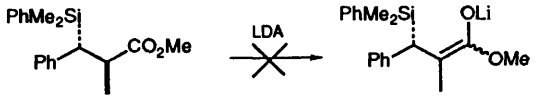
Two Unexpected but Understandable Reactions with Lithium Diisopropylamide (LDA)

Sarah C. Archibald and Ian Fleming*
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK

On treatment with LDA, the acylated oxazolidinones **3** and **10** gave the *N*-vinylamides **6**, **7** and **11** in low yields. The esters **13**, on treatment with an excess of LDA at 0 °C, gave a low yield of the β-aminovinyl ketones **15** in addition to the enolates. Methyl benzoate similarly gave the β-aminovinyl ketone **17**. Neither the formation of the *N*-vinylamides nor of the β-aminovinyl ketones was easily made high yielding.

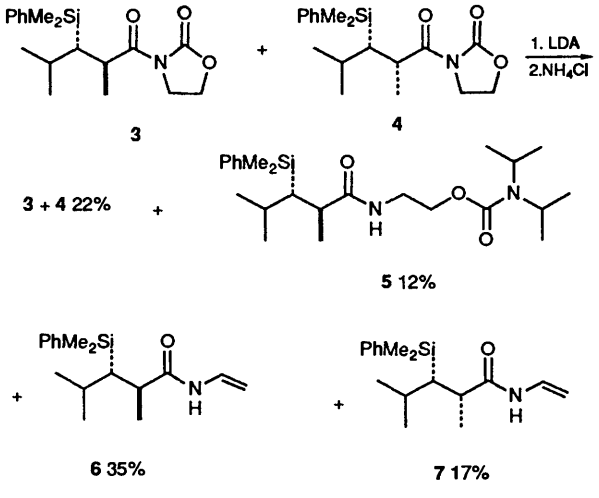
In an earlier paper,[1] we commented upon a difficulty that we have had in preparing an enolate from an ester carrying a silyl group in the β position when the proton to be removed is a methine proton. Thus, lithium diisopropylamide (LDA) did not give the enolate **2** of the ester **1**. In attempting to overcome this



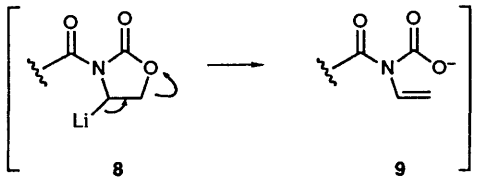
1 **2**

difficulty, which turns out not to have been as serious as we had thought, we have come across two unexpected reactions, which we now report in brief.

In the hope that we might be able to form the enolate of an acyloxazolidinone more easily than the enolate of an ester, we treated a mixture of the diastereoisomeric racemic acyl oxazolidinones **3** and **4**, rich (76:24) in the former, with LDA and quenched the mixture with aqueous ammonium chloride, hoping to find a mixture rich in the latter, which would have indicated the formation of the enolate and its reprotonation.[2] We found ourselves with three unexpected products, **5**, **6** and **7**, and some recovered starting material, but with no enrichment in favour of the stereoisomer **4**. The amide **5** is unexceptional—its

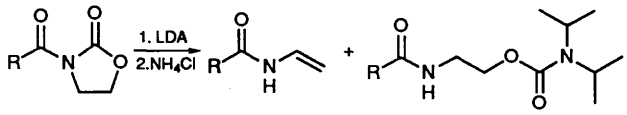


appearance among the products demonstrates again the difficulty of generating an enolate in this type of system, since it is the product of nucleophilic opening of the oxazolidinone ring, a problem not usually encountered when using LDA. It is known that nucleophiles attack hindered acyloxazolidinones more rapidly at the ring carbonyl than at the exocyclic *N*-acyl group.[3] The intriguing products were the pair of *N*-vinylamides **6** and **7**. These must have been produced by metallation on the methylene group adjacent to the nitrogen atom, followed by β-elimination **8** ⟶ **9** and subsequent decarboxylation, with the metallation step having precedent in Beak's work on the metallation of non-enolisable *N*-methylamides.[4]



8 **9**

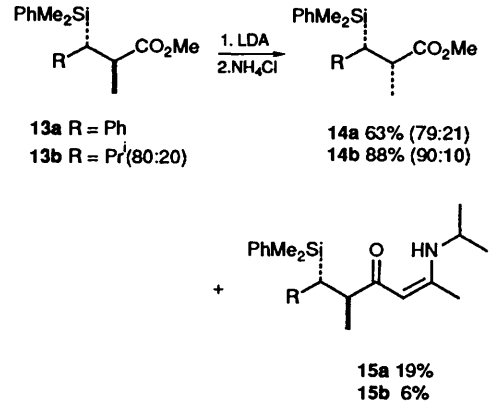
We investigated briefly the possibility that this might be a general reaction by preparing the acyloxazolidinones **10**, and repeating the reaction with them. In both cases, the *N*-vinylamides **11** were produced, but in yields that were not encouraging. In the non-enolisable case **10a**, there was marginally more nucleophilic opening than with the enolisable **10b**, which gave rather more *N*-vinylamide **11b**.



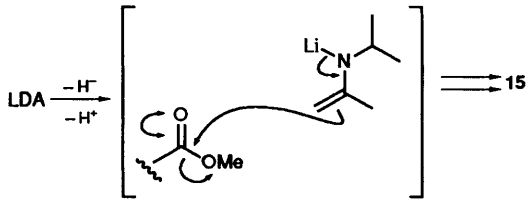
10a R = Bu^t **11a** 25% **12a** 59%
10b R = Pr^i **11b** 45% **12a** 8% + **10b** 13%

We therefore returned to the possibility of forming the enolate directly from an ester, choosing the ester **13a**, that we had looked at before, and the ester **13b** because we needed to be able to change the relative stereochemistry in a system like this into that of its diastereoisomer **14b** for our synthesis of ebelactone-a.[5] This indeed proved to be less of a problem than our earlier experience had led us to believe. The diastereoisomerically pure racemic ester **13a** reacted with 2.5 equiv. of LDA at 0 °C, as shown by reprotonation, which gave a mixture (63%) rich (79:21) in its diastereoisomer **14a**. Similarly, the ester **13b** (a racemic mixture with its stereoisomer **14b** in a ratio of 80:20) gave a mixture rich (varying from 83:17 to 90:10) in its diastereoisomer **14b**. At least 2 equiv. of LDA are necessary, the addition of lithium chloride making no difference to the yield, to the ratio of diastereoisomers on protonation, nor to the need for 2 equiv.; no deprotonation took place at −23 °C or lower.

We have therefore solved our problem, but these reactions always gave us small amounts, usually *ca.* 10%, of very visible (TLC) by-products, the enamino ketones **15**, which have



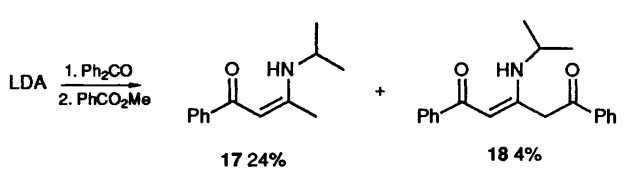
definitive ^{1}H NMR spectra. These products are those expected[6] from condensation of the aza enolate **16** with the ester **13**, and the aza enolate must have been produced by oxidation of LDA. Others[7,8] have observed that the reactions of LDA with ketones sometimes give by-products that must also have been produced from the aza enolate **16**. Wittig noted,[8] because he isolated the corresponding alcohol, that it was the ketone itself that had oxidised the LDA. Although we have no ketone present, and the ester seems an unlikely oxidising agent, no sample of LDA that we have used has been entirely free of this problem—we have always seen traces of the enamino ketones in the product mixtures when we used the 2 equiv. of LDA necessary for our deprotonations. However, when we used < 2 equiv. of LDA in the reaction with the ester **13b**, we did not detect the enamino ketone **15b**. On the other hand, using > 2 equiv. of LDA did not



16

seem greatly to increase the amount of enamino ketone produced. Products like these must be present in some of the reactions other people have carried out using ester enolates generated with LDA, but we have not been able to trace any earlier reports. It may be that this problem only surfaces when a substantial excess of LDA is needed or used.

In a brief attempt to increase the amount of this product, we deliberately oxidised a solution of 1 equiv. of LDA with benzophenone,[8,9] trapping the intermediate with methyl benzoate in place of the ester **13**. In addition to a reasonably good yield of diphenylmethanol, we obtained three products: a somewhat higher but still low yield of the enamino ketone **17**, a



17 24% **18** 4%

+ $PhCONPr^i_2$ 24% + Ph_2CHOH 67%

moderate yield of *N*,*N*-diisopropylbenzamide, and yet another by-product, the enamino ketone **18**, which is the result of a dianion of the enamino ketone **17** condensing with a second molecule of methyl benzoate. When we used *p*-chlorobenzaldehyde as the oxidant,[10] we obtained an even lower yield (4%) of the enamino ketone **17**, and when we used air as the oxidant, we could see none. Since enamino ketones are not difficult to make from aza enolates by conventional methods, we dropped this line of research.

Experimental

Preparation of LDA.—Butyllithium (*ca.* 1.6 mol dm^{-3} solution in hexane, titrated[11]; 1 mmol) was added dropwise to a solution of distilled diisopropylamine (1.1 mmol) in dry THF (*ca.* 1 cm^3) at 0 °C under argon. The solution was stirred at 0 °C for 20 min before use.

3-Dimethyl(phenyl)silyl-2,4-dimethylpentanoic Acid.—An 80:20 mixture of methyl (2*RS*,3*SR*)- and (2*RS*,*RS*)-3-dimethyl-(phenyl)sily-2,4-dimethylpentanoate[12] **13b** (4.17 g, 15 mmol) was refluxed with sodium hydroxide (4.8 g) in methanol (30 cm^3) and water (5 cm^3) for 2 h. The methanol was removed under reduced pressure and water (60 cm^3) added. The mixture was acidified (pH 1, universal indicator paper) with concentrated sulfuric acid and extracted with dichloromethane (4 × 150 cm^3). The organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give the *acid* (3.71 g, 94%); $\nu_{max}(CCl_4)/cm^{-1}$ 3600–2400 (OH), 1705 (C=O), 1250 (SiMe) and 1115 (SiPh); δ_H(250 MHz; $CDCl_3$) 11.1 (1 H, br s, CO_2OH), 7.56–7.75 (2 H, m, *o*-ArH), 7.35–7.29 (3 H, m, *m*- and *p*-ArH), 2.65 (1 H, dq, *J* 2.65 and 7.19, CSiC*H*Me), 2.04–1.84 (1 H, m, C*H*Me_AMe_B), 1.52 (1 H, dd, *J* 2.65 and 6.63, CHSi), 1.15 (3 H, d, *J* 7.15, CHSiCH*Me*), 0.94 (3 H, d, *J* 6.73, CH*Me*$_A$Me$_B$), 0.89 (3 H, d, *J* 6.83, CHMe$_A$*Me*$_B$), 0.41 (3 H, s, Si*Me*$_A$Me$_B$) and 0.38 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 249 (10.5%, M − Me), 187 (17, M − Ph), 143 (100, M − Ph − CO_2) and 135 (75, $PhMe_2Si$) (Found: M^+, 249.1320. $C_{15}H_{24}O_2Si$ − Me requires *M*, 249.1311).

Preparation of the Acid Chloride.—Oxalyl chloride (0.35 cm^3, 4 mmol) was added to a solution of the acid (0.528 g, 2 mmol) in dichloromethane (5 cm^3) at 0 °C under argon. The solution was allowed to warm to room temperature and stirred for 2 h. The solvent and excess reagent were removed under reduced pressure to give the acid chloride.

Preparation of the Oxazolidinones.—Typically, butyllithium (1.60 mol dm^{-3} solution in hexane; 6.2 cm^3, 10 mmol) was added dropwise to a solution of oxazolidin-2-one (0.87 g, 10 mmol) in dry THF (20 cm^3) under argon at −78 °C. The mixture was allowed to warm to room temperature over 1 h and freshly distilled acid chloride (15 mmol) was added. The mixture was stirred for 30 min at room temperature, quenched with aqueous sodium hydrogen carbonate (15 cm^3) and extracted with dichloromethane (4 × 75 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane) of the residue gave the following oxazolidinones.

(2RS,3SR)-N-[*3-Dimethyl(phenyl)silyl-2,4-dimethylpentanoyl*]-*oxazolidin-2-one* **3** (82%) as a mixture with its (2*RS*,3*RS*) diastereoisomer **4** in a ratio of 76:24; R_f(EtOAc–hexane 1:3) 0.24; $\nu_{max}(CDCl_3)/cm^{-1}$ 1785 and 1700 (C=O) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.59–7.52 (2 H, m, *o*-ArH), 7.36–7.28 (3 H, m, *m*- and *p*-ArH), 4.33–4.18 (2 H, m, CH_2O), 3.95–3.78 (2 H, m, NCH_2), 3.64–3.54 (1 H, m, C*H*Me), 2.08–1.99 (1 H, m, C*H*Me_2), 1.47 (1 H, dd, *J* 4.4 and 5.9, SiCH), 1.18 (3 H, d, *J* 7.0, *Me*CH), 0.93 (3 H, d, *J* 6.9, CH*Me*$_A$Me$_B$), 0.89 (3 H, d, *J* 7.0, CHMe$_B$), 0.44 (3 H, s, Si*Me*$_A$Me$_B$) and 0.39 (3 H, s, SiMe$_A$*Me*$_B$) with the *syn* diastereoisomer **4** detectable by signals at δ 1.82 (1 H, dd, *J* 3.2 and 8.5, SiCH) and 1.09 (3 H, d, *J* 7.0, *Me*CH); *m*/*z* 318 (5.34%, M − Me), 290 (27, M − Me_2CH) and

135 (100, $PhMe_2Si$) (Found: M^+, 318.1503. $C_{18}H_{27}NOSi$ – Me requires *M*, 318.1526).

N-(*Dimethylpropionyl*)*oxazolidin-2-one* **10a** (94%); R_f(Et-OAc–hexane 1:2) 0.28; $\nu_{max}(CDCl_3)/cm^{-1}$ 1780 and 1690 (C=O), 1490 and 1370 (Me_3C) and 1290 and 1200 (C–O); δ_H(250 MHz; $CDCl_3$) 3.36 (2 H, t, *J* 8.06, CH_2O), 3.99 (2 H, t, *J* 8.28, NCH_2) and 1.33 (9 H, s, Bu^t); *m/z* 156 (32%, M – Me), 128 (42, M – Me – CO), 88 (37, $C_3H_6NO_2$), 85 (12, Me_2CCO) and 57 (100, Bu^t) (Found: M^+ – Me, 156.0662. $C_8H_{13}NO_3$ requires *M* – Me, 156.0660).

N-(*Methylpropionyl*)*oxazolidin-2-one* **10b** (83%); R_f(EtOAc–hexane 1:2) 0.27; $\nu_{max}(CDCl_3)/cm^{-1}$ 1785 and 1700 (C=O), 1395 and 1370 (Me_2C) and 1260 and 1230 (C–O); δ_H(250 MHz; $CDCl_3$) 4.37 (2 H, t, *J* 8.08, CH_2O), 3.97 (2 H, t, *J* 8.21, NCH_2), 3.71 (1 H, septet, *J* 6.82, Me_2CH) and 1.14 (6 H, d, *J* 6.77, Me_2CH); *m/z* 157 (18%, M^+), 88 (100, $C_3H_6NO_2$) and 71 (49, Pr^{i}CO) (Found: M^+, 157.0737. $C_7H_{11}NO_3$ requires *M*, 157.0739).

N-*Vinyl*-3-*dimethyl*(*phenyl*)*silyl*-2,4-*dimethylpentanamide* **6** *and* **7**.—The oxazolidinone **3** (*anti*:*syn* 76:24) (167 mg, 0.5 mmol) in dry THF (1 cm^3) was added dropwise to a solution of LDA (0.5 mmol) in THF (1 cm^3), at –78 °C under argon. The mixture was stirred for 2 h at –78 °C, quenched with aqueous ammonium chloride (3 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Column chromatography (SiO_2, EtOAc–hexane) of the residue gave the (2RS,3SR)-*amide* **6** (50 mg, 35%); R_f(EtOAc–hexane 1:9) 0.25; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1690 and 1640 (C=O), 1505 (C=C), 1255 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.58–7.54 (2 H, m, *o*-ArH), 7.38–7.33 (3 H, m, *m*- and *p*-ArH), 6.89 (1 H, ddd, *J* 8.7, 10.9 and 15.7, CH=CH_2), 6.6 (1 H, br d, *J* 10.7, NH), 4.42 (1 H, d, *J* 15.7, CH=CH_AH_B), 4.30 (1 H, d, *J* 8.5, CH=CH_ACH_B), 2.41 (1 H, dq, *J* 3.1 and 7.2, MeC*H*), 2.09–2.00 (1 H, m, C*H*Me_2), 1.28 (1 H, dd, *J* 3.2 and 4.2, SiCH), 1.17 (3 H, d, *J* 7.2, *Me*CH), 0.98 (3 H, d, *J* 6.8, Me_AMe_BCH), 0.90 (3 H, d, *J* 6.7, Me_AMe_BCH), 0.43 (3 H, s, SiMe_AMe_B) and 0.42 (3 H, s, $SiMe_AMe_B$); *m/z* 274 (54%, M – Me), 247 (18, M – NHCH=CH_2), 246 (63, M – Pr) and 135 (100, Me_2PhSi) (Found: M^+, 274.1627. $C_{17}H_{27}NOSi$ – Me requires *M*, 274.1627); the (2RS,RS)-*amide* **7** (25 mg, 17%); R_f(EtOAc–hexane, 1:9) 0.18; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1690 and 1640 (C=O), 1505 (C=C), 1255(SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.56–7.52 (2 H, m, *o*-ArH), 7.36–7.32 (3 H, m, *m*- and *p*-ArH), 7.0–6.8 (2 H, m, NH and CH=CH_2), 4.49 (1 H, d, *J* 15.5, CH=CH_AH_B), 4.34 (1 H, d, *J* 8.3, CH=CH_ACH_B), 2.53 (1 H, quintet, *J* 7.1, MeC*H*), 1.92–1.87 (1 H, m, Me_2CH), 1.53 (1 H, dd, *J* 7.1 and 4.4, CHSi), 1.12 (3 H, d, *J* 7.1, *Me*CH), 0.95 (3 H, d, *J* 6.8, CHMe_AMe_B), 0.93 (3 H, d, *J* 6.9, CHMe_AMe_B) and 0.37 (6 H, s, $SiMe_2$); *m/z* 274 (41%, M – Me), 260 (13, M – C_2H_5), 247 (20, M – NHCH=CH_2), 246 (68, M – Pr^i) and 135 (100, $PhMe_2Si$) (Found: M^+, 274.1636. $C_{17}H_{27}NOSi$ – Me requires *M*, 274.1627); recovered starting material, which appeared (^{1}H NMR) to be only the *anti* isomer (36 mg, 22%); R_f(EtOAc–hexane 1:3) 0.24; and a mixture of (2RS,3SR)-N-(N′,N′-*diisopropylaminocarbonyloxyethyl*)-3-*dimethyl*(*phenyl*)*silyl*-2,4-*dimethylpentanamide* **5** and its (2RS,3RS)-*diastereoisomer* in a ratio of 77:23 (26 mg, 12%); R_f(EtOAc–hexane, 1:3) 0.16; $\nu_{max}(CDCl_3)/cm^{-1}$ 3470 (NH), 1680 (C=O), 1255 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) [(2*RS*,3*SR*)-diastereoisomer] 7.57–7.52 (2 H, m, *o*-ArH), 7.36–7.29 (3 H, m, *m*- and *p*-ArH), 6.1 (1 H, br s NH), 4.17 (2 H, t, *J* 5.2, CH_2O), 4.1–3.6 (2 H, v br m, 2 × Me_2CHN), 3.40 (2 H, q, *J* 5.2, $NHCH_2$), 2.45 (1 H, dq, *J* 3.3 and 7.2, MeC*H*), 2.01–1.93 (1 H, m, Me_2CH), 1.37 (1 H, dd, *J* 3.3 and 4.9, CHSi), 1.19 (6 H, d, *J* 6.8, 2 × Me_2CHN), 1.14 (3 H, d, *J* 7.2, *Me*CH), 0.92 (3 H, d, *J* 6.8, SiCHCHMe_A-Me_B), 0.84 (3 H, d, *J* 6.9, SiCHCHMe_AMe_B), 0.41 (3 H, s, SiMe_AMe_B) and 0.38 (3 H, s, $SiMe_AMe_B$) with the (2*RS*,3*RS*)-diastereoisomer detectable by a signal at δ 1.09 (3 H, d, *J* 7, 1, CH*Me*); *m/z* 419 (43%, M – Me), 172 (100, CH_2CH_2-OCONPr$_2$), 135 (100, $SiMe_2Ph$) and 128 (52, Pr_2NCO) (Found: M^+ – Me, 419.2762. $C_{24}H_{42}N_2O_3Si$ requires *M* – Me, 419.2729).

Treatment of the Oxazolidinones **10** *with LDA*.—Typically, the oxazolidinone (5 mmol) in dry THF (5 cm^3) was added dropwise to a solution of LDA (5.5 mmol), at –78 °C under argon and the mixture stirred for 2 h at –78 °C. The mixture was quenched with aqueous ammonium chloride (5 cm^3) and extracted with dichloromethane (4 × 50 cm^3) which was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. Column chromatography (SiO_2, EtOAc–hexane) gave the following compounds.

N-*Vinyl*-2,2-*dimethylpropionamide* **11a** (25%) as needles, m.p. 99–101 °C (from hexane); R_f(EtOAc–hexane 1:2) 0.41; $\nu_{max}(CDCl_3)/cm^{-1}$ 3470 (NH), 1685, 1645 and 1500 (C=O and C=C), 1405 and 1375 (Bu^t) and 1215 (C–O); δ_H(250 MHz; $CDCl_3$) 7.3 (1 H, br s, NH), 6.98 (1 H, ddd, *J* 8.74, 10.70 and 15.78, NHC*H*=CH_2), 4.60 (1 H, d, *J* 15.80, CH=CH_AH_B), 4.39 (1 H, d, *J* 8.72, CH=CH_AH_B) and 1.21 (9 H, s, Bu^t); *m/z* 127 (39%, M^+), 85 (18, Bu^{t}CO) and 57 (100, Bu^t) (Found: M^+, 127.0999. $C_7H_{13}NO$ requires *M*, 127.0997) (Found: C, 65.9; H, 10.35; N, 11.0. $C_7H_{13}NO$ requires C, 66.1; H, 10.3; N, 11.0%).

N-(*N′,N′-Diisopropylaminocarbonyloxyethyl*)-2,2-*dimethylpropionamide* **12a** (59%); R_f(EtOAc–hexane, 1:2) 0.14; $\nu_{max}(CDCl_3)/cm^{-1}$ 3490 (NH), 1680 and 1525 (C=O), 1375 (Bu^t) and 1225 (C–O); δ_H(250 MHz; $CDCl_3$) 6.5 (1 H, br s, NH), 4.22 (2 H, t, *J* 5.15, CH_2O), 4.1–3.6 (2 H, v br m, 2 × Me_2CHN), 3.45 (2 H, q, *J* 5.04, $NHCH_2$), 1.17 (12 H, d, *J* 6.83, 2 × Me_2-CHN) and 1.14 (9 H, s, Bu^t); *m/z* 272 (5%, M^+), 229 (33, M – Pr), 215 (17, M – Bu^t), 144 (10, Bu^{t}CONHCH$_2$CH$_2$O), 128 (100, $CONPr_2$) and 57 (40, Bu^t) (Found: M^+, 272.2150. $C_{14}H_{28}N_2O_2$ requires *M*, 272.2100).

N-*Vinyl*-2-*methylpropionamide* **11b** (46%) as needles, m.p. 57.5–59 °C (from hexane); R_f(EtOAc–hexane 1:2) 0.30; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1660 and 1520 (C=O and C=C) and 1225 (C–O); δ_H(250 MHz; $CDCl_3$) 7.6 (1 H, br s, NH), 6.95 (1 H, ddd, *J* 8.80, 10.74 and 15.85, NHC*H*=CH_2), 4.60 (1 H, d, *J* 15.86, CH=CH_AH_B), 4.36 (1 H, d, *J* 8.76, CH=CH_AH_B), 1.97 (1 H, sept, *J* 6.89, C*H*Me_2) and 1.15 (6 H, d, *J* 6.90, CHMe_2) (Found: C, 63.6; H, 9.9; N, 12.3. $C_6N_{11}NO$ requires C, 63.7; H, 9.8; N, 12.4%).

N-(N′,N′-*Diisopropylaminocarbonyloxyethyl*)-2-*methylpropionamide* **12b** (8%); R_f(EtOAc–hexane 1:2) 0.07; $\nu_{max}(CDCl_3)/cm^{-1}$ 3470 (NH) and 1680 and 1525 (C=O); δ_H(250 MHz; $CDCl_3$) 6.2 (1 H, br s, NH), 4.23 (2 H, t, *J* 5.18, CH_2O), 4.1–3.6 (2 H, v br m, 2 × Me_2CHN), 3.50 (2 H, q, *J* 5.11, $NHCH_2$), 2.35 (1 H, septet, *J* 6.92, Me_2CHCO), 1.19 (12 H, d, *J* 6.81, 2 × Me_2CHN) and 1.13 (6 H, d, *J* 6.95, Me_2CHCO); *m/z* 258 (59%, M^+), 215 (73, M – Pr), 128 (40, Pr$^i_2$NCO), 114 (100, Pr^{i}CONHCH$_2$CH$_2$) and 86 (26, Pr^{i}CONH) (Found: M^+, 258.1940. $C_{13}H_{26}N_2O_3$ requires *M*, 258.1944). In the reaction with the oxazolidinone **10b**, we also recovered starting material (13%).

Treatment of the Esters **13**[12,13] *with LDA*.—Typically, the ester (0.3 mmol) in THF (1 cm^3) was added dropwise at 0 °C under argon to a solution of LDA (0.6 mmol) in THF (3 cm^3) and the mixture stirred at 0 °C for 2 h, cooled to –78 °C, quenched with aqueous ammonium chloride (5 cm^3) and allowed to warm to room temperature. The mixture was extracted with dichloromethane (4 × 20 cm^3) and the combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Column chromatography (SiO_2, CH_2Cl_2–hexane) of the residue gave a mixture of the esters **13**

and **14**, rich in the latter (**13a** + **14a**,[13] 63% in a ratio of 21 : 79 as judged by integration of the signals at δ 0.98 and 1.13; **13b** + **14b**,[12] 88% in a ratio of 10 : 90 as judged by integration of the signals at δ 3.61 and 3.59). The following enamino ketones were prepared by this method.

(RS,RS)-(Z)-6-*Dimethyl(phenyl)silyl*-5-*methyl*-6-*phenyl*-2-(2-*propylamino*)*hex*-2-*en*-4-*one* **15a** (19%), $\nu_{max}(CDCl_3)/cm^{-1}$ 1605 and 1565 (C=O and C=C), 1270 (SiMe) and 1125 (SiPh); δ_H(250 MHz; $CDCl_3$) 10.95 (1 H, br d, *J* 7.6, NH), 7.39–6.83 (10 H, m, 2 × Ph), 4.95 (1 H, br s, CH=C), 3.69 (1 H, dsept, *J* 8.7 and 6.4, C*H*Me_2), 2.79 (1 H, dq, *J* 11.6 and 6.6, SiCHC*H*Me), 2.60 (1 H, d, *J* 11.6, SiCH), 1.96 (3 H, s, CH=CH*Me*), 1.24 (3 H, d, *J* 6.4, CH*Me*$_A$Me$_B$), 1.22 (3 H, d, *J* 6.4, CHMe$_A$*Me*$_B$), 0.87 (3 H, d, *J* 6.6, CHSiCH*Me*), 0.16 (3 H, s, Si*Me*$_A$Me$_B$) and 0.14 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 379 (27.3%, M^+), 364 (70, M − Me), 336 (20, M − Pr^i), 135 (100, $PhMe_2Si$) and 126 (80, COCH=CMeNHPr^i).

(5RS,6SR)(Z)-2-6-*Dimethyl(phenyl)silyl*-5,7-*dimethyl*-(2-*propylamino*)*oct*-2-*en*-4-*one* **15b** (6 mg, 6%) as a yellow oil, R_f(hexane–CH_2Cl_2 1 : 2) 0.23; $\nu_{max}(CDCl_3)/cm^{-1}$ 1600, 1565 and 1510 (C=O and C=C) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 10.6 (1 H, br s, NH), 7.58–7.54 (2 H, m, *o*-ArH), 7.34–7.29 (3 H, m), 4.76 (1 H, s, COC*H*=CMe), 3.78–3.61 (1 H, m, NC*H*Me_2), 2.50 (1 H, dq, *J* 3.6 and 7.0, MeC*H*CO), 2.1–1.9 (1 H, m, Me_2C*H*CSi), 1.90 (3 H, s, CH=CH*Me*), 1.42 (1 H, t, *J* 3.8, SiCH), 1.20 (6 H, d, *J* 6.4, NCH*Me*$_2$), 1.09 (3 H, d, *J* 7.1, *Me*CHCO), 0.94 (3 H, d, *J* 6.9, SiCHCH*Me*$_A$Me$_B$), 0.81 (3 H, d, *J* 7.0, SiCHCHMe$_A$*Me*$_B$), 0.40 (3 H, s, Si*Me*$_A$Me$_B$) and 0.36 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 345 (3%, M^+), 330 (50, M − Me), 302 (60, M − Pr^i), 155 (100, CH_3CH_2COCH=CMeNHPr^i) and 126 (58, COCH=CMeNHPr^i) (Found: M^+, 345.2499. $C_{21}H_{35}NOSi$ requires *M*, 345.2488). The minor diastereoisomer, although probably present, was not identifiable by any distinctive signals.

(*Z*)-1-*Phenyl*-3-(2-*propylamino*)*but*-2-*enone* **17**.—Benzophenone (0.364 g, 2 mmol) in THF (3 cm^3) was added dropwise to a solution of LDA (4.1 mmol) in THF (3 cm^3) at −78 °C under argon. After 15 min, methyl benzoate (0.249 cm^3, 2 mmol) was added to the mixture, which was then stirred for 1 h. Aqueous ammonium chloride (5 cm^3) was added to the mixture, which was then extracted with ether (3 × 50 cm^3). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography (SiO_2, Et_2O–hexane) of the residue gave diphenylmethanol (245 mg, 67%), R_f(Et_2O–hexane 1 : 2) 0.26; δ_H(90 MHz; $CDCl_3$) 7.5–7.2 (10 H, m, 2 × Ph), 5.8 (1 H, d, *J* 4, C*H*OH) and 2.3 (1 H, d, *J* 4, OH); the vinylogous amide[6] **17** (97 mg, 24%) as a yellow oil, R_f(Et_2O–hexane 1 : 2) 0.18; $\nu_{max}(CDCl_3)/cm^{-1}$ 1600, 1585 and 1550 (C=O and C=C); δ_H(250 MHz; $CDCl_3$) 10.3 (1 H, br s, NH), 7.86–7.81 (2 H, m, *o*-ArH), 7.52–7.32 (3 H, m, *m*- and *p*-ArH), 5.61 (1 H, s, COCH=C), 3.89–3.70 (1 H, m, Me_2C*H*N), 2.09 (3 H, s, CH=C*Me*) and 1.29 (6 H, d, *J* 6.5, *Me*$_2$CH); *m*/*z* 203 (100%, M^+), 160 (25, M − Pr^i), 105 (94, PhCO), 98 [70, Pr^i-NHC(=CH_2)CH_2] and 77 (57, Ph) (Found: M^+, 203.1297. $C_{13}H_{17}NO$ requires *M*, 203.1300); *N*,*N*-diisopropylbenzamide[14] (175 mg, 43%); R_f(Et_2O–hexane 1 : 2) 0.15; δ_H(90 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 3.8–3.5 (2 H, m, 2 × Me_2C*H*) and 1.4 (12 H, d, *J* 7, 2 × *Me*$_2$CH); and (Z)-1,5-*diphenyl*-3-(2-*propylamino*)*pent*-2-*enone* **18** (22 mg, 4%), R_f-(Et_2O–hexane 1 : 2) 0.08; $\nu_{max}(CDCl_3)/cm^{-1}$ 1700 (PhC=OCH_2), 1695 (PhCOC=C) and 1590 (C=C and Ph); δ_H(250 MHz; $CDCl_3$) 8.10–7.00 (10 H, m, 2 × Ph), 5.59 (1 H, s, C=CH), 4.03 (2 H, s, C*H*$_2$C=CH), 3.73–3.59 (1 H, m, Me_2C*H*N) and 1.29 (6 H, d, *J* 6.4, *Me*$_2$CHN); *m*/*z* 307 (54%, M^+), 202 (84, M − C_6H_5CO), 105 (100, PhCO) and 77 (53, Ph) (Found: M^+, 307.1564. $C_{20}H_{21}NO_2$ requires *M*, 307.1572). A similar reaction using *p*-chlorobenzaldehyde in place of the benzophenone gave the vinylogous amide **17** (4%), and recovered aldehyde (42%).

References

1 W. Engel, I. Fleming and R. H. Smithers, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1637.
2 I. Fleming, J. H. M. Hill, D. Parker and D. Waterson, *J. Chem. Soc., Chem. Commun.*, 1985, 318.
3 D. A. Evans, T. C. Britton and J. A. Ellman, *Tetrahedron Lett.*, 1987, **28**, 6141.
4 P. Beak, W. J. Zajdel and D. B. Reitz, *Chem. Rev.*, 1984, **84**, 471.
5 I. Fleming, *Pure Appl. Chem.*, 1990, **62**, 1879.
6 G. Bartoli, C. Cimarelli, G. Palmieri, M. Bosco and R. Dalpozzo, *Synthesis*, 1990, 895.
7 N. De Kimpe, M. Palamareva and N. Schamp, *J. Org. Chem.*, 1985, **50**, 2993.
8 G. Wittig and H. Reiff, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 7.
9 G. Wittig, H.-J. Schmidt and H. Renner, *Chem. Ber.*, 1962, **95**, 2377; M. Newcomb and M. T. Burchill, *J. Am. Chem. Soc.*, 1984, **106**, 2450 and 8276.
10 M. Majewski, *Tetrahedron Lett.*, 1988, **29**, 4057.
11 M. V. George, D. J. Peterson and H. Gilman, *J. Am. Chem. Soc.*, 1960, **82**, 403.
12 R. A. Crump, I. Fleming, J. H. M. Hill, D. Parker, N. L. Reddy and D. Waterson, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3277.
13 I. Fleming and D. Waterson, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1809.
14 N. A. Leister and D. S. Tarbell, *J. Org. Chem.*, 1958, **23**, 1152.

Paper 3/00278K
Received 18*th January* 1993
Accepted 28*th January* 1993