

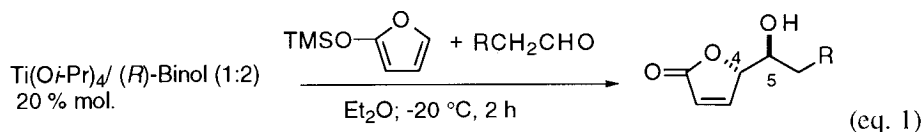
LIGAND EFFECTS ON THE CATALYTIC ASYMMETRIC AUTOINDUCTIVE ALDOL REACTION OF 2-TMSOF (2-TRIMETHYLSILYLOXYFURAN) WITH ALDEHYDES

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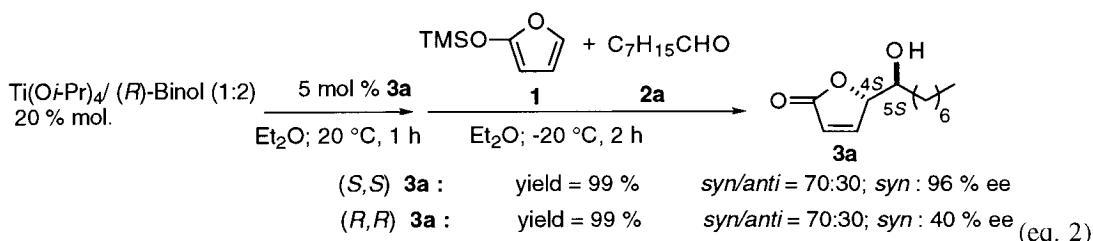
Abstract — We report herein some recent progress in the reaction of 2-TMSOF (2-trimethylsilyloxyfuran) with achiral aldehydes in the presence of a new catalytic system (which does not use the expensive Binol catalyst) yielding the corresponding butenolides with good diastereomeric ratios (d.e. = 90 %) and moderate e.e.'s (50 %).

Enantioselective addition of enol ethers to aldehydes and ketones to form cross coupled aldol products is now one of the most important reactions^{1,2} for the creation of carbon-carbon bonds. We have shown that an enantioselective aldolisation reaction between 2-trimethylsilyloxyfuran (2-TMSOF) and an achiral aldehyde can be performed leading to the corresponding butenolides with good to excellent yields as well as with good to excellent ee's, depending upon the time, solvent, and temperature.³ Furthermore, the butenolide moiety is very often encountered in naturally occurring products,⁴ and may also serve as useful chiral building blocks for the formation of polysubstituted γ -lactones⁵ as well as for the preparation of products possessing a 1,2-diol function.



Indeed, in the presence of (*R*)-1,1'-bi-2-naphthol (Binol) (0.4 equiv.) and Ti(Oi-Pr)_4 (0.2 equiv.), octanal reacted at $-20\text{ }^\circ\text{C}$ for 1.5 h in CH_2Cl_2 with 2-TMSOF, to yield a hardly separable 70:30 mixture of *syn/anti*-aldols in 95 % combined yield and with 57 % ee for the *syn* (or *threo*) (4*S*,5*S*)-product.³ However, when the reaction was run in ether, the enantioselectivity dramatically increased (87 % ee)

albeit in moderate yield (20 %).³ Then we showed that the major butenolide formed in this reaction acts as a co-catalyst, since when 5 molar % of the *syn*-adduct was added prior to the reaction, the corresponding butenolides were now obtained in quantitative yields with 96 % ee and 40 % ee for the major *syn*-compound, when the (*S,S*)- and (*R,R*)-aldols were used, respectively (Eq. 2); this was good evidence for the first catalytic autoinductive aldol reaction to be reported.



We now want to disclose the last results we obtained in this area, in order to both better understand the mechanism of this aldol reaction, and find better reaction conditions.

We first studied the influence of the enantiomeric purity of (*R*)-1,1'-bi-2-naphthol (Binol) on the enantiomeric excess of the product of the reaction (Table 1).

Table 1 : 2-TMSOF + 20 % molar of (*R*)-Binol₂Ti + octanal in Et₂O at -20 °C for 2 h

entry	ee of (<i>R</i>)-Binol	yield (%)	<i>syn/anti</i>	ee (%) of <i>syn</i> (abs. conf.)
1	2	99	65:45	2 (<i>S,S</i>)
2	25	80	60:40	57 (<i>S,S</i>)
3	50	90	60:40	80 (<i>S,S</i>)
4	75	90	60:40	92 (<i>S,S</i>)
5	99	50	57:43	90 (<i>S,S</i>)

The reactions were performed by mixing first (*R*)-Binol with Ti(O*i*-Pr)₄ in Et₂O at room temperature for 1 h prior to cooling at -20 °C and addition of octanal followed by TMSOF. After 2 h, the reaction mixture was quenched as usual, and after column chromatography purification, the butenolides were analyzed by ¹H NMR in the presence of europium salts (Eu(hfc)₃) for ee determination. These results show that a positive non linear effect (NLE)⁶ was observed since when a 50 % ee of (*R*)-Binol was used, the *syn*-butenolide was obtained in 80 % ee. This positive NLE, or amplification of the enantiomeric excess, should be rationalized by involving the autoinductive effect of the reaction. Indeed the self assembling of chiral Binol around Ti (IV) itself cannot explain these results; participation of the major adduct to the catalytic species through a chiral ligand accelerating effect, should encounter for the amplification observed. Then taking advantage of the catalytic autoinductive effect, the reaction was performed in a stepwise fashion, by adding at -20 °C in Et₂O the total amount of the couple TMSOF-octanal, but split into four portions (octanal/2-TMSOF : 0.032/0.049, 0.093/0.139, 0.125/0.188, 0.250/0.375 mmol), to

the reaction medium containing 20 % molar of the (*R*)-Binol₂Ti complex. This experimental procedure allows the formation of a small amount of aldols, after the first addition of reagents (aldehyde and nucleophile), which can be incorporated into new catalytic species prior to the second addition of reagents; thus this experiment mimics the procedure in which we added some pure aldol prior to addition of the aldehyde and 2-TMSOF. Under these conditions, we found that the time of the reaction was also crucial for the ee of the products : after 2 h, the *syn* (4*S*,5*S*)-isomer showed >96 % ee, and the *anti* (4*R*,5*S*)-isomer 90 % ee, in a combined 90 % chemical yield (Table 2).

Table 2 : 20 % molar of (*R*)-Binol₂Ti in Et₂O at -20 °C, then four additions of TMSOF-octanal

entry	time (h)	yield (%)	<i>syn/anti</i>	ee (%) of <i>syn</i> (abs. conf.)
6	24	99	55:45	80 (<i>S,S</i>)
7	6	99	57:43	88 (<i>S,S</i>)
8	2	90	60:40 ^a	>96 (<i>S,S</i>)
9	2 ^b	65	60:40	>95 (<i>S,S</i>)

a) *anti* (4*R*,5*S*)-isomer with 90 % ee; b) with 5 % molar of (*R*)-Binol₂Ti complex

It is noteworthy that longer reaction times, such as 6 h or 24 h, led to better chemical yields however with lower ee's (88 and 80 % ee, respectively). This illustrates that a retro-aldolization reaction occurred and not a partial decomposition of only one diastereomer (which should have led to a decrease in the combined chemical yield). A simple epimerization at the allylic position would have led only to different diastereomeric ratios, and not to a drop in the ee's. Finally, when the stepwise addition of the 2-TMSOF-octanal couple was performed to the reaction medium containing only 5 % molar of the (*R*)-Binol₂Ti complex, the desired butenolides were obtained in 65 % combined yield, with 60:40 diastereomeric ratio and >95 % ee for the major *syn*-aldol. Therefore, lowering the amount of catalyst resulted in decreased yield. However, optimisation of the stepwise addition should allow one to improve the chemical yield (e.g. continuous slow addition of the reagents).

We then studied the influence of the presence of a second chiral ligand in order to study a possible replacement of the expensive Binol reagent. We already showed that in the presence of 20 % molar mixture of (*R*)-Binol, (+)-Taddol and Ti(Oi-Pr)₄, in 1:1:1 ratio, a 60:40 mixture of *syn/anti*-butenolides was obtained in quantitative yield and with 90 % ee (for the major *syn*-compounds). The use of different alcohols ((+)- or (-)-Taddol) and phenols in combination with Ti(Oi-Pr)₄ was next studied and the results are shown in Table 3. It is noteworthy that in the sole presence of phenols and Ti(Oi-Pr)₄, no reactions occurred (results not shown). However when phenol, (-)-Taddol and Ti(Oi-Pr)₄, in a 2:1:1 ratio, were mixed in Et₂O at 20 °C for 1 h prior to the addition at -20 °C of octanal followed by 2-TMSOF, the formation of the desired butenolides was observed after 24 h, in 25 % combined yield and 60:40 diastereomeric ratio (in favor of the *syn*-butenolides) but in a racemic form (entry 10, Table 3). We next used 2,4,6-trimethylphenol with (-)-Taddol and Ti(Oi-Pr)₄ in a 2:1:1 ratio, and now observed formation of the butenolides after 24 h, in 23 % yield, as a 75:25 diastereomeric mixture with 35 % ee for the major *syn* (4*S*,5*S*)-compound (entry 11).

Table 3: 2-TMSOF + 20 % molar of (phenols)-Ti-Taddol + octanal in Et₂O at -20 °C for 24 h

entry	catalyst (ratio ^a) (20 % mol)	yield (%) of butenolides formed	<i>syn/anti</i>	ee % of all <i>syn</i> (abs. conf.)
10	phenol-Ti(-)-Taddol (2:1:1)	25	60:40	0
11	(Me) ₃ phenol-Ti(-)-Taddol (2:1:1)	23	75:25	35 (<i>S,S</i>)
12	(<i>t</i> Bu) ₃ phenol-Ti(-)-Taddol (2:1:1)	60	60:40	0
13	biphenol-Ti(-)-Taddol (1:1:1)	12	60:40	5 (<i>S,S</i>)
14	biphenol-Ti(-)-Taddol (2:1:0)	60	80:20	0
15	biphenol-Ti(-)-Taddol (2:1:1)	99	80:20	5 (<i>R,R</i>)
16	(Me) ₂ (<i>t</i> Bu) ₂ biphenol-Ti(+)-Taddol (2:1:1)	15	60:40	0
17	(Me) ₃ phenol-Ti(-)-Taddol (2:1:1) ^b	38	96:4	50 (<i>R,R</i>)
18	(Me) ₃ phenol-Ti(-)-Taddol (2:1:1) ^c	54	95:5	36 (<i>R,R</i>)
19	(Me) ₃ phenol-Ti(+)-Taddol (2:1:1) ^d	65	95:5	35 (<i>S,S</i>)
20	(<i>t</i> Bu) ₃ phenol-Ti(+)-Taddol (2:1:1) ^e	60	87:13	28 (<i>S,S</i>)
21	(Me) ₃ phenol-Ti(-)-Taddol (2:1:1) ^f	14	60:40	17 (<i>R,R</i>)
22	biphenol-Ti(+)-Taddol (1:1:1) ^d	49	75:25	10 (<i>S,S</i>)
23	biphenol-Ti(-)-Taddol (1:1:1) ^e	60	70:30	2 (<i>R,R</i>)
24	(Me) ₃ phenol-Ti(-)-Taddol (2:1:0) ^g	0	88:12	50 (<i>S,S</i>)

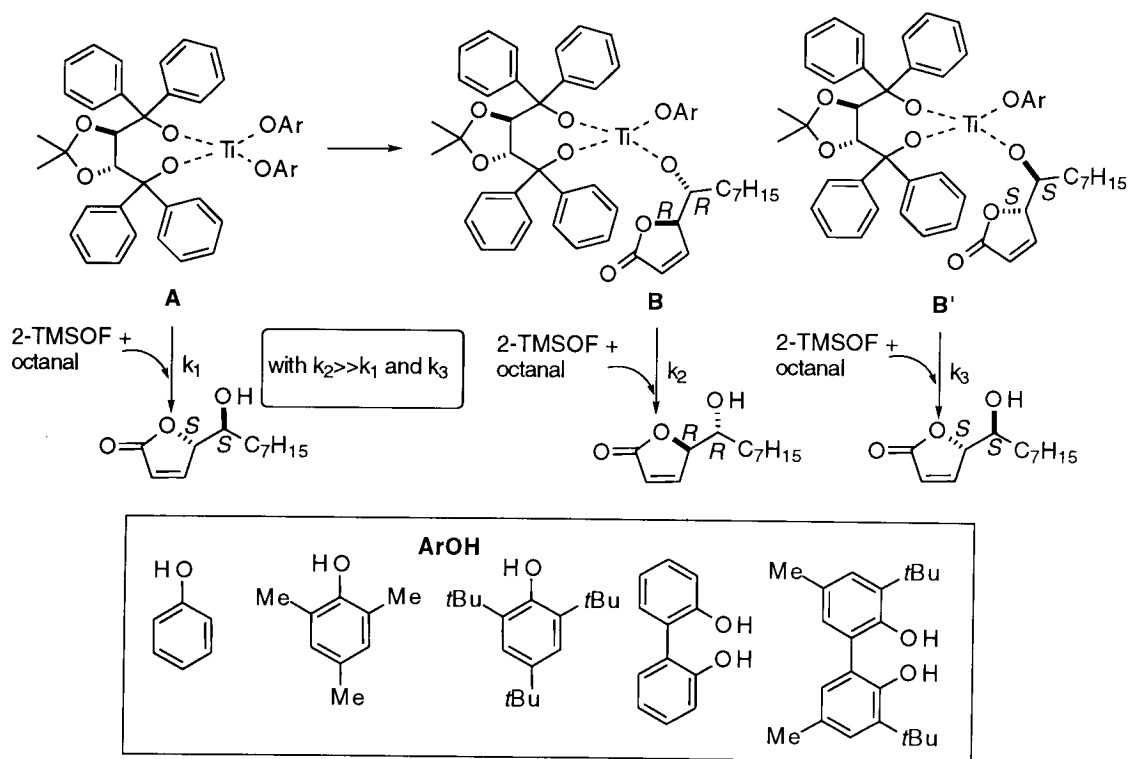
a) phenol:Ti:Taddol ratio; b) 45 h; c) with 5 % molar of pure (*S,S*)-aldol with 96 % ee; d) with 5 % molar of pure (*S,S*)-aldol with 50 % ee; e) with 5 % molar of pure (*S,S*)-aldol with 82 % ee; f) with addition of a pair of 2-TMSOF and octanal in four portions (octanal/2-TMSOF : 0.032/0.049, 0.093/0.139, 0.125/0.188, 0.250/0.375 mmol, respectively with 2, 4, 6 and 12 h of delay); g) with 15 % molar of pure (*S,S*)-aldol with 82 % ee.

We then thought that by using a more bulky phenol such as 2,4,6-tri-*tert*-butylphenol with (-)-Taddol and Ti(Oi-Pr)₄ in a 2:1:1 ratio, we should increase the ee. However, we did obtain the desired butenolides with a good yield (60 %) and with a 60:40 diastereomeric ratio but in a racemic form (entry 12). We thus decided to use biphenol with (-)-Taddol and Ti(Oi-Pr)₄ in a 1:1:1 ratio, and observed the formation of the desired butenolides in 12 % yield, 60:40 diastereomeric ratio with 5 % ee for the major *syn* (4*S*, 5*S*)-compound (entry 13). This disappointing result led us to try the following conditions: a 2:1:1 biphenol, (-)-Taddol and Ti(Oi-Pr)₄ mixture was used in Et₂O at -20 °C for 24 h (entry 15). The corresponding butenolides were thus obtained in 99 % yield with 80:20 diastereomeric ratio but with 5 % ee for the major *syn*-compound but with the *opposite* absolute configurations (4*R*,5*R*)! The high chemical yield obtained in this last experiment should be compared with the yield obtained in the sole presence of a 2:1 ratio of biphenol and Ti(Oi-Pr)₄ mixture (where the butenolides were formed in 60 % yield as a 80:20 diastereomeric mixture, entry 14). However inversion of the absolute configurations depending on the amount of the achiral ligand is troublesome. This indicated that biphenol is too reactive

or/and that the (-)-Taddol accelerating ligand effect was not sufficient enough to induce the enantioselectivity of the reaction. We then used the 5,5'-dimethyl-3,3'-di-*tert*-butyl-2,2'-biphenol with (+)-Taddol and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 2:1:1 ratio, and observed the formation of the desired butenolides in 15 % chemical yield, with 60:40 diastereomeric ratio but in a racemic form (entry 16). Since reactions performed in the presence of phenols were quite slow, we were curious to check if a longer reaction times would improve both the chemical yield and the ee. Thus we performed the reaction with 2,4,6-trimethylphenol, (-)-Taddol and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 2:1:1 ratio, and after 45 h we obtained in 38 % yield a 96:4 *syn/anti*-mixture showing a 50 % ee for the major *syn*-product, possessing the (4*R*,5*R*) absolute configurations (entry 17)! To our knowledge it is the first time that under the same reaction conditions (compare entries 11 and 17) both enantiomers can be obtained after either 24 h or 45 h. This result is quite surprising but is confirmed by the following experiment. We have had already shown that by introducing 5 % mol of the *syn*-isomer in the reaction medium containing 20 % mol of the $(\text{Binol})_2\text{Ti}$ complex, prior to octanal and 2-TMSOF, ee's and yields were dramatically increased (Eq. 2) due to the autoinductive effect. However, the addition of the minor *anti*-compound had no effects (result not shown). Thus, when the reaction was performed with 2,4,6-tri-*tert*-butylphenol, (-)-Taddol and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 2:1:1 ratio in the presence of 5 % molar of (4*S*,5*S*)-aldol product with 96 % ee, prior to addition at once of octanal followed by 2-TMSOF, the expected butenolides were now obtained in 54 % yield as a 95:5 *syn/anti*-mixture with 36 % ee for the major (4*R*,5*R*)-adduct (entry 18). Comparison of this result with those obtained in entry 17 shows that a reverse induction also occurred by comparison with the results obtained in entry 11. These experiments seem to show that a first catalytic complex induces the formation of the *syn* (4*S*,5*S*)-adduct with low efficiency, and then a new catalytic species more active than the former one induces now the formation of the (4*R*,5*R*)-compound; indeed on 0.5 mmol scale reaction, after 24 h about 11.9 mg of (4*S*,5*S*)-compound is formed which is roughly the same quantity obtained after 45 h (9.2 mg). It seems that (-)-Taddol₂Ti complexe is responsible for the formation of the (4*S*,5*S*)-aldol and small amount of (4*R*,5*R*)-aldol. Both compounds can then participate to the new catalytic species leading to the major (4*R*,5*R*)-compound; in other words the (-)-Taddol:(4*S*,5*S*)-aldol:Ti complex forms a mismatch catalytic species whereas (-)-Taddol:(4*R*,5*R*)-aldol pair forms a match catalytic species (Scheme 1). We then performed the reaction using 2,4,6-trimethylphenol with the enantiomer of Taddol, (+)-Taddol, and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 2:1:1 ratio, in the presence of 5 % molar of (4*S*,5*S*)-aldol product (possessing only 50 % ee), and obtained the expected butenolides in a 95:5 *syn/anti*-mixture with 35 % ee for the major *syn* (4*S*,5*S*)-isomer (entry 19). This result is in accord with what expected if we compare this experiment with entry 18, where the other enantiomer of Taddol was employed. These results together with those obtained above, seem to indicate that both the aldol and Taddol are crucial for the enantioselection of the reaction, and that probably the aldols produced in the reaction participate to the catalytic species to form match and mismatch pairs of ligands around Ti (IV). Indeed, when the reaction is run in the absence of Taddol, no reaction occurred, neither in the lack of phenol. Therefore, we propose that three different complexes **A**, **B**, and **B'** are formed with different catalytic activities (Scheme 1). In the presence of (-)-Taddol, **A** is first responsible for the beginning of the reaction leading to the major (4*S*,5*S*)-isomer with small amount of its enantiomer, then the more active **B** catalytic species

containing (-)-Taddol and the minor (4*R*,5*R*)-isomer gives rise to the *syn* (4*R*,5*R*)-isomer. Nevertheless more experiments in order to tentatively isolate the complexes are needed.

Scheme 1



We then used 2,4,6-*tert*-butylphenol with (+)-Taddol and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 2:1:1 ratio, in the presence of 5 % molar of (*S,S*)-aldol product with 82 % ee (entry 20). In that case, we observed after 24 h the formation of the desired butenolides in 60 % yield, as a 87:13 *syn/anti*-mixture with 28 % ee for the major *syn* (4*S*,5*S*)-aldol. This last experiment did not allow us to increase significantly the ee, as expected. Then we performed the reaction using biphenol with (+)-Taddol and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 1:1:1 ratio, in the presence of 5 % molar of (*S,S*)-aldol product (possessing a 50 % ee), and obtained the expected butenolides in a 75:25 *syn/anti*-mixture with 10 % ee for the major *syn* (4*S*,5*S*)-isomer (entry 22). This result is in accord with the above results, if we compare entry 22 with entry 13: the (4*S*,5*S*)-isomer was obtained either with (-)-Taddol, or with the enantiomer of Taddol but in the presence of (4*S*,5*S*)-aldol. Repeating the reaction with (-)-Taddol and $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 1:1:1 ratio, in the presence of 5 % molar of (*S,S*)-aldol product with 96 % ee, allowed us to obtain a 70:30 *syn/anti* mixture with 2 % ee for the major *syn* (4*R*,5*R*)-isomer in 60 % combined yield (entry 23). These last two experiments show that biphenol is not as good as 2,4,6-trimethylphenol as catalyst for this reaction, as far as ee are concerned. We then performed the reaction with 2,4,6-trimethylphenol, with $\text{Ti}(\text{O}i\text{-Pr})_4$ in a 2:1 ratio and with 15 % molar of the *syn* (*S,S*)-aldol product showing 82 % ee, prior to addition at once of octanal followed by 2-TMSOF. After stirring 3 h at -20 °C, the reaction was quenched as usual and after purification, we

recovered only the quantity of aldol that we have had introduced in the reaction mixture. Interestingly, analysis of ^1H NMR spectrum showed that the pure *syn*-aldol was now a 88:12 mixture of *syn/anti*-compounds and that ee of the major *syn*-product was now only 50 %. This result is in accord with a retro-aldolization reaction, which was further demonstrated by the above results. Finally when the reaction was performed in a stepwise fashion, disappointing results were obtained (entry 21) but in accord with experiments 17 and 18, where the first minor (*4R,5R*)-aldol formed at the early stage of the reaction will then induce the formation of the (*4R,5R*)-product.

Absolute configurations of the adducts, as reported in Tables 1-4, were determined, after hydrogenation of the double bonds, by comparisons of the sign of the specific rotations of the reduced products with related compounds.^{7,8}

We have had already applied this new methodology to the synthesis of natural muricatacin,³ a natural metabolite of the bioactive annonaceous acetogenins,⁹ and showed that the major *syn*-product could be obtained with 80 % ee (in 80 % combined yield) when the reaction was run in CH_2Cl_2 .³ However, when the reaction was run in Et_2O instead (entry 25), the major *syn*-product was now obtained with 90 % ee, but in only 20 % overall chemical yield.³ We thus decided to test the new reaction conditions, derived from the results obtained above, to the aldol addition of 2-TMSOF to tridecanal (Table 4).

Table 4 : application to muricatacin synthesis: addition of 2-TMSOF to tridecanal in Et_2O at $-20\text{ }^\circ\text{C}$ in the presence of chiral Lewis acid

entry	20 % molar of catalyst (ratio; time h)	yield (%)	<i>syn/anti</i>	ee % of <i>syn</i> (abs. conf.)
25	(<i>R</i>)-Binol-Ti (2:1; 2 h)	20	60:40	90 (<i>S,S</i>)
26	(<i>R</i>)-Binol-(+)-Taddol-Ti (1:1:1; 4.5 h)	72	70:30	93 (<i>S,S</i>)
27	(<i>R</i>)-Binol-Ti (2:1, + 5 % molar of <i>S,S</i> -aldol ^a ; 6 h)	72	70:30	78 (<i>S,S</i>)
28	(<i>R</i>)-Binol-Ti (2:1, + 4 additions of couple 2-TMSOF-aldehyde, 6 h)	80	60:40 ^b	>96 (<i>S,S</i>)

a) from octanal; b) with >90 % ee for (*4R,5S*) *anti*-isomer

Thus, when the reaction was run in Et_2O at $-20\text{ }^\circ\text{C}$ for 4 h and catalyzed by a 1:1:1 (*R*)-Binol:(+)-Taddol:Ti(IV) mixture, we observed an increase of both the chemical yield and the ee (72 % and 93 %, respectively, entry 26, Table 4). Then we thought that by adding, prior to the reaction, 5 % molar of the *syn*-butenolide obtained from octanal (with 82 % ee) to the reaction mixture containing 20 % molar of (*R*)-Binol:Ti (IV) complex, we should observe an increased chemical yield. This was the case, since the desired butenolides were now obtained in 72 % combined yield and 78 % ee for the major *syn*-isomer, after 6 h of stirring at $-20\text{ }^\circ\text{C}$ (entry 27). This interesting result shows that a product-like aldol may also co-catalyze the reaction.¹⁰ Finally, taking advantage of the autoinductive process we added in four portions the couple 2-TMSOF-tridecanal to the reaction medium containing 20 % molar of the complex (*R*)-Binol₂Ti in Et_2O at $-20\text{ }^\circ\text{C}$, and quenched the reaction after a total of 6 h of stirring. The butenolides

were obtained in 80 % combined chemical yield, with 60:40 diastereomeric ratio and 96 % ee for the major *syn*-butenolide (entry 28). Interestingly the minor isomer was found to have >90 % ee and the (4*R*,5*S*) absolute configuration. Therefore, epimerization at the allylic position through basic treatment would lead to the (4*S*, 5*S*)-isomer, and thus would convert the total amount of butenolides into the sole *syn*-adduct.

In conclusion, these results confirm the catalytic autoinductive enantioselective aldol reaction of 2-TMSOF to aldehydes. Replacement of chiral Binol by an achiral phenol, such as 2,4,6-trimethylphenol, in the presence of (+)- or (-)-Taddol, allowed us to get the desired butenolides in good yields, with excellent diastereomeric excess and moderate enantiomeric excess. Furthermore, to our knowledge it is the first time that a sole *TIME* effect is reported on asymmetric catalytic aldol reaction, in order to obtain either enantiomer as the major product of the reaction. These results are in accord with a possible participation of several catalytic active complexes, with a co-catalytic effect of the aldol products. The stepwise addition of the couple 2-TMSOF-achiral aldehyde to the reaction medium containing 20 % molar of (*R*)-Binol₂Ti complex in Et₂O at -20 °C led to the expected butenolides in a highly enantiomeric pure form (>96 % ee) and in excellent chemical yields (nearly quantitative).¹¹ These results bring some new insights onto the mechanism of such an aldolisation, together with evidences that a perfect control of a new process (e.g. time of reaction, order of addition, temperature, etc..) in asymmetric reactions is crucial to get both high yields and excellent ee's.

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REFERENCES AND NOTES

1. a) T. Mukaiyama, K. Narasaka, and K. Banno, *Chem. Lett.*, **1973**, 1011; b) T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, 1974, **96**, 7503.
2. a) S. Kobayashi and M. Horibe, *J. Am. Chem. Soc.*, 1994, **116**, 9805; b) S. Kobayashi and T. Hayashi, *J. Org. Chem.*, 1995, **60**, 1098; c) S. Kobayashi and M. Horibe, *Tetrahedron*, 1996, **52**, 7277; d) M. Sodeoka, K. Ohrai, and M. Shibasaki, *J. Org. Chem.*, 1995, **60**, 2648; e) K. Mikami, M. Terada, and T. Nakai, *J. Am. Chem. Soc.*, 1989, **111**, 1940; f) K. Mikami, M. Terada, and T. Nakai, *J. Am. Chem. Soc.*, 1990, **112**, 3949; g) K. Mikami and S. Matsukawa, *J. Am. Chem. Soc.*, 1993, **115**, 7039; h) K. Mikami and S. Matsukawa, *J. Am. Chem. Soc.*, 1994, **116**, 4078; i) E.M. Carreira, R. A. Singer, and W. Lee, *J. Am. Chem. Soc.*, 1994, **116**, 8837; j) E. M. Carreira, W. Lee, and R. A. Singer, *J. Am. Chem. Soc.*, 1995, **117**, 3649; k) R. A. Singer and E. M. Carreira, *Tetrahedron Lett.*, 1997, **38**, 927; l) G. Keck and D. Krishnamurthy, *J. Am. Chem. Soc.*, 1995, **117**, 2363.
3. M. Szlosek, X. Franck, B. Figadère, and A. Cavé, *J. Org. Chem.*, 1998, **63**, 5169.

4. G. Pattenden, in *Progress in the Chemistry of Organic Natural Products*, Springer-Verlage, Wien, 1978, p. 133.
5. a) B. Figadère, J.-F. Peyrat, and A. Cavé, *J. Org. Chem.*, 1997, **62**, 3428; b) B. Figadère, C. Chaboche, J.-F. Peyrat, and A. Cavé, *Tetrahedron Lett.*, 1993, **34**, 8093; c) J.-F. Peyrat, B. Figadère, A. Cavé, and J. Mahuteau, *Tetrahedron Lett.*, 1995, **36**, 7653.
6. C. Girard and H. B. Kagan, *Angew. Chem. Int., Ed. Engl.*, 1998, **37**, 2922-2959
7. M. Larchevêque and J. Lalande, *Bull. Soc. Chim. Fr.*, 1987, 116.
8. B. Figadère, J.-C. Harmange, A. Laurens, and A. Cavé, *Tetrahedron Lett.*, 1991, **32**, 7539.
9. M. J. Rieser, J. F. Koslowski, K. V. Wood, and J. L. McLaughlin, *Tetrahedron Lett.*, 1991, **32**, 1137.
10. T. Volk, T. Korenaga, S. Matsukawa, M. Terada, and K. Mikami, *Chirality*, 1998, **10**, 717.
11. For an alternative enantioselective aldol addition of TMSOF to aldehydes and ketones, see : D. A. Evans, M. C. Kozlowski, J. A. Murry, C. S. Burgey, K. R. Campos, B. T. Connell, and R. J. Staples, *J. Am. Chem. Soc.*, 1999, **121**, 669.

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