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Concerning the Diastereofacial Selectivity of the Reaction of (*E*)-β-Nitroenones with Ketone Enolates

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Abstract: Stereoselectivity of the reaction of acyclic ketone enolates with (*E*)-β-nitroenones was investigated according to the nature of the base used to accomplish deprotonation. The stereoselectivity and the regioselectivity of the reaction of ketone enolates with (*E*)-β-nitroenones could be enhanced by the use of trichlorotitanium enolates, which allowed the formation of diastereomeric mixture of (*E*)-3-hydroxy-5-nitroalk-4-enones **3** where the amount of product of (*l*) configuration is increased compared to results obtained with lithium enolates.

Introduction

Nitroalkenes are versatile synthetic intermediates[1] and have frequently been used in carbon-carbon bond forming reactions among which, reactions with bis-activated methylene compounds, ketone and ester enolates have been well documented.[2]

We have during last years reported a convenient procedure for the synthesis of β-nitroenones,[3] which are potentially useful intermediates for the preparation of functionalized nitro or nitrofree compounds.[4] We showed that bis-activated methylene compounds enolates entered α to the carbonyl functionality of β-nitroenones with high regioselectivity.[5] The behaviour of ketone and ester enolates was quite different.[6] Under kinetic control at -78°C reactions of ketone and ester enolates with β-nitroenones occured at the carbonyl group. When the temperature was allowed to warm up to -10°C before hydrolysis, only the Michael adducts on the α-nitroalkene moiety were obtained with ketone enolates, while complex mixtures were obtained with ester enolates (Scheme 1).

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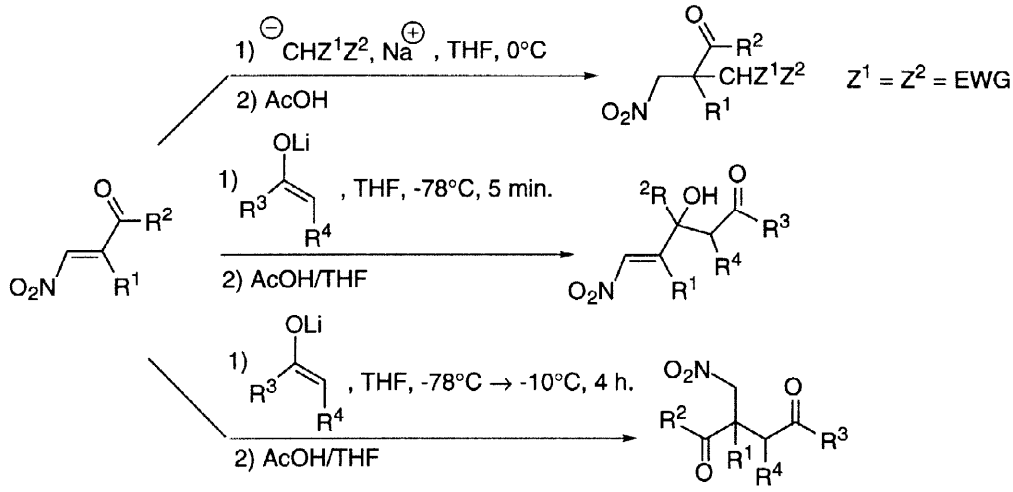
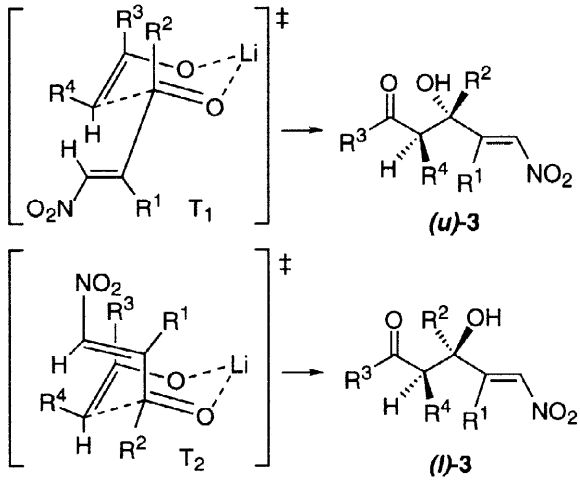
The stereoselectivity observed during the nucleophilic attack on the carbonyl group has been discussed according to enolates geometry, mainly (*E*) cyclic Li-enolates, and steric factors using a "pericyclic" chairlike six-membered ring transition state derived from the pioneering contribution of Zimmerman and Traxler (Scheme 2).[7]



Scheme 1



R^1	R^2	R^3 R^4	*u/l*
CH_3	CH_3	$(CH_2)_3$	70/30
CH_3	CH_3	$(CH_2)_4$	75/25
CH_3	CH_2CH_3	$(CH_2)_4$	44/56
CH_3	$(CH_2)_4CH_3$	$(CH_2)_4$	37/63
CH_3	$CH(CH_3)_2$	$(CH_2)_4$	0/100
CH_2CH_3	CH_3	$(CH_2)_4$	70/30

Scheme 2. Transition states for the reaction of cycloalkanones-Li-enolates with (*E*)-β-nitroenones

The diastereofacial selectivities were generally poor except in the case of hindered β-nitroenone bearing an *i*-Pr group on the carbonyl where the diastereomeric *u/l* ratio reached 0/100.

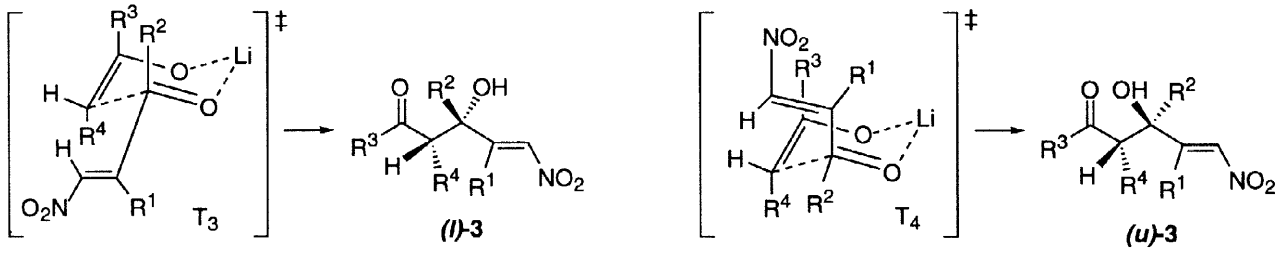
The relationship between enolate geometry and product stereostructure is well established and several types of metal enolates have been developed for the stereocontrolled synthesis of acyclic molecules. In this paper, we report our results on stereoselection in the reaction of acyclic lithium and trichlorotitanium enolates of ketones with (*E*)-β-nitroenones.

Results and Discussion

We began our investigations by surveying the stereochemistry of the products resulting from the addition of preformed lithium enolates of pentan-3-one or 2-methylpentan-3-one using different bases such as lithium diisopropylamide (LDA), lithium 2,2,6,6-tetramethylpiperidide (LTMP) and lithium hexamethyldisilazine (LHMDS). The nature of the base used to accomplish deprotonation influences considerably the *E/Z* ratio in the enolates produced and consequently the stereostructure of the formed products.[8] As it was described by Heathcock, LDA and LTMP give more *E* enolate, while LHMDS gives more *Z* enolate.[8f] Results obtained for different β-nitroenones are collected in Table 1. Reaction stereoselectivity was determined by ^{1}H NMR analyses of the crude reaction products. The chemical shift of the hydrogens of the methyl group adjacent to the hydroxyl group was higher in *l*-**3** than in *u*-**3** products by comparison with the chemical shift observed for the hydrogen adjacent to the hydroxyl group in classical aldol reaction $\delta(l(H)) > \delta(u(H))$.[6,9] It is clear from Table 1 that the *E/Z* ratio of the enolate has a substantial effect on the stereochemical outcome of the reaction.

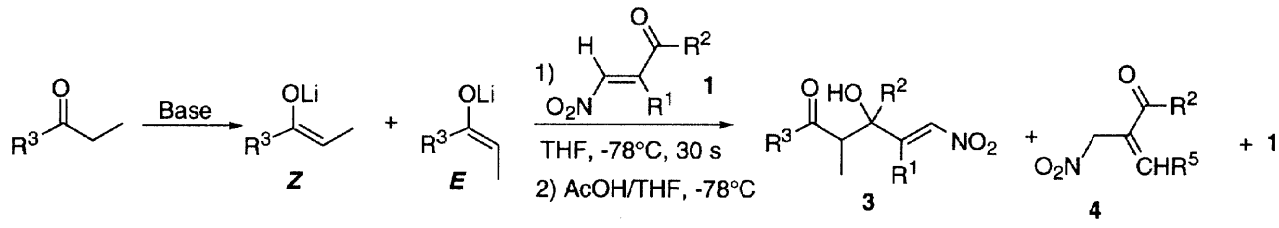
For less hindered β-nitroenones ($R^2 = CH_3$), the use of LDA or LTMP, giving more *E* enolate, produces *u/l* mixtures where the products of unlike configuration slightly predominate (entries 1, 2, 7, 8 and 13), while the use of LHMDS, giving more *Z* enolate, produces preferentially *u/l* mixtures where the products of like configuration predominate (entries 3, 6 and 9). An increase of the size of R^2 from Me to larger Et or *i*-Pr changes the diastereoselectivity in favor of the (*l*)-products (entries 4, 5, 6, 11 and 12). These results are compatible with the six center transition state previously reported.[6] For *E* enolates, there is an important interaction between R^3 and R^2. Thus when R^2 = Me, the transition state T_1 has a lower energy than T_2, and affords mostly the unlike stereomer. When R^2 is larger, the like stereomer can be seen to arise from the transition state T_2, which has the largest substitutent in quasi equatorial conformation (Scheme 2). In a similar manner, stereoselectivities observed with *Z* enolates can be explained by transition states T_3 and T_4 (Scheme 3).

When R^2 = Me, transition state T_3 is preferred in order to minimize diaxial interactions with R^3, while with larger R^2 substituents (like Et or *i*-Pr) transition state T_4 is preferred.



Scheme 3. Transition states for the reaction of (*Z*)-Li-enolates with (*E*)-β-nitroenones

Table 1. Effect of lithium enolate geometry on the stereostructure of products **3**

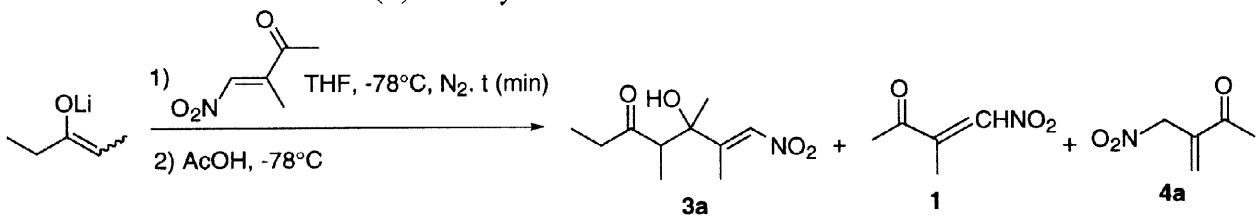


Entry	Product	Base	*E*/*Z*[a]	R^1	R^2	R^3	R^5	**3** Yield (%)[b]	**3** Diastereomeric ratio[c,d]	Relative ratio of products[d] **3**	(*E*)-**1**	(*Z*)-**1**	**4**
1	**3a**	LDA	70/30	CH_3	CH_3	CH_2CH_3	H	98	52/48	100	0	0	0
2	**3a**	LTMP	80/20	CH_3	CH_3	CH_2CH_3	H	85	69/31	87	9	3	1
3	**3a**	LHMDS	34/66	CH_3	CH_3	CH_2CH_3	H	84	46/54	87	13	0	0
4	**3b**	LDA	70/30	CH_3	CH_2CH_3	CH_2CH_3	H	62	22/78	62	23	11	4
5	**3b**	LTMP	80/20	CH_3	CH_2CH_3	CH_2CH_3	H	40	30/70	42	27	15	16
6	**3b**	LHMDS	34/66	CH_3	CH_2CH_3	CH_2CH_3	H	88	6/94	88	8	4	0
7	**3c**	LDA	70/30	CH_2CH_3	CH_3	CH_2CH_3	CH_3	96	53/47	100	0	0	0
8	**3c**	LTMP	80/20	CH_2CH_3	CH_3	CH_2CH_3	CH_3	89	54/46	89	5	6	0
9	**3c**	LHMDS	34/66	CH_2CH_3	CH_3	CH_2CH_3	CH_3	78	33/67	78	14	8	0
10	**3d**	LDA	60/40	CH_3	CH_3	$CH(CH_3)_2$	H	88	47/53	88	7	5	0
11	**3e**	LDA	60/40	CH_3	CH_2CH_3	$CH(CH_3)_2$	H	82	17/81	86	6	8	0
12	**3f**	LDA	60/40	CH_3	$CH(CH_3)_2$	$CH(CH_3)_2$	H	6	0/100	8	43	37	16
13	**3g**	LDA	60/40	CH_2CH_3	CH_3	$CH(CH_3)_2$	CH_3	80	60/40	82	8	10	0

[a] According to reference 8f. [b] Isolated yields of adducts (*l*) and (*u*)-**3**. [c] Assumed to be *u*/*l* ; for this assignment see text. [d] Determined from the 400 MHz ^{1}H NMR analysis of the crude products.

Contrary to the results obtained in our previous paper,[6] Michael addition products have never been detected after 30 s in the crude reaction mixture. Only starting (*E*)-β-nitroenone and various amounts of isomerized β-nitroenone ((*Z*)-β-nitroenone and α-(nitromethyl)enone **4**) were observed in some cases. In order to investigate the mechanism of formation of these compounds, we examined ratio of products resulting from the reaction of pentan-3-one lithium enolate with 3-methyl-4-nitrobut-3-en-2-one with time. The results are summarized in Table 2.

Table 2. Products formed by reaction of pentan-3-one lithium enolate and (*E*)-3-methyl-4-nitrobut-3-en-2-one with time

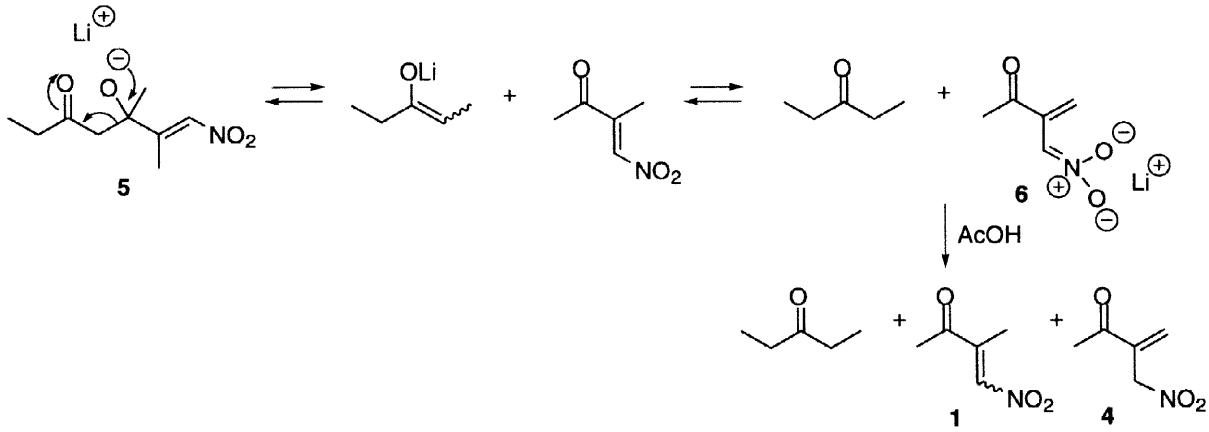


3a **1** **4a**

Entry	t (min)	**3** *u/l*	Relative ratio of products[a]			
			3	**1*E***	**1*Z***	**4**
1	0.5	52/48	100	0	0	0
2	10	61/39	90	7	2	1
3	60	59/41	58	29	9	5
4	120	59/41	40	40	12	8
5	180	60/40	6	54	18	21

[a] Determined from the 400 MHz ^{1}H NMR analyses of the crude products.

It is clear from Table 2 that ketolates **5**, initially formed, undergo retroketolization to afford more stable compound which could be the nitronate **6** resulting from the deprotonation of the starting β-nitroenone by lithium enolate. Quenching with acetic acid allows to obtain β-nitroenone with partial loss of the carbon-carbon double bond geometry and α-(nitromethyl)enone **4** (Scheme 4).



5 **6** **1** **4**

Scheme 4

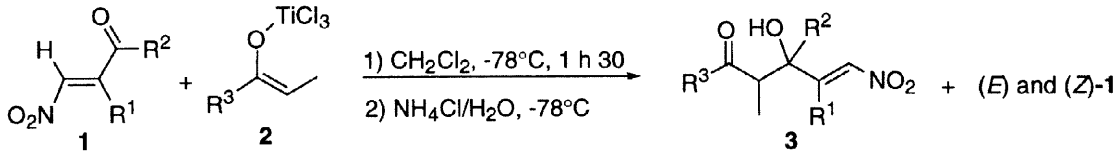
Explanations for these differences in reactivity may lie in the fact that disubstituted enolates derived from pentan-3-one are less nucleophilic and more basic than the enolates derived from alkylmethylketones previously studied.[6]

Over the last decade, the stereochemical outcome of the aldol reaction has been improved through the introduction of architecturally refined enolate metal centers among which boron enolates have been well documented.[10] All attempts to use such enolates failed and prompted us to investigate titanium enolates which are also described to provide high levels of stereoselection.[11]

Kuwajuma has reported that trichlorotitanium enolates exhibit highly erythro selective aldol reaction irrespective of their (Z)-geometry.[11b] The conventional chair transition states fail to offer adequate explanations and a new boat transition state has been proposed to explain these stereoselectivities. Taken into account these results, we decide to exploit the potential advantages of titanium enolates to improve the stereocontrol of the reaction of ketone enolates with β-nitroenones.

Sequential addition of 1.1 eq. of $TiCl_4$ and 1.2 eq. of triethylamine to a cold (-78°C) solution of the ketone in CH_2Cl_2, according to Harrison procedure, [11c] allowed the formation of (Z)-trichlorotitanium enolates. Their reaction with (E)-β-nitroenones were generally very clean compared to those with lithium enolates. The results are summarized in Table 3. Ketols **3** were prepared in good yields ranging from 50 to 99 % using 1.3 eq. of titanium enolate excepted compounds **3f** and **3g** obtained respectively with 13 and 12 % yields. These compounds were prepared in better yields, respectively 30 and 38 %, using 2 eq. of enolate.

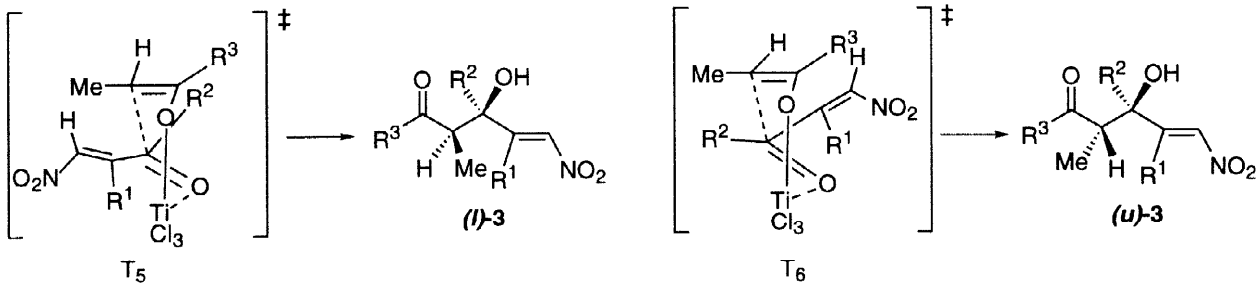
Table 3. Adducts **3** prepared from (E)-β-nitroenones **1** and trichlorotitanium enolates **2**



Entry	Product	R^1	R^2	R^3	3		Relative ratio of products[c]		
					Yield (%)[a]	Diastereomeric ratio[b,c]	3	(E)-1	(Z)-1
1	**3a**	CH_3	CH_3	CH_2CH_3	87	20/80	93	7	0
2	**3b**	CH_3	CH_2CH_3	CH_2CH_3	85	21/79	88	12	0
3	**3c**	CH_2CH_3	CH_3	CH_2CH_3	65	16/84	70	29	1
4	**3d**	CH_3	CH_3	$CH(CH_3)_2$	99	50/50	99	1	0
5	**3e**	CH_3	CH_2CH_3	$CH(CH_3)_2$	78	25/75	78	12	0
6	**3f**	CH_3	$CH(CH_3)_2$	$CH(CH_3)_2$	30[d]	0/100	35	63	2
7	**3g**	CH_2CH_3	CH_3	$CH(CH_3)_2$	50	60/40	53	47	0
8	**3h**	CH_3	$CH(CH_3)_2$	CH_2CH_3	38[d]	0/100	42	56	2

[a] Isolated yields of adducts (*l*) and (*u*)-**3**. [b] Assumed to be *u*/*l* ; for this assignment see text. [c] Determined from the 400 MHz ^1H NMR analysis of the crude products. [d] 2 Equivalents of titanium enolates were used instead of 1.3.

The stereoselectivity is in favour of the like stereomer except in the case of the addition of the trichlorotitanium enolate of 2-methylpentan-3-one to (*E*)-3-ethyl-4-nitrobut-3-en-2-one (entry 8). Stereochemical outcome of these additions can be rationalized by considering the boat transition states, first proposed by Kuwajima,[11a] as the lowest energy transition states. Such transition states seem reasonable according to the relatively long Ti-O bond length,[12] the well established Bürgi-Dunitz trajectory in the nucleophilic attack to a carbonyl group[13] and orbital interactions favoring the "endo" arrangement of the reactants[14]. Proposed transition states T_5 and T_6 are depicted in Scheme 5.



Scheme 5. Transition states for the reaction of (*Z*)-trichlorotitanium enolates with (*E*)-β-nitroenones

The disposition of the reactants in these boat TS makes the like selectivity of T_5 more favorable than the alternative T_6 in which steric interactions between R^2 and Me are more important. Introduction of an isopropyl group (R^2 = *i*-Pr) raises the energy of T_6 compared to T_5, which gives exclusively the (*l*)-stereomer. In any case, in spite of a small excess of triethylamine, no α-(nitromethyl)enone **4** was detected. Only starting (*E*)-β-nitroenone and, sometimes, small amounts of (*Z*)-β-nitroenones were obtained as by-products. A comparison of the reactions of trichlorotitanium and lithium enolates with the same β-nitroenones reveals that the formers are less reactive and more regioselective than the other ones. We speculate that this lower reactivity permits to avoid the formation of isomerized products resulting from the deprotonation of β-nitroenones. Retroketolization, used to explain the presence of β-nitroenone, seems not likely under these conditions according to the fact that low yields of products were obtained when the reactions were carried out for shorter times.

Conclusion

The previous studies highlight the regio and stereocontrol of reactions of (*E*)-β-nitroenones with lithium and trichlorotitanium acyclic ketone enolates. The observed stereochemistry could be explained using chair or boat transition states according, respectively, to *E*/*Z* ratio of different preformed lithium enolates and *Z* geometry of titanium enolates. Although the later are less reactive, they allow a better regiocontrol and stereocontrol of the reaction affording mainly (*E*)-3-hydroxy-5-nitroalk-4-enones.

Experimental section

All experiments were performed under N_2. Commercially available reagents were purchased from Aldrich or Lancaster. The ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AM 400 or Bruker AC 250 spectrometers and the chemical shifts are reported as δ values with units of ppm. ^1H NMR spectra are referenced to TMS at 0.00 ppm as an internal standard and ^{13}C NMR spectra are referenced to $CDCl_3$ at 77.00 ppm. IR spectra were recorded as thin films between NaCl plates on a Mattson Genesis Series FTIR. All reactions were monitored by TLC carried out on Macherey-Nagel SIL G/UV_{254} silica gel plates. Separations were accomplished by column chromatography on silica gel 60 (70-230 mesh) at normal pressure. All organic solvents were appropriately dried and purified before use.

General procedure for the addition of lithium enolate of ketones with (*E*)-β-nitroenones (3). To a solution of 2.06 ml (3.3 mmol) of *n*-BuLi 1.6 M in hexanes in 10 ml of dry THF at -50°C was added dropwise 333 mg (3.3 mmol) of diisopropylamine in 1 ml of THF before cooling to -78°C. The temperature was slowly raised to 20°C. 3.15 mmol of the ketone in 1 ml of THF was added dropwise over 1 min. After addition, the mixture was stirred at -78°C for 30 min and then 3.10 mmol of (*E*)-β-nitroenone in 15 ml of THF was added rapidly by means of a syringe. After 30 s, 744 mg of AcOH (12.4 mmol) in 5 ml of THF was added and the reaction was warmed to room temperature. The reaction mixture was diluted with water (30 ml), extracted with CH_2Cl_2 (4 x 35 ml). The combined extracts were washed with 5% aqueous $NaHCO_3$ solution (45 ml), water (45 ml), brine (45 ml) and dried over $MgSO_4$. Evaporation of the solvent afforded crude material which was analyzed by ^1H NMR. Purification of 3-hydroxy-5-nitroalk-4-enones was achieved by column chromatography on silica gel using AcOEt/hexane (5/95) as eluent.

A similar procedure was employed for the condensation of lithium enolate formed with lithium 2,2,6,6-tetramethylpiperidide (LTMP). For lithium hexamethyldisilylazine (LHMDS), the reaction with ketones was run for 1 h at -78°C instead of 30 min in order to assure complete deprotonation.

General procedure for the addition of trichlorotitanium enolates of ketones with (*E*)-β-nitroenones. To a solution of 2.6 mmol of ketone (for compounds **3f** and **3h**, 4 mmol of ketone were used) in 6 ml of dry CH_2Cl_2 at -78°C was added successively 2.86 mmol of $TiCl_4$ (4.4 mmol for **3f** and **3h**) followed after 15 min by 3.12 mmol of triethylamine (4.8 mmol for **3f** and **3h**) in 1 ml of CH_2Cl_2. After 1 h 30 min of stirring at -78°C, 2.0 mmol of (*E*)-β-nitroenone in 6 ml of CH_2Cl_2 was added rapidly by means of a syringe. After 1 h 30 min, 12 ml of saturated aqueous NH_4Cl solution was added and the reaction mixture was warmed to room temperature. The reaction mixture was then extracted with CH_2Cl_2 (4 x 20 ml). The combined organic layers were washed with brine (10 ml) and dried over $MgSO_4$. Evaporation of CH_2Cl_2 afforded crude material

which was analyzed by ^{1}H NMR before purification by chromatography on silica gel using AcOEt/hexane (5/95) as eluent.

(*E*)-3-Hydroxy-2,3,4-trimethyl-1-nitrohept-1-en-5-one (3a): oil; IR (film): 3346, 3127, 1695, 1517 and 1347 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ (*u*) stereomer: 7.32 (brs, 1H), 4.43 (OH), 3.05 (q, J = 7.0 Hz, 1H), 2.80-2.30 (m, 2H), 2.16 (s, 3H), 1.30 (s, 3H), 1.27 (d, J = 7.0 Hz, 3H), 1.00 (t, J = 7.0 Hz, 3H); (*l*) stereomer: 7.42 (brs, 1H), 4.72 (OH), 2.93 (q, J = 7.0 Hz, 1H), 2.80-2.30 (m, 2H), 2.11 (s, 3H), 1.37 (s, 3H), 1.10 (t, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*u*) stereomer: 216.0, 156.7, 136.7, 76.6, 49.2, 36.6, 27.1, 14.6, 11.9, 7.6; (*l*) stereomer: 218.4, 152.6, 137.3, 76.3, 48.7, 37.7, 26.5, 12.9, 12.7, 7.6. Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.6; H, 7.8; N, 6.3.

(*E*)-3-Ethyl-3-hydroxy-2,4-dimethyl-1-nitrohept-1-en-5-one (3b): oil; IR (film): 3440, 3120, 1695, 1631, 1531 and 1350 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (*u*) stereomer: 7.27 (s, 1H), 4.24 (OH), 3.03 (q, J = 7.1 Hz, 1H), 2.72-2.31 (m, 2H), 2.13 (s, 3H), 1.90-1.40 (m, 2H), 1.23 (d, J = 7.1 Hz, 3H), 1.01 (t, J = 7.5 Hz, 3H), 0.78 (t, J = 7.5 Hz, 3H); (*l*) stereomer 7.38 (s, 1H), 4.46 (OH), 2.89 (q, J = 6.8 Hz, 1H), 2.69 (qd, J = 18.6 and 7.3 Hz, 1H), 2.54 (qd, J = 18.1 and 7.3 Hz, 1H), 2.05 (s, 3H), 1.75-1.45 (m, 2H), 1.09 (t, J =7.3 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.79 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*u*) stereomer: 218.1, 154.7, 138.1, 79.1, 49.4, 36.7, 32.9, 15.6, 11.8, 8.0, 7.4; (*l*) stereomer: 218.9, 150.7, 138.7, 79.5, 48.7, 38.1, 31.0, 14.2, 12.8, 7.8, 7.6. Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.9; H, 8.0; N, 6.1.

(*E*)-3-Hydroxy-3,4-dimethyl-2-ethyl-1-nitrohept-1-en-5-one (3c): oil; IR (film): 3460, 3120, 1694, 1631, 1521 and 1347 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (*u*) stereomer: 7.21 (s, 1H), 3.62 (OH), 3.03 (q, J = 7.1 Hz, 1H), 2.80-2.25 (m, 4H), 1.32 (s, 3H), 1.27 (d, J = 7.1 Hz, 3H), 1.12 (t, J = 7.3 Hz, 3H), 1.01 (t, J = 7.5 Hz, 3H); (*l*) stereomer 7.36 (s, 1H), 4.63 (OH), 2.93 (q, J = 7.1 Hz, 1H), 2.80-2.25 (m, 4H), 1.39 (s, 3H), 1.19 (t, J = 7.5 Hz, 3H), 1.11 (t, J = 7.3 Hz, 3H), 1.03 (d, J = 7.1 Hz, 3H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (*u*) stereomer: 217.8, 162.5, 143.6, 76.6, 49.7, 36.9, 24.4, 22.6, 13.5, 11.9, 7.4; (*l*) stereomer: 218.3, 158.2, 137.3, 76.4, 48.9, 37.7, 26.4, 20.1, 13.2, 13.0, 7.5. Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.7; H, 8.0; N, 6.0.

(*E*)-3-Hydroxy-2,3,4,6-tetramethyl-1-nitrohept-1-en-5-one (3d): oil; IR (film): 3446, 1695, 1635, 1517 and 1351 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (*u*) stereomer: 7.30 (s, 1H), 4.65 (OH), 3.15 (q, J =

4.0 Hz, 1H), 2.72-2.61 (m, 1H), 2.18 (s, 3H), 1.33 (s, 3H), 1.29 (d, J = 8.0 Hz, 3H), 1.12 (d, J = 4.0 Hz, 3H), 1.05 (d, J = 4.0 Hz, 3H); (*l*) stereomer: 7.45 (s, 1H), 4.85 (OH), 3.04 (q, J = 8.0 Hz, 1H), 2.84-2.72 (m, 1H), 2.13 (s, 3H), 1.37 (s, 3H), 1.18 (d, J = 8.0 Hz, 3H), 1.16 (d, J = 8.0 Hz, 3H), 1.04 (d, J = 8.0 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*u*) stereomer: 221.4, 156.4, 137.7, 76.7, 47.9, 42.0, 26.8, 18.4, 17.8, 15.8, 12.9; (*l*) stereomer: 221.2, 152.4, 137.4, 76.4, 47.3, 41.4, 27.2, 18.3, 18.1, 14.6, 12.2. Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.6; H, 8.1; N, 5.7.

(*E*)-3-Ethyl-3-hydroxy-2,4,6-trimethyl-1-nitrohept-1-en-5-one (3e): oil; IR (film): 3446, 1695, 1635, 1517 and 1351 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (*u*) stereomer: 7.39 (s, 1H), 4.56 (OH), 3.01 (q, J = 7.0 Hz, 1H), 2.86-2.63 (m, 1H), 2.07 (s, 3H), 1.77-1.60 (m, 1H), 1.58-1.40 (m, 1H), 1.16 (d, J = 5.0 Hz, 3H), 1.14 (d, J = 5.0 Hz, 3H), 1.02 (d, J = 7.5 Hz, 3H), 0.80 (t, J = 7.5 Hz, 3H); (*l*) stereomer: 7.23 (s, 1H), 4.62 (OH), 3.13 (q, J = 7.1 Hz, 1H), 2.70-2.57 (m, 1H), 2.14 (s, 3H), 1.90-1.77 (m, 1H), 1.55-1.42 (m, 1H), 1.25 (d, J = 7.1 Hz, 3H), 1.11 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H), 0.79 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*u*) stereomer: 221.8, 154.4, 138.3, 79.2, 48.2, 41.5, 32.9, 18.0, 17.8, 14.9, 12.1, 8.1; (*l*) stereomer: 221.3, 150.5, 138.9, 79.6, 47.5, 42.3, 31.2, 18.1, 17.8, 14.3, 13.0, 7.9. Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.2; H, 8.70; N, 5.76. Found: C, 59.0; H, 8.8; N, 5.7.

(*E*)-3-Hydroxy-2,4,6-trimethyl-3-isopropyl-1-nitrohept-1-en-5-one (3f): oil; IR (film): 3444, 1694, 1638, 1517 and 1350 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (*l*) stereomer: 7.39 (s, 1H), 4.99 (OH), 3.14 (q, J = 7.0 Hz, 1H), 2.72-2.50 (m, 1H), 2.10 (s, 3H), 1.99-1.88 (m, 1H), 1.23 (d, J = 7.0 Hz, 3H), 1.18 (d, J = 2.8 Hz, 3H), 1.16 (d, J = 2.6 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*l*) stereomer: 221.8, 152.3, 138.5, 82.2, 45.5, 42.4, 35.9, 18.8, 18.5, 18.2, 18.1, 15.2, 14.6. Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.6; H, 8.8; N, 5.5.

(*E*)-3-Hydroxy-3,4,6-trimethyl-2-ethyl-1-nitrohept-1-en-5-one (3g): oil; IR (film): 3446, 1695, 1635, 1517 and 1351 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ (*u*) stereomer: 7.16 (s, 1H), 4.70 (OH), 3.15 (q, J = 7.1 Hz, 1H), 3.00-2.80 (m, 1H), 2.70-2.57 (m, 1H), 2.32-2.20 (m, 1H), 1.34 (s, 3H), 1.26 (d, J = 7.1 Hz, 3H), 1.18 (t, J = 7.3 Hz, 3H), 1.09 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H); (*l*) stereomer 7.39 (s, 1H), 4.75 (OH), 3.04 (q, J = 7.1 Hz, 1H), 2.82-2.65 (m, 3H), 1.37 (s, 3H), 1.20 (t, J = 7.5 Hz), 1.17 (d, J = 7.1 Hz, 3H), 1.15 (d, J = 7.5 Hz, 3H), 1.03 (d, J = 7.1 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*u*) stereomer: 221.3, 162.3, 136.7, 76.8, 48.6, 41.7, 24.3, 22.5, 18.3, 17.9, 13.8, 12.4; (*l*) stereomer: 221.5, 158.1, 137.5, 76.7, 47.6, 42.2, 26.8, 21.5, 18.4, 17.8, 13.5, 13.5. Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.4; H, 8.8; N, 5.8.

(*E*)-3-Hydroxy-2,4-dimethyl-3-isopropyl-1-nitrohept-1-en-5-one (3h): oil; IR (film): 3460, 3120, 1694, 1631, 1521 and 1347 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ (*l*) stereomer: 7.42 (brs, 1H), 5.13 (OH), 2.97 (q, J = 7.5 Hz, 1H), 2.70-2.26 (m, 2H), 2.10 (s, 3H), 2.02-1.88 (m, 1H), 1.09 (t, J = 7.5 Hz, 3H), 1.02 (d, J = 7.5 Hz, 3H), 0.87 (d, J = 7.5 Hz, 3H), 0.83 (d, J = 7.5 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (*l*) stereomer: 218.6, 152.4, 138.5, 81.9, 46.7, 37.2, 36.0, 18.7, 18.4, 14.6, 13.8, 7.6. Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.2; H, 8.6; N, 5.5.

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