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Titanium Enolates and "ate" Complexes of N,N-Disubstituted Amides and Thioamides in the Michael Reaction.

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Abstract: The synthetic potential, regio- and stereoselectivity of titanium dialkylamide and dialkylthioamide enolates and "ate" complexes in reaction with some conjugate carbonyl compounds are investigated. Titanium enolates react preferentially in 1,2-position while "ate" complexes afford 1,4-regiocontrol. The stereochemical behaviour of the latter follows in general the lithium and potassium precursors. Marked influence of solvent and of electrophile geometry on 1,4-stereoselectivity was found with the amides but not with the thioanalogs. The stereochemistry of the amide titanium "ate" complexes is correlated with a cyclic transition state. The solvent effect is explained by involvement into the transition structure. Some advantages of the titanium "ate" complexes are discussed.

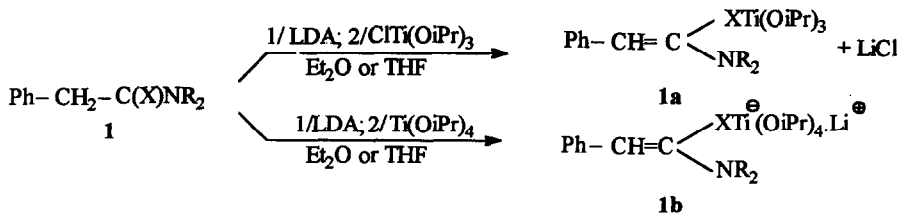
The wide variety of data concerning simple diastereoselectivity of the Michael reaction with alkali metal enolates allowed some useful generalisations to be made, connecting the structural features of the reactants with the stereochemical outcome by means of a cyclic eight - membered transition state.[1] Our continued investigations on diastereoselective C-C bond formation in bifunctionalized 2,3-diphenyl- or 2-phenyl-3-methyl propanic model systems contribute to and are entirely consistent with the above generalisations.[2-8]

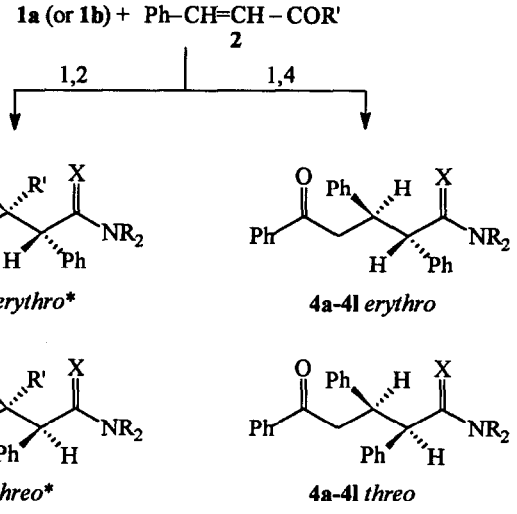
Meanwhile, new types of reagents displaying some advantages over classical enolates appeared. Of special interest are organotitanium compounds. It had been discovered that titanation of the classical carbanions results in species with reduced basicity and reactivity, thus providing in general better chemo-, regio- and stereoselectivity. On the other hand the different number of ligands in enolates and "ate" complexes alters the steric environment of the titanium center and the formal charge in the titanium compounds, consequently their reactivity and stereochemical behaviour.[9]

While titanium reagents are widely used in the aldol addition[9], the examples of the vinylogous Michael reaction are scarce.[10-16] In a recent study, the stereoselectivity of conjugate addition of ketone and ester enolate "ate" complexes was systematically investigated.[17] It was established that the stereochemical outcome parallels or opposes that of the parent lithium enolates depending on the donor and acceptor used. The results were not rationalised in terms of the transition state models assumed.

Having in hand our previous results with lithium enolates, it came natural to turn attention to the titanium reagents. Herein we report our investigations on the synthetic utility, regioselectivity and stereochemistry of the titanium mediated conjugate addition of phenylacetic acid N,N-dialkylamides and thioamides to cinnamic aldehyde, benzalacetone, chalcone and *E*- and *Z*-configurated methyl cinnamate (**Scheme 1**). Both types of reagents - enolates **1a** and "ate" complexes **1b** were used. An attempt has been made to connect the stereochemical data with probable transition state geometry.

Scheme 1





	X	R	R'		X	R	R'		X	R	R'
3a	O	CH_3	H	**4a**	O	CH_3	CH_3	**4g**	S	CH_3	H
3b**	O	CH_3	CH_3	**4b**	O	CH_3	Ph	**4h**	S	CH_3	CH_3
3c	O	CH_3	Ph	**4c**	O	CH_3	OCH_3	**4i**	S	CH_3	Ph
3d	S	CH_3	H	**4d**	O	C_2H_5	OCH_3	**4j**	S	CH_3	OCH_3
3e	S	CH_3	Ph	**4e**	O	C_6H_{11}	OCH_3	**4k**	S	C_6H_{11}	OCH_3
				4f	O	i-C_3H_7	OCH_3	**4l**	S	i-C_3H_7	OCH_3

* Concerning *erythro,threo* convention for 1,2-additional products see ref.4.

** The relative configurations have not been assigned.

RESULTS AND DISCUSSION

Titanium enolates and enethiolates

The behaviour of the representative N,N-dimethylphenylacetamide and N,N-dimethylphenyl - thioacetamide was examined. Titanation was performed with $ClTi(OiPr)_3$ in Et_2O or THF *via* the corresponding lithium enolates.[18] Having in mind the possible interference of the lithium salt in the regio- and stereochemistry

control[19], we varied the quantity of $ClTi(OiPr)_3$ from 1 to 4 equivalents. The syntheses were carried out at -40°C for 30 min and the results are listed in **Table 1**.

Table 1. Addition of Titanium Enolates of N,N-Dimethylphenylacetamide (X = O) and N,N-Dimethylphenylthioacetamide (X = S) to Cinnamic Aldehyde (R' = H) and Chalcone (R' = Ph).

Entry	X	R'	Metallating agent (equiv.)	Solvent	%	1,2/1,4	*erythro/threo*$_{1,2}$	*erythro/threo*$_{1,4}$
1	O	H	$ClTi(OiPr)_3$ (1→4)	Et_2O	65	100/0	23/77	-
2	O	H	LDA[a]	Et_2O	69	100/0	28/72	-
3	O	H	$ClTi(OiPr)_3$ (1→4)	THF	67	100/0	25/75	-
4	O	H	LDA[a]	THF	85	100/0	27/73	-
5	S	H	$ClTi(OiPr)_3$ (1→4)	Et_2O	62	100/0	10/90	-
6	S	H	$ClTi(OiPr)_3$ (1)	THF	56	48/52	12/88	50/50
7	S	H	$ClTi(OiPr)_3$ (2→4)	THF	64	95/5	10/90	-
8	S	H	LDA[a]	THF	63	46/54	12/88	52/48
9	O	Ph	$ClTi(OiPr)_3$ (1→4)	Et_2O	57	90/10	38/62	22/78
10	O	Ph	LDA	Et_2O	60	0/100	-	37/63
11	O	Ph	$ClTi(OiPr)_3$ (1)	THF	48	0/100	-	35/65
12	O	Ph	$ClTi(OiPr)_3$ (2→4)	THF	53	95/5	30/70	-
13	O	Ph	$ClTi(OiPr)_3$ (2→4)	THF	47	0/100	-	5/95[b]
14	O	Ph	LDA[a]	THF	49	0/100	-	38/62
15	S	Ph	$ClTi(OiPr)_3$ (1→4)	Et_2O	29	70/30	50/50	12/88
16	S	Ph	$ClTi(OiPr)_3$ (1)	THF	69	0/100	-	83/17
17	S	Ph	$ClTi(OiPr)_3$ (2→4)	THF	32	83/17	45/55	15/85
18	S	Ph	$ClTi(OiPr)_3$ (2→4)	THF	35	0/100	-	5/95[c]
19	S	Ph	LDA[a]	THF	89	0/100	-	83/17

[a] The data are taken from ref. 8; [b] 22°C 24 h; [c] 22°C 3h.

The inspection of the table data shows that the lithium interference effect works only in THF when less than 2 equivalents of $ClTi(OiPr)_3$ are used, while in Et_2O 1 equivalent is sufficient (compare entries 6 and 8; 11 and 14; 16 and 19). Obviously the stronger solvating ability of THF relative to Et_2O prevents the shifting of the equilibrium to the titanium species and requires excess of titanating reagent.

Titanium oxoamide enolate reacts with cinnamic aldehyde 1,2-regioselectively, analogously to the parent lithium enolate (entries 1 and 2; 3 and 4). In all other cases, titanation of both amide and thioamide dramatically reverses (compare entries 9 and 10; 12 and 14; 15, 17 and 19) or reinforces (compare entries 5, 7 and 8) the regioselectivity course to the aldol addition. The thioamide gives greater proportion of the conjugate product than the oxoanalog in accordance with its softer character (compare entries 9 and 15; 12 and 17).[20] Concerning 1,4-diastereofacial selectivity, the *threo* form predominates in both cases (see entries 9, 15 and 17).However it is difficult to decide if it is a result of kinetic control since the lowering of the temperature or shortening of the reaction time strongly decreases the reaction yields and the proportion of 1,4 addition. The work at ambient temperature provides the *threo* isomer with high diastereoselectivity (entries 13 and 18).

Titanium "ate" complexes

Addition to cinnamic aldehyde and α,β-unsaturated ketones

Titanium "ate" complexes were prepared from lithium enolates by treating with equimolar quantity of $Ti(OiPr)_4$.[21] Their actual structure (coordination number and aggregation state) is currently unknown. Concerning the enolate double bond geometry, according to recent data[22] it remains unchanged during titanation.

The behaviour of the N,N-dimethylphenylacetamide and N,N-dimethylphenylthioacetamide titanium "ate" complexes was examined in Et_2O and THF. The kinetic origin of the diastereoisomeric ratios was unambiguously proved by control experiments carried out for a very short reaction time (15 sec). (Only decrease of the yields and no change in stereochemistry was observed). The data obtained are presented in **Table 2** and compared with the corresponding lithium precursors in the same solvent (the data in brackets). The results with lithium in Et_2O are newly obtained.

Table 2. Addition of N,N-Dimethylphenylacetamide (X = O) and N,N-Dimethylphenylthioacetamide (X = O) Enolate-$Ti(OiPr)_4$ "ate" Complexes to Cinnamic Aldehyde and α,β-unsaturated Ketones at -78°C.[a]

Entry	X	R'	Solvent	%	1,2/1,4	*erythro/threo*$_{1,2}$	*erythro/threo*$_{1,4}$
1	O	H	THF	65 (86)[b]	100/0 (100/0)	30/70 (27/73)	-
2	S	H	THF	67 (63)[c]	87/13 (46/54)	20/80 (12/88)	54/46 (52/48)
3	O	CH_3	Et_2O	81 (54)	40/60 (46/54)	72/28 (80/20)[e]	77/23 (36/64)
4	O	CH_3	THF	75 (58)	38/62 (40/60)	80/20 (75/25)[e]	78/22 (70/30)
5	S	CH_3	Et_2O	52 (49)	0/100 (0/100)	- -	90/10 (82/18)
6	S	CH_3	THF	64 (60)[d]	0/100 (5/95)	- -	89/11 (88/12)
7	O	Ph	Et_2O	79 (83)	0/100 (0/100)	- -	56/44 (36/64)
8	O	Ph	THF	90 (75)[b]	0/100 (0/100)	- -	56/44 (37/63)
9	S	Ph	Et_2O	50 (75)	0/100 (0/100)	- -	54/46 (38/62)
10	S	Ph	THF	64 (89)[c]	0/100 (0/100)	- -	87/13 (87/13)

[a] The data in brackets concern lithium enolates and are given for comparison; [b] ref. 4; [c] ref. 8; [d] ref. 23; [e] A/B ratio.

The regio- and diastereoselectivity of both amide and thioamide titanium "ate" complexes follow in general the behaviour of the lithium precursors. Being a softer nucleophile, the thioamide shows greater trend to 1,4-addition than the oxoanalog (compare entries 1 and 2; 3, 4 and 5, 6). Titanation does not alter the regioselectivity as far as benzalacetone and chalcone are concerned but significantly increases the 1,2 proportion with cinnamic aldehyde (entry 2).

Conjugate addition occurs with *erythro* diastereofacial selectivity which varies from poor with chalcone (entries 7-9; entry 10 is an exception) to moderate (entries 3 and 4) and high with benzalacetone (entries 5 and 6).The *erythro* proportion increases (in different extend) from lithium to titanium species (compare with the data in brackets) as well as from amide to thioamide (compare entries 3, 4 and 5, 6; 8 and 10). The solvent effect on the stereoselectivity, where it exists, (entries 3 and 4, lithium enolates and 9 and 10, both lithium and titanium species), is connected with increase of the *threo* form in Et_2O relative to THF.

Addition to E- and Z-configurated methyl cinnamate.

The data collected in **Table 3** are obtained under kinetic control conditions. The results with the lithium precursors are given for comparison. Since lithium species had been investigated in THF only, some additional experiments in Et_2O were performed.

The ethereal solvents show substantial effect on the lithium enolates stereochemistry. The change of THF to Et_2O is accompanied by increase of the *threo* form with ***E***-methyl cinnamate (compare entries 1-4 and 9-12, Li) to extend of braking the dependence on the acceptor geometry found before.[7] With ***Z***-acceptor the effect is the opposite (entries 5-8 and 13-16, Li) and in both cases the selectivity diminishes for bulkier donors (R = C_6H_{11}, i-C_3H_7).

The titanium "ate" complexes react 1,4-regioselectively. They have in the prevailing number of cases higher reactivity relative to the starting enolates. It is noteworthy that the lithium enethiolates failed to react and potassium gave poor yields.[8] Obviously, in appropriate cases titanation might serve as an important instrument in organic synthesis.

The solvent effect observed with lithium works only with the titanium species of the amides. Their stereochemical behaviour was found to parallel (in general) the parent lithium enolates. Thus, in THF (entries 3 and 4, Ti) the bulky amides (R = C_6H_{11}, i-C_3H_7) form with ***E***-methyl cinnamate preferentially *erythro* isomer, selectivity somewhat growing up in comparison with the case of lithium. When R is relatively small (R = CH_3, C_2H_5, entries 1 and 2) the *threo* form predominates. The stereochemical course with a ***Z***-acceptor (entries 5-8, Ti) favours the *threo* adduct and the selectivity is comparable to that in the case of lithium.

In Et_2O titanium "ate" complexes follow the lithium precursors towards the ***E***-acceptor (see entries 9-12, Ti), while with ***Z***-acceptors (entries 13-16, Ti) the sterically hindered amides give reversed ratios in favour of the *erythro* form.

The thioamide-Ti(OiPr)$_4$ "ate" complexes demonstrate by analogy with the potassium salts high *erythro* selectivity which does not depend on the solvent used and the electrophile geometry.

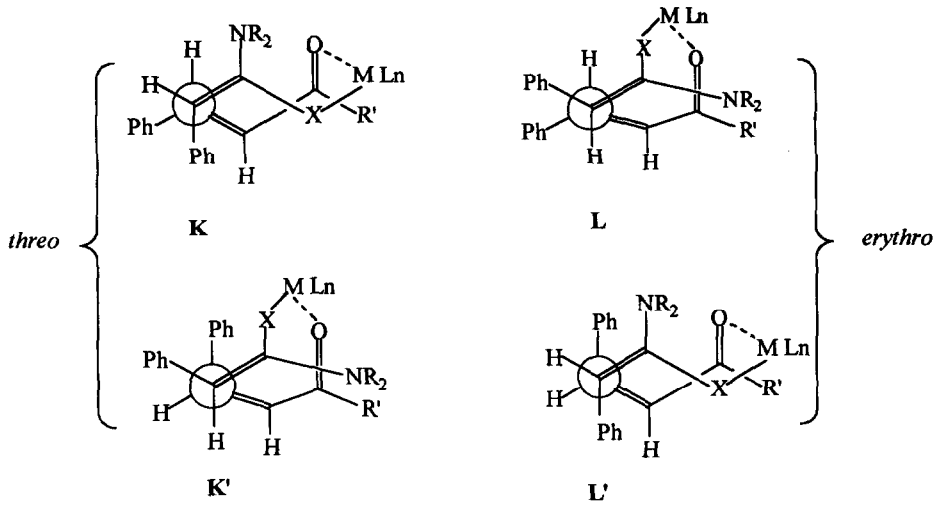
Table 3. Addition of N,N - Dialkylphenylacetamide (X = O) and N,N - Dialkylphenylthioacetamide (X = S) Enolate - $Ti(OiPr)_4$ "ate" Complexes to *Z* - and *E*-configurated Methyl Cinnamate at -40°C.

Entry	X	R	Confi-guration	Solvent	*erythro/threo* (%) Ti	*erythro/threo* (%) Li
1	O	CH_3	*E*	THF	17/83 (89)	47/53 (48)[a]
2	O	C_2H_5	*E*	THF	40/60 (78)	70/30 (43)
3	O	C_6H_{11}	*E*	THF	85/15 (86)	76/24 (59)[a]
4	O	i-C_3H_7	*E*	THF	84/16 (80)	78/22 (69)[a]
5	O	CH_3	*Z*	THF	5/95 (88)	0/100 (55)[a]
6	O	C_2H_5	*Z*	THF	5/95 (82)	6/94 (43)
7	O	C_6H_{11}	*Z*	THF	14/86 (72)	9/91 (46)[a]
8	O	i-C_3H_7	*Z*	THF	8/92 (80)	10/90 (57)[a]
9	O	CH_3	*E*	Et_2O	9/91 (92)	22/78 (67)
10	O	C_2H_5	*E*	Et_2O	29/71 (52)	28/72 (42)
11	O	C_6H_{11}	*E*	Et_2O	33/67 (85)	41/59 (47)
12	O	i-C_3H_7	*E*	Et_2O	37/63 (75)	38/62 (64)
13	O	CH_3	*Z*	Et_2O	5/95 (88)	10/90 (45)
14	O	C_2H_5	*Z*	Et_2O	15/85 (33)	5/95 (33)
15	O	C_6H_{11}	*Z*	Et_2O	60/40 (34)	40/60 (43)
16	O	i-C_3H_7	*Z*	Et_2O	70/30 (22)	38/62 (10)
17	S	CH_3	*E*	Et_2O	95/5 (59)	-
18	S	CH_3	*E*	THF	95/5 (45)	100/0 (23)[b]
19	S	C_6H_{11}	*E*	Et_2O	85/15 (52)	-
20	S	C_6H_{11}	*E*	THF	90/10 (42)	82/18 (18)[b]
21	S	i-C_3H_7	*E*	Et_2O	90/10 (60)	-
22	S	CH_3	*Z*	Et_2O	95/5 (24)	-
23	S	C_6H_{11}	*Z*	Et_2O	82/18 (59)	-
24	S	i-C_3H_7	*Z*	Et_2O	88/12 (67)	-
25	S	i-C_3H_7	*Z*	THF	86/14 (40)	-

[a] The data are taken from ref. 7; [b] Potassium enolates, ref. 8.

Two are the essential findings in the present study: 1/ the solvent effect over the adduct configuration in the case of oxoamides; 2/ similarity (in general) in the stereochemical behaviour of the titanium "ate" complexes and the corresponding lithium and potassium enolates.

Scheme 2. Reaction Transition States.



where: M = Li, Ln = solvent
M = Ti, Ln = Oi-C_3H_7 groups and solvent

The ethereal solvents can affect the reaction stereochemistry by either general solvation effect or involvement into the transition structure. The first assumption is not consistent with the experimental data since it would cause a later transition state and therefore enhanced diastereoselectivity in Et_2O.[24,25]

The solvent association to the transition structure has been considered to explain the stereochemistry of aldol reactions.[26] We assume binding of both Et_2O and THF to lithium. The smaller THF molecule does not alter steric priorities in the simplified cyclic models which explain well our previous results.[2-8] The larger Et_2O obviously becomes an important steric parameter and determines new diastereofacial selectivity.

This hypothesis seems to be in good agreement with the molecular models inspection. With *E*-configurated acceptors (benzalacetone, chalcone and methyl cinnamate) (**Scheme 2**, transition states **K** and **L**) the additional ligands cause stronger R/Solv. and R'/Solv. repulsive interactions in **K** thus favouring the *threo* form. With the bulky amides (R = C_6H_{11}, i-C_3H_7) the hindrance R'/Solv. in transition state **L** becomes significant and decreases the selectivity. The lack of the solvent effect when R' = Ph is probably due to the flat and sterically less demanding character of this conjugate group.

With *Z*-acceptor the accumulation of repulsive interactions in **K'** favours again the formation of the *threo* form. The increase of R lowers the selectivity by reasons analogous to these discussed in the previous paragraph.

The considerations above are supported by the fact that the reaction of lithium N,N-dicyclohexylphenylacetamide enolate with *E*-methyl cinnamate in i-Pr_2O favours additionally the *threo* isomer formation (*erythro/threo* = 17/83).

Our attempt to rationalise the behaviour of the titanium oxoamide "ate" complexes is based on the stereochemical similarity with the lithium precursors. This suggests the idea about the same chelated type of transition state where the isopropoxy groups have not special influence on the stereochemistry.[27] It is noteworthy that though the Ti-O bond (1.7-1.9Å) is shorter than the Li-O one (1.9-2.0Å) it may vary up to 2.1Å.[9] The possibility to explain the stereochemistry with the participation of a mixture of lithium and titanium enolates as a result of fast equilibrium[9] is unlikely (titanium enolates do not react with methyl cinnamate). The solvent most probably operates as in the case of lithium with hepta- or octa coordinated titanium.[28]

The behaviour of the thioamide titanium "ate" complexes seems more complicated. A cyclic transition state is in a good agreement with the strong *erythro* preference possibly conditioned by a more favourable mode of chelation with sulfur donors[29] but fails to explain the independence on the acceptor geometry as well as the lack of solvent effect in the predominant number of cases. Although all data are consistent with an open antiperiplanar transition state it is difficult at present to decide between the two reaction mechanisms.

The present study contributes to the elucidation of the synthetic potential and the stereochemical behaviour of titanium reagents in conjugate addition reactions. Titanation by means of Ti(Oi-Pr)$_4$ improves in general the reaction yields under close or higher level of diastereofacial selectivity. Though some uncertainties remain, possible transition state structures are discussed.

EXPERIMENTAL

All reactions were run in anhydrous conditions and under argon atmosphere. Tetrahydrofurane (THF) was freshly distilled from $LiAlH_4$ immediately prior to use. Diethyl ether (Et_2O) and diisopropyl ether (i-Pr_2O) were dried by standard techniques and stored over sodium wire. Melting points were determined on a Kofler apparatus and are uncorrected. IR spectra were measured on a Bruker JSS-113v spectrometer. ^{1}H NMR spectra were recorded on a Bruker WM-250 spectrometer; tetramethylsilane was used as internal standard and the chemical shifts are reported as δ-values (ppm). Analytical TLC was performed on Kieselgel Mark 60 F_{254} plates. *erythro/threo* ratios were determined by ^{1}H NMR using the difference in location of appropriate protons.

Stereostructural assignments

The diastereoisomeric pairs **3a, 3c, 3d, 4b-4g** and **4i-4l** ***erythro*** and ***threo***, their relative configurations and the ^{1}H NMR differences used for analysis of the reaction mixtures have been described in our previous papers.[4,8,30-32]

The relative stereochemistry of the diastereoisomeric *3-hydroxy-2,3,5-triphenyl-4-pententhioic acids dimethylamides* **3e *erythro* and 3e *threo*** was assigned using the ^{1}H NMR correlation between the H-4 and H-5 protons chemical shifts and the stereostructure found in the oxo- sery.[4] Thus, *erythro* configuration was attributed to the isomer with down-field shifting of the H-4 and H-5 protons.

The diastereoisomeric *3-acetyl-2,3-diphenyl-thiobutyric acids dimethylamides* **4a *erythro*** and **4a *threo*** have been obtained by Gaudemar et *al.*[23] but their configurations have not been assigned. In order to determine

the products stereostructure the ^1H NMR similarity with dimethylamides of the diastereoisomeric *4-methoxy-carbonyl-2,3-diphenyl- and 4-benzoyl-2,3-diphenyl-thiobutyric acids* was used.[8] *Erythro* configuration was attributed to the isomer with up-field location of the $CON(CH_3)_2$ signals.

General procedure for formation of titanium enolates 1a and titanium "ate" complexes 1b and their reactions with conjugate carbonyl compounds.

The lithium amide and thioamide enolates were generated using LDA or BuLi as it has been described before [4,8]. Thus, to 1.1 mmol of the metallating agent in 1 ml of the corresponding solvent 1 mmol of the donor in 1 ml of the same solvent was added dropwise and at stirring at appropriate temperature. After the metallation was completed the reaction mixture was cooled to -40°C and 1→4 equivalents (as described) of $ClTi(OiPr)_3$ (2M in Et_2O or THF) or 1 equivalent of neat $Ti(OiPr)_4$ was added. Stirring was continued for 30 min at -40°C in the case of titanium enolates and for 60 min in the case of titanium "ate" complexes. Then the mixture was allowed to reach the desired temperature and the solution of 1 mmol of the electrophile in 1 ml was added. At the end of the reaction time the mixture was quenched with an aqueous NH_4Cl solution. After standard working-up procedure the reaction yields were determined by means of preparative TLC.

3-Hydroxy-3-methyl-2,5-diphenyl-4-pentenoic acids dimethylamides (**3b A** and **3b B**).

Compound **3b A** and **3b B** were isolated by column chromatography (eluent ether : petroleum ether = 1 : 1) from reaction mixture obtained with titanium reagent in THF.

Compound **3b A:** m.p. 83-85°C (ether - hexane); R_f= 0.42 (ether : petroleum ether = 2 : 1); IR (3.10^{-3} mol/l in CCl_4), ν (cm^{-1}) : 1632 (CO amide), 3375 (OH--OC); ^1H NMR ($CDCl_3$) δ(ppm): 1.07(s, 3H, CH_3), 2.86, 2.91(d, 6H, $N(CH_3)_2$), 3.80(s, 1H, H-2), 6.37(s, 1H, OH), 6.37, 6.43(d, 1H, H-4, J = 15.9 Hz), 6.66, 6.72(d, 1H, H-5, J = 15.9 Hz), 7.18 - 7.43(m, 10H, $2xC_6H_5$); Found : C, 77.60 ; H, 7.50; $C_{20}H_{23}O_2N$ requires C, 77.64; H, 7.49.

Compound **3b B**: m.p. 136 -138°C (EtOH); R_f = 0.29 (ether : petroleum ether = 2 : 1); IR (3.10^{-3} mol/l in CCl_4) ν cm-1 : 1632 (CO amide), 3400 (OH--OC); ^1H NMR ($CDCl_3$) δ (ppm) : 1.56(s, 3H, CH_3), 2.91, 2.97 (d, 6H, $N(CH_3)_2$), 3.78(s, 1H, H-2), 5.93, 5.99(d, 1H, H-4, J = 16 Hz), 5.98(s, 1H, OH), 6.29, 6.36(d, 1H, H-5, J = 16 Hz), 7.13 - 7.49(m, 10H, $2xC_6H_5$); Found: C, 77.45; H, 7.45; $C_{20}H_{23}O_2N$ requires C, 77.64; H, 7.49.

3-Hydroxy-2,3,5-triphenyl-4-pententhioic acids dimethylamides (**3e *eryhtro*** and **3e *threo***).

The diastereoisomers **3e *erythro*** and **3e *threo*** were not isolated. All attempt for purification by column chromatography were accompanied by retrocondensation and coupling reaction of the starting thioamide. TLC and ^1H NMR data are taken from the crude reaction mixture obtained with titanium enolate and benzalacetone in Et_2O.

Compound **3e *erythro*** : R_f = 0.47(ether : petroleum ether = 3 : 2); ^1H NMR ($CDCl_3$) δ (ppm) : 3.23, 3.33(d, 6H, $N(CH_3)_2$), 4.57(s, 1H, H-2) 6.64, 6.70, 6.74, 6.80(dd, 2H, H-4 + H-5).

Compound **3e *threo*** : R_f = 0.41(ether : petroleum ether = 3 : 2); ^1H NMR ($CDCl_3$) δ (ppm): 3.36, 3.41(d, 6H, $N(CH_3)_2$), 4.87(s, 1H, H-2), 6.06, 6.12, 6.16, 6.22(dd, 2H, H-4 + H-5).

4-Acetyl-2,3-diphenyl-butiric acids dimethylamides (**4a *erythro*** and **4a *threo***).

Compound **4a *erythro*** was isolated from the reaction mixture obtained with lithium reagent at 22°C for 2h in THF (affording only conjugate additional adducts in ratio *erythro/threo* = 60/40) after recristallization from EtOH; m.p.: 190 - 192°C; R_f = 0.68 (ether); IR ($CHCl_3$) ν (cm^{-1}) : 1708 (CO ketone), 1640 (CO amide); ^1H NMR ($CDCl_3$) δ (ppm) : 1.79 (s, 3H, $COCH_3$), 2.39 - 2.61(m, 2H, H-4), 2.67, 2.82(d, 6H, $N(CH_3)_2$), 4.02 -

4.14(m, 2H, H-3 + H-2), 7.01 - 7.47(m, 10H, 2xC_6H_5). Found: C, 77.51; H, 7.60. $C_{20}H_{23}O_2N$ requires C, 77.64; H, 7.49.

Compound **4a *threo*** was isolated from the mother liquor by preparative TLC (ether); m.p.: 144-146°C (EtOH); R_f = 0.23(ether), IR ($CHCl_3$) ν (cm^{-1}): 1708(CO ketone), 1640(CO amide); ^1H NMR ($CDCl_3$) δ (ppm) : 2.01(s, 3H, CH_3), 2.87 - 3.05(m, 2H, H-4), 2.94(s, 6H, $N(CH_3)_2$), 3.83 - 3.93(m, 1H, H-3), 3.96, 4.00(d, 1H, H-2, J = 10.01 Hz), 6.94 - 7.29(m, 10H, 2xC_6H_5); Found: C, 77.60; H, 7.40; $C_{20}H_{23}O_2N$ requres C, 77.64; H, 7.49.

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