Regioselective Aldol Condensations of Boron and Tin Furanolates with Aldehydes: an Improved Synthesis of 2-(1′-Hydroxyalkyl)butenolides

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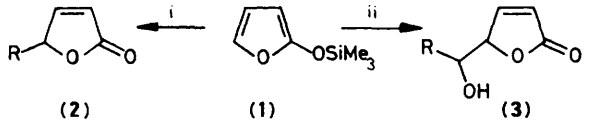
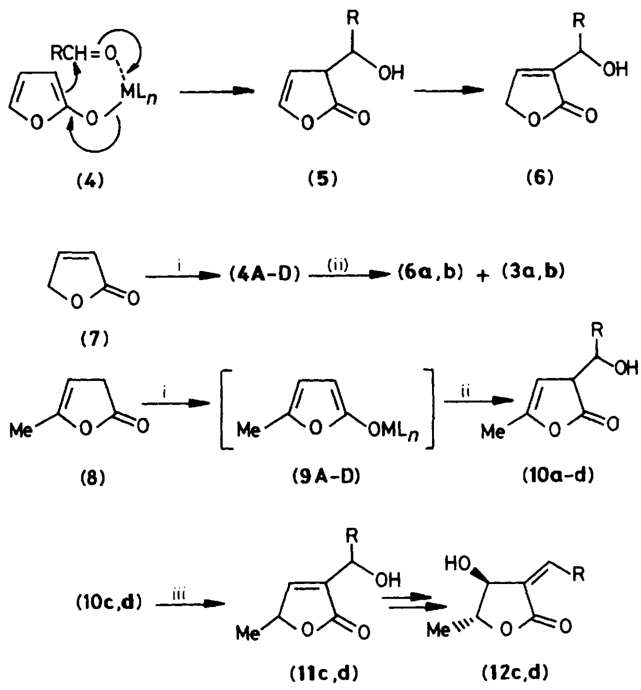
Boron and tin(II) 2-furanolates generated *in situ* from 2-(5*H*)-furanone and α-angelica lactone undergo regioselective aldolization with aldehydes to furnish the corresponding 2-(1′-hydroxyalkyl)butenolides in good yields; a new formal synthesis of (±)-litsenolide C1 and (±)-dihydromahubanolide is described.

We have recently shown that 2-trimethylsiloxyfuran (**1**) is a powerful reagent for the quick assembly of butenolides.[1,2] Under the appropriate conditions, (**1**) demonstrates the particularity of undergoing alkylation and aldolization exclusively at the C(5) position to give (**2**) and (**3**) respectively (Scheme 1). In view of the demonstrated synthetic utility of 2-(1′-hydroxyalkyl)butenolides (**6**),[3] the alternative regioselective aldolization of a suitable furanolate (**4**) at the C(3) position offers an economical solution for their preparation, especially as few methods are available.[4] Chelation-controlled condensation of an aldehyde through a cyclic transition state ought to deliver butenolide (**5**) and the desired product (**6**) by isomerization (Scheme 2).

We now report that some new tin and boron furanolates, generated *in situ*, behave exactly as anticipated and provide convenient access to (**6**). Conversion of 2-(5*H*)-furanone (**7**) to the tin(II) furanolate (**4A**) using stannous trifluoromethanesulphonate (triflate = Tf) and N-ethylpiperidine,[5] followed by addition of capronaldehyde gave the 2-substituted butenolide (**6a**) as the major product although a small amount of the regioisomer (**3a**) was also obtained (entry 1, Table 1). The regioselectivity was markedly improved when tetramethylethylenediamine (TMEDA)[5] was added to the mixture containing (**4A**), presumably owing to the formation of the furanolate intermediate (**4B**) (entry 2, Table 1).



Scheme 1. *Reagents*: i, RX; ii, RCHO.



A; ML$_n$ = SnOTf   a; R = n-pentyl
B; ML$_n$ = SnOTf·TMEDA   b; R = Pr^i
C; ML$_n$ = Bu$^n_2$ c; R = n-$C_{13}H_{27}$
D; ML$_n$ = B(cyclopentyl)$_2$ d; R = n-$C_{15}H_{31}$

Scheme 2. *Reagents and conditions*: i, TfOML$_n$, amine, CH_2Cl_2, −78 °C; ii, RCHO, −78 °C to 20 °C; iii, DBU, CH_2Cl_2, −20 °C.

Table 1. Regiocontrolled aldolization of boron and tin 2-furanolates.

Entry	Furanolate	RCHO (R =)	Products[a,b]	Ratio[c] (**6**) : (**3**)	Total % yield[d]
1	(**4A**)	n-Pentyl	(**6a**), (**3a**)	7 : 1	58
2	(**4B**)	n-Pentyl	(**6a**), (**3a**)	13 : 1	52
3	(**4C**)	n-Pentyl	(**6a**), (**3a**)	>40 : 1	98
4	(**4D**)	n-Pentyl	(**6a**), (**3a**)	>40 : 1	97
5	(**4A**)	Pr^i	(**6b**), (**3b**)	12 : 1	56
6	(**4B**)	Pr^i	(**6b**), (**3b**)	11 : 1	61
7	(**4D**)	Pr^i	(**6b**), (**3b**)	>40 : 1	71
8	(**9A**)	n-Pentyl	(**10a**)	—	53
9	(**9D**)	n-Pentyl	(**10a**)	—	79
10	(**9A**)	Pr^i	(**10b**)	—	55
11	(**9D**)	Pr^i	(**10b**)	—	80
12	(**9C**)	n-$C_{13}H_{27}$	(**10c**)	—	72
13	(**9D**)	n-$C_{15}H_{31}$	(**10d**)	—	73

[a] All new compounds (**6a,b**) and (**10a—d**) exhibited satisfactory analytical and spectral data. [b] Butenolides (**3a,b**) and (**10a—d**) were obtained as pairs of diastereoisomers. [c] Determined by ^1H n.m.r. (360 MHz). [d] Yield of chromatographically purified product(s).

Next, the boron furanolates (**4C**) and (**4D**) were generated by treating (**7**) with the corresponding dialkylboron triflates and di-isopropylethylamine.[6] Subsequent addition of capronaldehyde in both instances afforded (**6a**) with essentially total regiocontrol and in excellent yield (entries 3 and 4, Table 1). When capronaldehyde was replaced by isobutyraldehyde, higher regioselectivity was again experienced with the boron furanolate (**4D**) than with the tin derivatives (**4A**) and (**4B**).

A further test and an application of the foregoing methodology was presented by α-angelica lactone (**8**). Stannylation and borylation were accomplished as before and the resulting furanolates (**9**) were treated with aldehydes. Only the corresponding C(3)-substituted products (**10a—d**) were obtained regardless of the procedure used (entries 8—13, Table 1). On account of the C(5)-methyl substituent, the aldols so formed did not equilibrate to the conjugated isomers during work-up. However, the aldols arising from tridecanal and heptadecanal (**10c**) and (**10d**) were readily isomerized[7] by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2 at −20 °C to furnish (**11c**) and (**11d**) in *ca.* 70% yield. Consequently, this last process amounts to a formal synthesis of (±)-litsenolide C1 (**12c**) and (±)-dihydromahubanolide (**12d**) respectively as the intervening steps in both cases are the same and have been described.[8]

The advantage of the present procedure is simplicity in that it enables a variety of butenolides to be assembled in a regiocontrolled manner and in a single operation. Access to chiral products should also be possible by recourse to enantioselective aldolization.[5,9] Such applications and the preparation of highly functionalized lactones of marine origin will be reported elsewhere.

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References

1 C. W. Jefford, A. W. Sledeski, and J. Boukouvalas, *Tetrahedron Lett.*, 1987, **28**, 949; *J. Chem. Soc., Chem. Commun.*, 1988, 364.

2 C. W. Jefford, D. Jaggi, and J. Boukouvalas, *Tetrahedron Lett.*, **28**, 4037.

3 B. M. Trost, M. K.-T. Mao, J. M. Balkovec, and P. Buhlmayer, *J. Am. Chem. Soc.*, 1986, **108**, 4965; R. J. Capon, E. L. Ghiselberti, and P. R. Jefferies, *J. Chem. Res.* (*S*), 1987, 118.

4 M. Watanabe, K. Shirai, and T. Kumamoto, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 3318; J. H. Näsman, N. Kopola, and G. Pensar, *Tetrahedron Lett.*, 1986, **27**, 1391.

5 T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, *Tetrahedron*, 1984, **40**, 1381; T. Mukaiyama and N. Iwasawa, *Chem. Lett.*, 1984, 753.

6 D. A. Evans, J. V. Nelson, E. Vogel, and T. R. Taber, *J. Am. Chem. Soc.*, 1981, **103**, 3099.

7 For a precedent see: G. A. Kraus and B. Roth, *J. Org. Chem.*, 1978, **43**, 4923.

8 R. W. Wollenberg, *Tetrahedron Lett.*, 1980, **21**, 3139; K. Tanaka, M. Terauchi, and A. Kaji, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 3935.

9 *Cf.* I. Paterson, M. A. Lister, and C. K. McClure, *Tetrahedron Lett.*, 1986, **27**, 4787; S. Masamune, T. Sato, B.-M. Kim, and T. A. Wollman, *J. Am. Chem. Soc.*, 1986, **108**, 8279.