Promoted Transesterification of Thioimide Aldol Adduct **4**.

entry	nucleophile	DMAP [equiv]	t (h)	yield[a] (%)	$[\alpha]_D^{25}$ (c , CH_2Cl_2)	adduct
1	MeOH	0.2	20	90	+23.1 (1.4)[b]	**5a**
2	H_2O	1.0	18	88	+13.7 (1.1)	**5b**
3	CH_2=$CHCH_2OH$	0.2	20	93	+14.8 (0.8)	**5c**
4	$PhCH_2OH$	0.2	24	96	+6.5 (1.0)	**5d**
5	PhOH	0.2	24	91	-20.4 (1.2)	**5e**
6	$BrCH_2CH_2OH$	0.2	20	94	+7.4 (1.5)	**5f**
7	$Me_3SiCH_2CH_2OH$	0.2	36	92	+5.3 (1.0)	**5g**

[a] Isolated yield. [b] Literature rotation: $[\alpha]_D^{25}$ +23.5° (c 3.2, $CHCl_3$)[3]; $[\alpha]_D^{25}$ +23.2° (c 3.2, $CHCl_3$)[1a].

Using the above standard conditions, the transesterification of hindered aldol **6** was also easily effected with no detectable levels of epimerization.[4] Thus the DMAP promoted methanolysis of **6** afforded methyl ester **7a**, $[\alpha]^{25}_D$ -7.8° (c 1.1, CH_2Cl_2); [lit.[1a] $[\alpha]^{25}_D$ -7.9° (c 5.7, $CHCl_3$)], in 87% yield (Scheme 1).

The remarkable facility of this DMAP-promoted oxazolidinethione "deacylation" opens the question of the importance of the nature of chiral heterocycles on further useful transformations of the initial chiral adducs.

References and Notes

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4. New compounds have been characterized spectroscopically. *Selected data* for **5g**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.32 (m, 5 H, C_6H_5), 5.06 (d, J = 3.6 Hz, 1 H, $CHOH$), 4.14 (m, 2 H, OCH_2CH_2), 3.07 (bs, 1 H, OH), 2.72 (dq, J = 7.2, 3.6 Hz, 1 H, $CHCHCH_3$), 1.10 (d, J = 7.2 Hz, 3 H, $CHCH_3$), 0.92 (m, 2 H, $CH_2CH_2Si(CH_3)_3$), 0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 141.3, 128.1, 127.3, 125.9, 73.6, 63.1, 46.5, 17.4, 10.8, -1.4