# Addition of Ketone and Ester Lithium Enolates to (*E*)-β-Nitroenones

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Under kinetic control at −78 °C, reactions of ketone or ester lithium enolates with (*E*)-β-nitroenones **2** occurred at the carbonyl group giving (*E*)-3-hydroxy-5-nitroalk-4-enones **6** or (*E*)-3-hydroxy-5-nitroalk-4-enoates **13**, respectively, with good regioselectivity. When the temperature of the reaction between **2** and lithium ketone enolates was allowed to warm up to −10 °C before hydrolysis, solely the 2-(nitromethyl) 1,4-diketones **8** were obtained. Steric factors which might influence the observed stereoselectivities during the nucleophilic attack on β-nitroenones are discussed.

## Introduction

Nitroalkenes are potentially useful substrates in carbon–carbon bond-forming reactions and have frequently been used in organic synthesis.[1] Their reactions with ketone and ester enolates have been widely investigated during recent years.[2] The many further transformations possible on either the intermediate nitronate or the γ-nitro carbonyl derivative obtained after hydrolysis make these compounds attractive synthetic intermediates.[3]

As reported in our previous papers, we have investigated a method for the preparation of β-nitroenones **2** which involves the regioselective ring-opening of nitroepoxides **1** with silica gel or aluminum isopropoxide, followed by oxidation of the γ-hydroxy-α-nitroalkenes thus obtained with PCC (**1** → **2**, Scheme 1).[4] Later, we showed that reactions of compounds **2** with enolates of bis-activated methylene compounds[5] with unsaturated alkoxides[6] and with thiophenolate[7] proceeded smoothly. These nucleophiles entered α to the carbonyl functionality with high regioselectivity (**2** → **3**, Scheme 1).

The potential utility of the obtained adducts **3** has been demonstrated by the synthesis of heterocycles containing a 2-isoxazole moiety (e.g. 6,6-disubstituted furo[3,4-*c*]-isoxazoles, 7,7-disubstituted pyrano[3,4-*c*]isoxazoles, or 5-hydroxy-4-(phenylthio)-2-isoxazoline 2-oxides) that can be used for further structural modifications.[6,7]

As an extension of this work into other useful synthetic areas, we have initiated the study of the addition of more reactive nucleophiles, namely the lithium enolates of esters and ketones, to β-nitroenones. However, a key issue needed to be addressed: will the carbonyl function compete with the nitroalkene, and if this is the case, will it be possible to control the regioselectivity of the reactions? Our interest in such work was motivated by the versatility of the nitro group, which could provide a tool for further interesting transformations of the resulting addition compounds.

## Results and Discussion

The lithium enolates **4**, generated from the corresponding ketones and LDA, reacted with the (*E*) isomer (>97% according to $^1$H NMR analysis) of β-nitroenones **2** in THF at −78 °C to yield, after immediate hydrolysis with acetic acid at −78 °C, products **6** resulting from addition to the carbonyl group (Table 1). Smaller quantities of the Michael adduct **8** were also formed (less than 5% from unhindered ketones, up to 22% from cyclohexanone enolate). The 3-hydroxy-5-nitroalk-4-enones **6** were isolated mainly as the more stable (*E*) isomers ($^1$H NMR: vinylic proton in the 7.38–7.27 ppm region) but small amounts of (*Z*) isomers ($^1$H NMR: vinylic proton in the 6.65–6.51 ppm region) were also obtained (always less than 5% according to the $^1$H NMR spectra). In some cases, the $^1$H NMR spectra of the crude reaction products also indicated the presence of the (*Z*) isomer (δ vinylic proton = 6.80 ppm) of the β-nitroenone **2** (no (*E*) starting material remaining). These results imply an equilibrium involving either the nitronates **7** or, more probably, the epoxides **9** (Scheme 2).

On the other hand, when the temperature was gradually (4 h) allowed to increase to −10 °C before quenching, only compound **8**, the Michael adduct on the nitroalkene functionality, was isolated (Table 1). Transformation of

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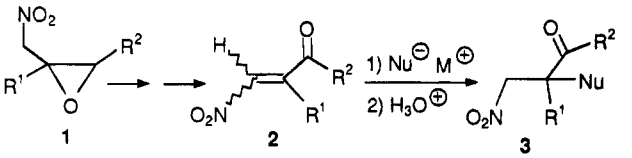
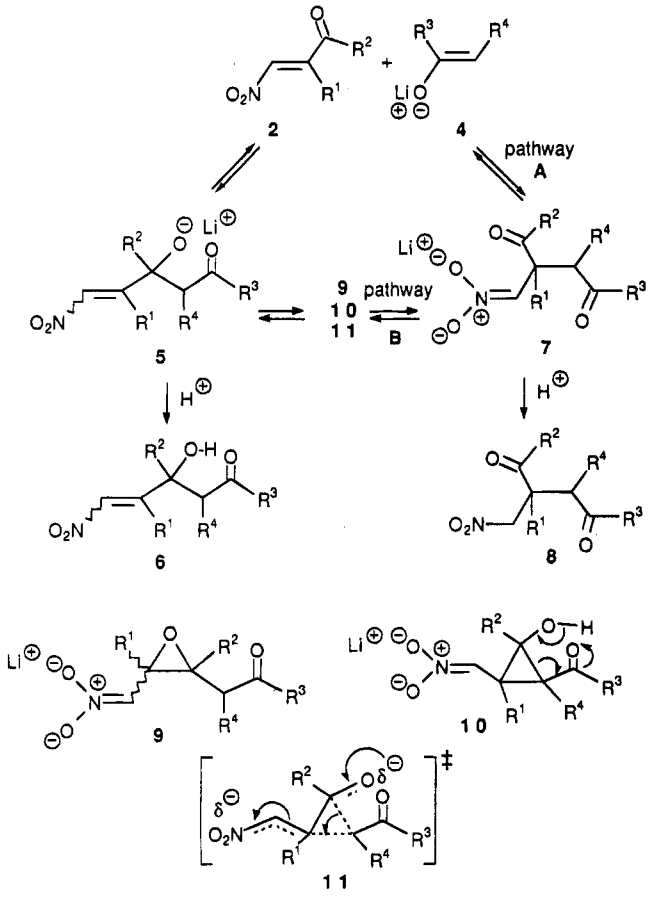
**Scheme 1**



$R^1$, $R^2$ = alkyl

$Nu^{\ominus}M^{\oplus}$ = $NaCR^3Z^1Z^2$, Na(K)OR or $(Et_3NH)SPh$ with $R^3$ = H, $CH_3$ or OAc and $Z^1$, $Z^2$ = EWG

**Scheme 2. Proposed Mechanism for the Addition of Ketone Lithium Enolates to (*E*)-β-Nitroenones**



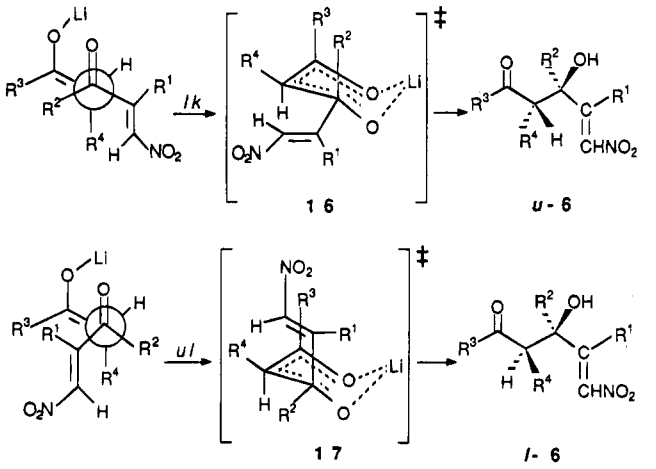
**5** to **7** could be occurring either *via* **2** and **4** (pathway A, Scheme 2) or by a process involving the epoxide **9** or cyclopropanic structures such as **10** or **11** (pathway B).

In a similar manner, when (*E*)-β-nitroenones **2** were treated with lithium ester enolates **12** under kinetic control (5 min, −78 °C), the (*E*)-3-hydroxy-5-nitroalk-4-enoates **13** were obtained as the sole or the main products (Table 2).

Contrary to the results obtained with the ketone enolates, adducts **13** were also obtained from the lithium ester enolates **12** at −10 °C after 4 h. Increasing the reaction time to 12 h at room temperature led to more complex mixtures containing compounds **13** and **14** and an unexpected product, the 3-hydroxy-4-(nitromethyl)-alk-4-enoate **15**, resulting from the isomerization of the carbon−carbon double bond of compound **13**. The results obtained with various β-nitroenones are collected in Table 3. The regioselectivity and the stereochemical outcome of these reactions deserve comment.

**Reactions under Kinetic Control.** At −78 °C in THF, lithium enolates of ketones and esters react cleanly and preferentially by 1,2-addition to the carbonyl group

**Scheme 3**[a]



[a] Only one of the two enantiomeric transition states and products is shown.

of β-nitroenones affording compounds **6** and **13**, respectively, in good to excellent yields (Scheme 2). The proportion of Michael addition products increases with cyclic enolates (up to 22% from the Li enolate of cyclohexanone and 2-ethyl-4-nitrobut-3-en-2-one, entry o, Table 1). Increasing the size of $R^1$, $R^2$, or $R^3$ has the same effect, but the amounts of Michael adducts **8** and **14** obtained are significantly less.

As with the reactions of lithium ester enolates with α,β-unsaturated carbonyl systems, kinetic addition occurs at the carbonyl carbon atom and equilibration leads to conjugate addition.[8] It should also be noted that sodium or lithium enolates of bis-activated methylene compounds did not react with β-nitroenones at low temperature and so only the thermodynamic adducts were obtained.

All of the addition reactions of Li enolates were very rapid (less than 5 min) and kinetically controlled. With the exception of compound **6k**, the diastereoselectivities obtained were poor, ranging from 44/56 to 75/25. However, it was shown that the size of the $R^2$ substituent of the starting β-nitroenone influences the stereoselectivity of the reaction. A remarkable reversal in stereoselectivy is observed with cyclohexanone and (δ)-valerolactone Li enolates when $R^2$ increases from Me to Et or *n*-Pent (entries d, g, j, and o, Table 1; entries d, i, and p, Table 2). This striking reversal of diastereofacial selectivity was markedly enhanced in the case of the cyclopentanone Li enolate (entries c and k, Table 1). Thus, an increase in size of the $R^2$ group from Me to the larger *i*-Pr changes the diastereomeric ratio from 75/25 to 0/100.

The aldol reaction between (*E*)-Li enolates and carbonyl compounds was reported to proceed preferentially with relative topicity (*lk*) giving mainly the product of unlike configuration.[9] The reaction is generally considered to proceed via the "pericyclic" chairlike six-membered ring transition state first proposed by Zimmerman and Traxler.[10] In our case, we have to consider the models **16** and **17** depicted in Scheme 3. When $R^2 = CH_3$ (entries c, d, and o, Table 1; entries d and p, Table 2), the favored product can be seen to arise from the

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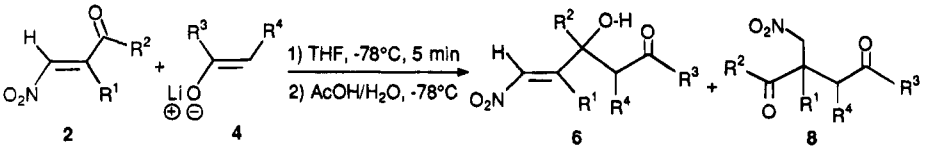
(10) Zimmerman, H. E.; Traxler, M. D. J. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

**Table 1. Adducts 6 and 8 Independently Prepared from (*E*)-β-Nitroenones 2 and Enolates of Ketones 4**

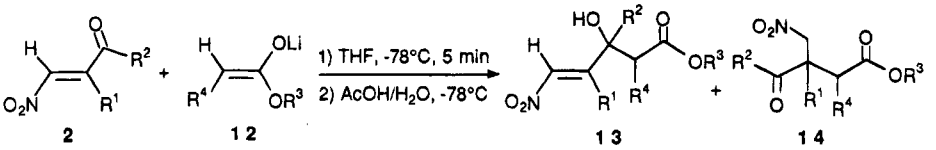



2 4 6 8

| | | | | | preparation of **6**[a] | | | preparation of **8**[b] | |
|---|---|---|---|---|---|---|---|---|---|
| entry | $R^1$ | $R^2$ | $R^3$ | $R^4$ | yield (%)[c] | **8** (%)[d] | diastereomeric ratio[d,e] | yield (%)[f] | diastereomeric ratio[d,e] |
| a | $CH_3$ | $CH_3$ | $CH_2CH_3$ | H | 98 | 0 | | 37 | |
| b | $CH_3$ | $CH_3$ | $(CH_2)_2CH{=}C(CH_3)_2$ | H | 83 | 5 | | | |
| c | $CH_3$ | $CH_3$ | $(CH_2)_3$ | | 88 | 3 | 70/30 | 73 | 40/60 |
| d | $CH_3$ | $CH_3$ | $(CH_2)_4$ | | 74 | 10 | 75/25 | 59 | 65/35 |
| e | $CH_3$ | $CH_2CH_3$ | $CH_2CH_3$ | H | 90 | 0 | | 52 | |
| f | $CH_3$ | $CH_2CH_3$ | $(CH_2)_2CH{=}C(CH_3)_2$ | H | 78 | 4 | | | |
| g | $CH_3$ | $CH_2CH_3$ | $(CH_2)_4$ | | 73 | 18 | 44/56 | 77 | 40/60 |
| h | $CH_3$ | $(CH_2)_4CH_3$ | $CH_2CH_3$ | H | 91 | 1 | | 47 | |
| i | $CH_3$ | $(CH_2)_4CH_3$ | $(CH_2)_2CH{=}C(CH_3)_2$ | H | 78 | 4 | | | |
| j | $CH_3$ | $(CH_2)_4CH_3$ | $(CH_2)_4$ | | 64 | 17 | 37/63 | 87 | 47/53 |
| k | $CH_3$ | $CH(CH_3)_2$ | $(CH_2)_3$ | | 81 | 16 | 0/100 | 78 | 58/42 |
| l | $CH_3$ | $CH(CH_3)_2$ | $(CH_2)_4$ | | | | | 87 | 80/20 |
| m | $CH_2CH_3$ | $CH_3$ | $CH_2CH_3$ | H | 88 | 4 | | 35 | |
| n | $CH_2CH_3$ | $CH_3$ | $(CH_2)_2CH{=}C(CH_3)_2$ | H | 85 | 12 | | | |
| o | $CH_2CH_3$ | $CH_3$ | $(CH_2)_4$ | | 61 | 22 | 70/30 | 46 | 35/65 |

[a] THF, −78 °C, 5 min; AcOH, THF, −78 °C. [b] THF, −78 °C; 1 h → −10 °C, 4 h; AcOH, $H_2O$. [c] Isolated yield of isomers **6** and **8**. [d] Determined from the 400 MHz $^1H$ NMR analyses of the crude products. [e] Assumed to be *u*/*l*; for this assignment see text. Correspondence between ratios in the series is proved by $^1H$ NMR. [f] Isolated yield.

**Table 2. Reaction of Lithium Esters Enolates with (*E*)-β-Nitroenones under Kinetic Control**

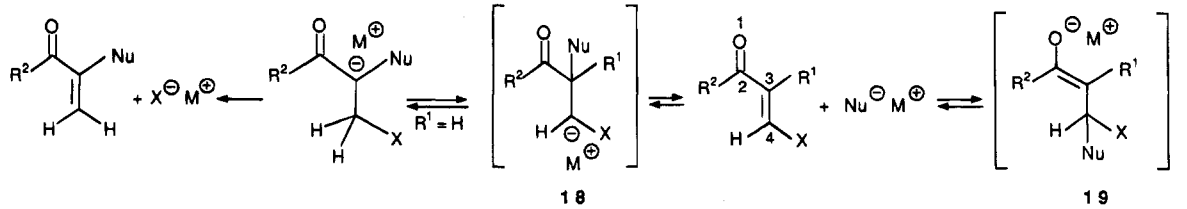



2 12 13 14

| entry | $R^1$ | $R^2$ | $R^3$ | $R^4$ | yield (%)[a] | **14** (%)[b] | **13** diastereomeric ratio[b-d] |
|---|---|---|---|---|---|---|---|
| a | $CH_3$ | $CH_3$ | $CH_3$ | H | 90 | 0 | |
| b | $CH_3$ | $CH_3$ | $CH_2CH_3$ | H | 82 | 0 | |
| c | $CH_3$ | $CH_3$ | $CH(CH_3)_3$ | H | 96 | 1 | |
| d | $CH_3$ | $CH_3$ | $(CH_2)_3$ | | 86 | 2 | 61/39 |
| e | $CH_3$ | $CH_2CH_3$ | $CH_3$ | H | 87 | 1 | |
| f | $CH_3$ | $CH_2CH_3$ | $CH_2CH_3$ | H | 64 | 1 | |
| g | $CH_3$ | $CH_2CH_3$ | $CH(CH_3)_2$ | H | 96 | 5 | |
| h | $CH_3$ | $CH_2CH_3$ | $CH_2CH_3$ | $CH_3$ | 32 | 6 | 55/45 |
| i | $CH_3$ | $CH_2CH_3$ | $(CH_2)_3$ | | 96 | 11 | 40/60 |
| j | $CH_3$ | $(CH_2)_4CH_3$ | $CH_3$ | H | 94 | 2 | |
| k | $CH_3$ | $(CH_2)_4CH_3$ | $CH_2CH_3$ | H | 95 | 4 | |
| l | $CH_3$ | $(CH_2)_4CH_3$ | $CH(CH_3)_2$ | H | 98 | 7 | |
| m | $CH_2CH_3$ | $CH_3$ | $CH_3$ | H | 94 | 3 | |
| n | $CH_2CH_3$ | $CH_3$ | $CH_2CH_3$ | H | 94 | 6 | |
| o | $CH_2CH_3$ | $CH_3$ | $CH(CH_3)_2$ | H | 85 | 9 | |
| p | $CH_2CH_3$ | $CH_3$ | $(CH_2)_3$ | | 93 | 16 | 70/30 |
| q | $(CH_2)_2CH_3$ | $CH_2CH_3$ | $CH_3$ | H | 92 | 4 | |
| r | $(CH_2)_2CH_3$ | $CH_2CH_3$ | $CH_2CH_3$ | H | 99 | 5 | |
| s | $(CH_2)_2CH_3$ | $CH_2CH_3$ | $CH(CH_3)_2$ | H | 85 | 9 | |

[a] Isolated yield of isomers **13** and **14**. [b] Determined from the 400 MHz $^1H$ NMR analyses of the crude products. [c] Correspondence between ratios in the series is proved by $^1H$ NMR. [d] Assumed to be *u*/*l*; for this assignment see text.

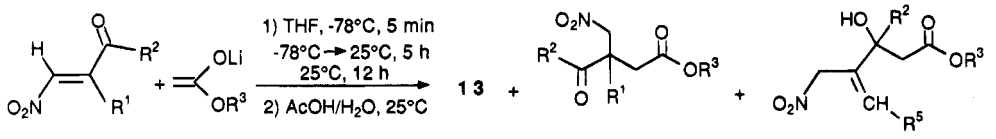
**Scheme 4**




18 19

transition structure **16** ((*lk*) approach of the reactants) which has the largest carbonyl substituent, $C(R^1){=}CHNO_2$, in a quasiequatorial conformation. However, when $R^2$ increases to Et or *n*-Pent (entries g and j, Table 1; entries h and i, Table 2), the diastereoselectivity inverts ((*ul*) approach of the reactants and $R^2$ in a quasiequatorial

**Table 3. Ratios of Isomers from Addition of Lithium Ester Enolates to (*E*)-β-Nitroenones after 12 h at 25 °C**




2 12

| | | | | | | | relative ratio of products[b] | | |
|---|---|---|---|---|---|---|---|---|---|
| entry | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | isolated yield (%)[a] | **13** | **14** | **15** |
| a | $CH_3$ | $CH_3$ | $CH_2CH_3$ | H | H | 55 | 0 | 94 | 6 |
| b | $CH_3$ | $CH_2CH_3$ | $CH_2CH_3$ | H | H | 42 | 0 | 82 | 18 |
| c | $CH_2CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | 61 | 20 | 0 | 80 |

[a] Isolated yield of compounds **13**–**15**. [b] Determined by 400 MHz $^1$H NMR analyses of the crude reaction products.

**Table 4. Selected $^1$H NMR Data of Compounds 6 and 13 (δ values, $CDCl_3$)**

| compound | δ(H)[ethylenic] | δ(OH) | δ($CH_3$)[$R^1$] | δ($CH_3$)[$R^2$] |
|---|---|---|---|---|
| (*u*)-**6c** | 7.29 | 3.97 | 2.23 | 1.39 |
| (*l*)-**6c** | 7.38 | 3.97 | 2.15 | 1.73 |
| (*u*)-**6d** | 7.34 | 3.79 | 2.16 | 1.28 |
| (*l*)-**6d** | 7.37 | 4.22 | 2.09 | 1.52 |
| (*u*)-**6g** | 7.32 | 3.74 | 2.13 | – |
| (*l*)-**6g** | 7.27 | 4.03 | 2.04 | – |
| (*u*)-**6j** | 7.32 | 3.77 | 2.14 | – |
| (*l*)-**6j** | 7.27 | 4.08 | 2.05 | – |
| (*u*)-**6k** | – | – | – | – |
| (*l*)-**6k** | 7.30 | 3.72 | 2.15 | – |
| (*u*)-**6o** | 7.28 | 3.94 | – | 1.27 |
| (*l*)-**6o** | 7.31 | 4.21 | – | 1.53 |
| (*u*)-**13d** | 7.28 | 4.17 | 2.25 | 1.41 |
| (*l*)-**13d** | 7.42 | 3.85 | 2.15 | 1.68 |
| (*u*)-**13i** | 7.28 | 4.30 | 2.22 | – |
| (*l*)-**13i** | 7.33 | 3.66 | 2.06 | – |
| (*u*)-**13p** | 7.24 | 4.30 | – | 1.41 |
| (*l*)-**13p** | 7.37 | 3.85 | – | 1.71 |

rather than in a quasiaxial conformation). The models **16** and **17** satisfactorily rationalize the inversion of diastereoselectivity caused by an increase in the size of $R^2$. The addition of Li enolates to (*E*)-β-nitroenones under kinetic control seems to be dominated by the tendency to minimize the destabilizing interaction between $R^2$ and $R^3$.

Selected chemical shifts of the $^1$H NMR spectra of compounds **6** and **13** are listed in Table 4. The diastereomeric ratios in Tables 1 and 2 were determined by integration of the $^1$H NMR signals of the ethylenic hydrogens, the OH hydrogens, and the hydrogens of the $R^1$ and $R^2$ methyl groups (identical ratios were obtained in each case).

Structural assignments for compounds **6** and **13**, based on the mechanistic arguments described above, were confirmed by the $^1$H NMR chemical shifts of the hydrogens of the methyl group adjacent to the hydroxyl group C($CH_3$)(OH), δ(*l*($CH_3$)) > δ(*u*($CH_3$)), by comparison with the chemical shifts observed for the C*H*(OH) hydrogen in classical aldol rections δ(*l*(H)) > δ(*u*(H)).[11] The small variations of the ethylenic protons chemical shifts and the reversal observed for the OH ones between adducts **6** and **13** prevented the use of these data for the structural assignments.

**Michael Addition to the Nitroalkene Functionality.** As noted in the previous papers of this series[5-7] and contrary to 3-nitrocyclohex-2-en-1-one[12] and vinylsulfones bearing a β carbonyl group,[13] the regioselectivity of the Michael addition to the nitroalkene functionality is complete since products deriving from an attack β to the carbonyl group have never been detected. Explanations for these differences in reactivity and regioselectivity are proposed in Scheme 4.

Both the β-substituted α,β-unsaturated carbonyl systems mentioned above are not α-alkylated ($R^1$ = H); therefore, irreversible elimination of $NO_2^-$ or $PhSO_2^-$ from β-addition product **18** occurs. With our α-alkylated β-nitroenones, this elimination is impossible. Therefore, nucleophiles added exclusively on position 3 of the α,β-unsaturated carbonyl system giving an intermediate nitronate carbanion **18**, which is more stable than the corresponding enolate carbanion **19**.

In order to investigate the mechanism of the formation of compounds **8** (Scheme 2), crossover experiments were performed. We found that adding (*E*)-3-hydroxy-5-nitroalk-4-enones **6k** and **6o** to 2 equiv of LDA in THF at −78 °C and allowing the temperature to warm up to −10 °C before quenching afforded Michael adducts **8k**, **8o**, and **8l**. The $^1$H NMR spectrum of the crude reaction products showed three different signals for the CH of the isopropyl group: the first between 3.10 and 2.99 ppm for both diastereomers of compound **8k**, the second and third, respectively, between 3.25–3.14 ppm and 3.43–3.33 ppm for the main and the minor diastereomer of compound **8l**. This observation clearly points out that the transformation of **6** into **8** occurred *via* pathway A.

There are three other factors that migh support pathway A: (1) retroketolization occurs with loss of the carbon–carbon double bond geometry since various amounts of (*Z*)-β-nitroenone were detected after 5 min reaction at −78 °C. Therefore, the (*lk*) approach of the two trigonal centers generally observed when cyclic ketone enolates reacted with (*E*)-nitroalkenes cannot be considered with our substrates.[2,14] Complex and poor diastereoselectivities obtained for 2-(nitromethyl) 1,4-diketones **8** support the mechanism proposed. (2) For cyclic ketones (except entry o, Table 1), adducts **8** were obtained in good yields ranging from 59 to 87%. Lower yields (37–52 %) were obtained for unsymmetrical aliphatic ketones due to the generation of isomeric enolates, with the most hindered ones adding only with difficulty to β-nitroenones. (3) The difference observed between the reactions of ketones and esters tends also to support that enolates or enolate-like species might be involved in the transformation **5** → **7** and **13** → **14**. However, pathway

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B (Scheme 2) cannot be totally excluded. Transformation of **5** to **7** may also occur either *via* the epoxide **9** or *via* cyclopropanic structures such as **10** or **11**.

## Conclusion

We have shown that, under kinetic control, ketone and ester lithium enolates reacted preferentially by 1,2-addition with (*E*)-β-nitroenones to afford the corresponding (*E*)-3-hydroxy-5-nitroalk-4-enones **6** and (*E*)-3-hydroxy-5-nitroalk-4-enoates **13**, respectively, in good yields. When an equilibrium was allowed, only the ketone adducts **5** rearranged cleanly to the 2-(nitromethyl) 1,4-diketones **8**, which could be considered the Michael adducts to the nitroalkene moiety. We believe the compounds reported herein will be useful in organic synthesis due to their novel structures and several functional groups. Further investigations, in particular on the stereochemical control of the reactions, are in progress.

## Experimental Section

General experimental conditions and details of instrumentation have been previously reported.[6] All reactions were carried out under a nitrogen atmosphere in flame-dried glassware.

**General Procedure: Addition of Lithium Ketone Enolates under Kinetic Control (6).** To a solution of LDA (prepared from diisopropylamine (3.197 mmol) and *n*-BuLi (3.197 mmol, 2.0 mL, 1.6 M in hexanes) in THF (10 mL) at −78 °C was added dropwise a solution of the ketone (3.045 mmol) in THF (1 mL) over 10 min at the same temperature. After stirring the mixture for 1 h, a solution of the β-nitroenone **2** (3.0 mmol) in THF (15 mL) was added over 2 min. The resulting mixture was stirred for 5 min at −78 °C and immediately quenched with acetic acid (12.0 mmol) in THF (5 mL). After warming to rt, the mixture was poured into water (30 mL) and extracted with $CH_2Cl_2$ (4 × 30 mL). The combined organic layers were washed with 5% aqueous $NaHCO_3$ solution (40 mL), water (40 mL), and brine (40 mL), dried with $MgSO_4$, and concentrated. The crude 3-hydroxy-5-nitroalk-4-enone **6** was purified by column chromatography on silica gel.

**(*E*)-3-Hydroxy-2,3-dimethyl-1-nitrohept-1-en-5-one (6a):** oil; yield 98%; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38 (brs, 1 H), 4.52 (OH), 2.92 (d, 1 H, *J* = 17.5 Hz), 2.72 (d, 1 H, *J* = 17.5 Hz), 2.47 (qd, 2 H, *J* = 3.9, 7.3 Hz), 2.14 (d, 3 H, *J* = 1.2 Hz), 1.39 (s, 3 H), 1.07 (t, 3 H, *J* = 7.3 Hz); $^{13}$C NMR (100.6 MHz, $CDCl_3$) δ 212.0, 155.4, 135.7, 74.0, 48.9, 37.1, 26.6, 14.8, 6.9; IR (neat) 3482, 1638, 1517, 1347 cm$^{-1}$. Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72, H, 7.51, N, 6.96. Found: C, 53.5, H, 7.8, N, 7.1.

**General Procedure: Addition of Lithium Ester Enolates under Kinetic Control (13).** These compounds were prepared according to the procedure described for compounds **6**.

**Methyl (*E*)-3-hydroxy-3,4-dimethyl-5-nitropent-4-enoate (13a):** oil; yield 90%; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39 (brs, 1 H), 4.24 (OH), 3.73 (s, 3 H), 2.79 (d, 1 H, *J* = 16.1 Hz), 2.67 (d, 1 H, *J* = 16.1 Hz), 2.16 (d, 3 H, *J* = 1.5 Hz), 1.43 (s, 3 H); $^{13}$C NMR (100.6 MHz, $CDCl_3$) δ 171.8, 154.4, 136.0, 73.5, 51.9, 42.7, 26.6, 14.7; IR (neat) 3496, 1720, 1638, 1517, 1347 cm$^{-1}$. Anal. Calcd for $C_8H_{13}NO_5$: C, 46.82 H, 7.37 N, 6.83. Found: C, 46.8, H, 7.3, N, 6.7.

**General Procedure: Michael Addition of Lithium Ketone Enolates (8).** The procedure for the preparation of 2-(nitromethyl) 1,4-diketones **8** was the same as those described above for compounds **6** except that after addition of the β-nitroenone **3**, the mixture was first stirred 1 h at −78 °C and then the temperature was slowly raised to −10 °C (4 h). The mixture was then poured into a 2% aqueous acetic acid solution (30 mL) and worked-up as described above.

**3-Methyl-3-(nitromethyl)heptane-2,5-dione (8a):** oil; yield 37%; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.77 (d, 1 H, *J* = 11.9 Hz), 4.66 (d, 1 H, *J* = 11.9 Hz), 2.95 (d, 1 H, *J* = 18.3 Hz), 2.84 (d, 1 H, *J* = 18.3 Hz), 2.45 (qd, 2 H, *J* = 2.1, 7.3 Hz), 2.23 (s, 3 H), 1.33 (s, 3 H), 1.06 (t, 3 H, *J* = 7.3 Hz); $^{13}$C NMR (100.6 MHz, $CDCl_3$) δ 208.3, 207.7, 80.2, 47.2, 35.8, 25.3, 20.4, 7.2; IR (neat) 1710, 1556, 1375 cm$^{-1}$. Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72, H, 7.51, N, 6.96. Found: C, 53.4, H, 7.6, N, 7.0.

For more detailed procedures and for all characterization data, see the supporting information.

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**Supporting Information Available:** Experimental procedures and characterization data for **6a−k,m−o**, **8a,c−e,g,h,j−m,o**, **13a−s** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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