Regioselective α-Alkylation of Extended Enolates Derived from Enamines of β-Keto Esters. Studies Relating to the Synthesis of 2-Substituted 2-Alkoxycarbonylcycloalkanones

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Enamines **4a–c**, **5a–c** and **6** have been prepared (from the corresponding 5-, 6- and 7-ring cyclic β-keto esters) and converted into enolates of general structure **2**. These extended enolates react with alkyl halides at the α-site exclusively and the resulting adducts, exemplified by **7**, have been hydrolysed to the corresponding 2-substituted 2-alkoxycarbonylcycloalkanones. These results are discussed in the context of the regioselectivity that has been reported for related enolates which tend, depending on the structure, to show a preference for γ-selectivity in their reactions with electrophiles. The asymmetric variant of the alkylation sequence described has also been examined but only modest enantioselectivity (up to 33% e.e.) has been attained by incorporation of (*S*)-2-methoxymethylpyrrolidine **25**, *via* enamine **26**. Further progress was blocked by problems encountered in the synthesis of the requisite enamines when the more hindered C_2-symmetric amines, such as (2*R*,5*R*)-2,5-dimethylpyrrolidine **27**, were used, thereby limiting the more general synthetic utility and scope of these extended enolates.

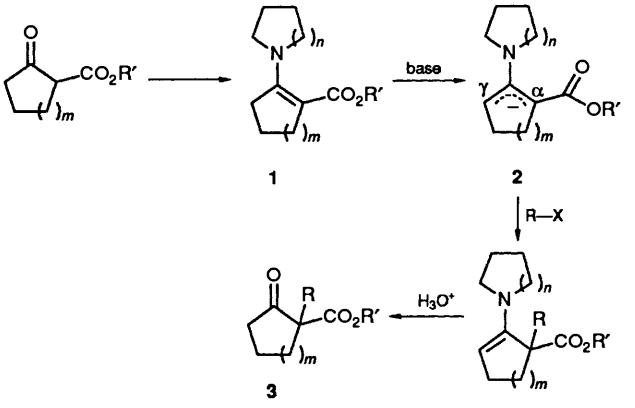
The alkylation of β-keto esters under basic conditions represents a widely used and synthetically flexible process. Much effort has been applied to the problems that are associated with this reaction and although reaction yields, the ratio of *C*- to *O*-alkylation and the competition between mono- and di-alkylation are subject to a number of variables, many of these factors are now well defined.[1] In addition, the ability to achieve the asymmetric alkylation of β-keto esters is important and this process offers an entry into a range of highly functionalised and enantiomerically pure substrates. Although this area has also witnessed a series of significant advances over recent years, the efficiency and generality of the synthetic solutions that are available with which to address this problem remain somewhat limited.[2]

Our interest in this area was stimulated by the opportunities that were offered by a series of biologically-useful targets for the development of new synthetic methodology. Our initial objective was to explore a general approach to 2-substituted 2-alkoxycarbonylcycloalkanones **3** that was amenable to the production of enantiomerically pure products. The strategy that we adopted, which is outlined in Scheme 1, was to study the reactivity of enolates **2** derived from enamines of cyclic β-keto esters **1**. These enolates are classic examples of nucleophiles capable of displaying ambident reactivity and may react with electrophiles, such as alkyl halides (RX), at either the α- or the γ-site, or at oxygen. Alkylation at nitrogen, a process that often accompanies enamine alkylation, may also participate.

If α-alkylation of enolate **2** can be achieved, then hydrolysis of the resulting adduct would give the corresponding 2-substituted cycloalkanone **3**. This chemistry should then allow for the incorporation of an enantiomerically pure secondary amine into **2** for use as a chiral auxiliary and provide a mechanism for the control of absolute stereochemistry.

It is also worth noting that enamines derived from β-keto esters are useful nucleophiles in their own right, having first been used in alkylation processes by Collie.[3] However their reactivity, in terms of the preference exhibited for α *vs.* γ selectivity, is complicated by a number of factors that limit their value in the synthesis of adducts of general structure **3**.†

In this paper we described the generation of a series of enolates related to **2**, together with the reactivity of these ambident nucleophiles towards alkyl halides. A number of structural variations relating to the ring sizes of both the starting β-keto esters and the secondary amine have been examined as has the possibility of developing the asymmetric variant of the sequence shown in Scheme 1. While some progress towards this latter goal has been made, our results in this aspect of the study have now led us to redefine the basic problems that remain to be solved.



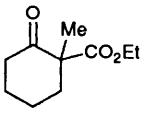
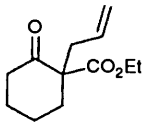
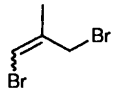
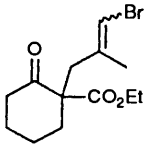
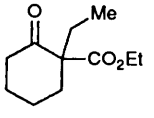
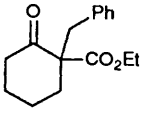
Scheme 1

Results and Discussion

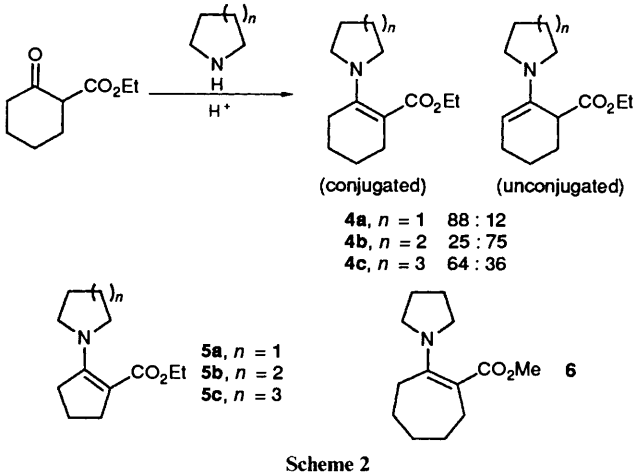
The first phase of this study was focused on the alkylation of commercially available 2-ethoxycarbonylcyclohexanone using enamines **4a**, **4b** and **4c** derived from pyrrolidine, piperidine and hexahydroazepine, respectively. These substrates were all prepared using literature procedures and in each case a mixture of the 'conjugated' and 'unconjugated' enamine isomers was

† Enamines **1**, as well as the corresponding acyclic variants, can exist as mixtures of the conjugated and unconjugated isomers (see Scheme 2). The observed preference for γ-regioselectivity observed in alkylation of these neutral systems has been attributed to the higher reactivity of the unconjugated form, although the nature of the electrophilic component has also been shown to influence site selectivity.[4,5]

Table 1

Entry	Enamine	R–X	Adduct		Yield (%)
1	**4a**	MeI		**9**	80[a]
2	**4a**	$H_2C{=}CHCH_2Br$		**10**	30[a], 70[c]
3	**4b**	MeI	**9**		100[a], 79[b]
4	**4b**	$H_2C{=}CHCH_2Br$	**10**		85[a], 62[b]
5	**4b**			**11**	26[a], 20[b], 40[c]
6	**4b**	EtI		**12**	40[a]
7	**4b**	$PhCH_2Br$		**13**	55[a], 42[b]
8	**4c**	MeI	**9**		60[a]
9	**4c**	$CH_2{=}CHCH_2Br$	**10**		50[a], 85[c]

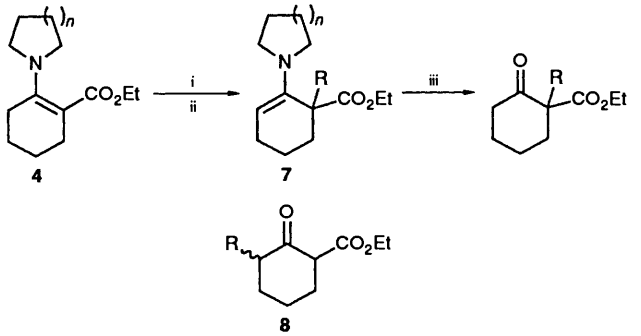
[a] Yield based on ^1H NMR and GC analysis. [b] Isolated yield. [c] Yield (^1H NMR–GC) when alkylation was carried out using DMPU as co-solvent.



Scheme 2

obtained in the proportions shown in Scheme 2.[5] The presence of this isomer mixture did not, however, appear to complicate our subsequent studies. We have also included within the scope of this study enamines **5a–c** and **6** derived from 2-ethoxycarbonylcyclopentanone and 2-methoxycarbonylcycloheptanone, respectively. In all of these latter cases the 'conjugated' form of the enamine predominated (≥95% as determined by ^1H NMR spectroscopy), although the low reactivity of the cycloheptanone carbonyl made only the synthesis of the pyrrolidine derivative **6** feasible.

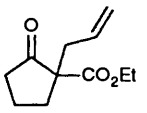
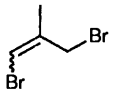
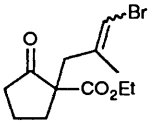
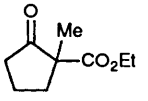
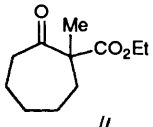
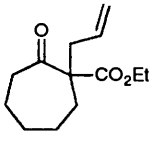
The results of the alkylation study relating to the cyclohexyl derivatives **4a–c** are shown in Table 1. The reaction sequence followed is shown in Scheme 3 and involved deprotonation of **4** using lithium diisopropylamide (LDA) in THF at −78 °C for 1 h. The resulting anion was then treated with the electrophile (an alkyl or allylic halide) and the reaction mixture was allowed to warm to room temperature. The initially-formed adduct **7** was not sufficiently stable to be isolated and fully characterised but was immediately treated with aqueous acid to effect enamine hydrolysis and the resulting substituted β-keto ester was obtained following chromatography.



Scheme 3 *Reagents and conditions:* i, LDA, THF, −78 °C; ii, R–X (see Table 1), −78 °C to room temp.; iii, H_3O^+

The yields shown in Table 1 refer to either isolated material or to the extent of conversion which was determined by ^1H NMR spectroscopic analysis of the crude reaction mixture (after acid hydrolysis) and reflects the ratio of alkylated adduct to 2-ethoxycarbonylcyclohexanone derived from unchanged

Table 2

Entry	Enamine	R–X	Adduct		Yield (%)
1	**5a**	$H_2C{=}CHCH_2Br$		**14**	100[c]
2	**5a**			**15**	50[c], 16[b]
3	**5b**	MeI		**16**	90[c]
4	**5b**	$H_2C{=}CHCH_2Br$	**14**		40[a]
5	**5c**	MeI	**16**		43[c]
6	**5c**	$H_2C{=}CHCH_2Br$	**14**		100[c]
7	**6**	MeI		**17**	70[a]
8	**6**	$H_2C{=}CHCH_2Br$		**18**	67[a], 30[b]

[a] Yield based on ^{1}H NMR and GC analysis. [b] Isolated yield. [c] Yield (^{1}H NMR–GC) when alkylation was carried out using DMPU as co-solvent.

enamine. A similar study was conducted using the cyclopentanone- and cycloheptanone-derived enamines **5a–c** and **6** and the results of this aspect of the investigation are shown in Table 2.

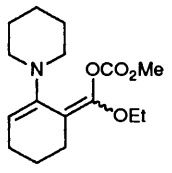
In all cases examined (Tables 1 and 2), the *only* alkylated product that was observed corresponded to the α-adduct (≥95% as determined by ^{1}H NMR spectroscopy and GC) and we were unable to detect the formation of the isomeric γ-adducts **8**. Care was taken to ensure the homogeneity of the alkylated products and a number of authentic samples were prepared for purposes of comparison. Direct alkylation of 2-ethoxycarbonylcyclohexanone (EtOH–EtONa or NaH–THF, RX) provided independent access to adducts **9**, **10** and **11**. The methylated cyclopentanone **16** and cycloheptanone **17** were prepared in a similar fashion. In other cases a comparison of spectroscopic data with that reported in the literature allowed unambiguous regiochemical assignments to be made. Using the conditions described by Huckin and Weiler, methylation of the dianion of 2-ethoxycarbonylcyclohexanone provided the γ-adduct **8** (R=Me) in 83% yield.[6] Once again, this material was useful as a GC standard in the investigation of reaction mixtures but this only served to confirm the conclusions reached by ^{1}H NMR spectroscopic analysis.

Several general comments need to be made at this point. The use of 1,3-dibromo-2-methylpropene[7] (as an *E*/*Z* mixture) as an alkylating agent was of interest in relation to a longer term synthetic objective but in this, and in other cases, the influence of *N*,*N*′-dimethylpropylene urea (DMPU) was marked. While it is not clear exactly what role this co-solvent plays, significantly higher yields were observed when this reagent was employed. Interestingly we were unable, despite several attempts, to achieve methylation of enamine **5a** under these anionic conditions.* We have also examined the reactivity of the enolate derived from **4b** with aldehydes. Although reaction is facile, we obtained complex product mixtures and we have been unable to draw any useful conclusions from this aspect of the study.

As stated in the introductory section, enolate **2** is also capable of reacting through oxygen and this mode of reaction was observed when acylation of **4b** was examined. Deprotonation of **4b** under the usual conditions followed by addition of methyl chloroformate to the resulting allylic anion gave, on workup (no acid hydrolysis step), a 1:1 mixture of **4b** and the *O*-acylated adduct **19**. This structural assignment, which must be regarded as tentative since the sensitivity of this product to hydrolytic cleavage precluded purification and full characterisation, was based on ^{1}H NMR [δ_H 5.12 (1 H, t, *J* 4, vinyl CH), 3.65 (3 H, s, OMe)] and mass spectral analysis [*m*/*z* (EI) 295 (100%, M^+)].

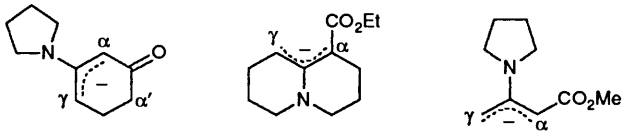
The results shown in Tables 1 and 2 also illustrate that the nature of the secondary amine component did not have a significant influence in terms of α *vs.* γ-regioselectivity.

* The possibility of *O*-alkylation was also considered since acidic hydrolysis would regenerate an unsubstituted β-keto ester. Using methyl iodide with an enolate derived from **5a** we have not been able to observe the *O*-alkylated adduct in the ^{1}H NMR spectrum of the crude reaction mixture (following aqueous quench but prior to hydrolysis). A similar study was conducted with enamine **26** but, once again, no evidence was obtained for *O*-alkylation. The low yields obtained with **26** may reflect the involvement of alternative pathways or may be a consequence of the more hindered nature of this system. We cannot, however, exclude that alkylation of nitrogen occurs in these cases. At first sight, this process would appear to be less favoured than alkylation of an enolate but we have observed that methylation of tertiary amines does occur in the presence of reactive allylic anions derived from ketene-*S*,*S*-acetals (P. Brough, University of Bath, unpublished results).



19

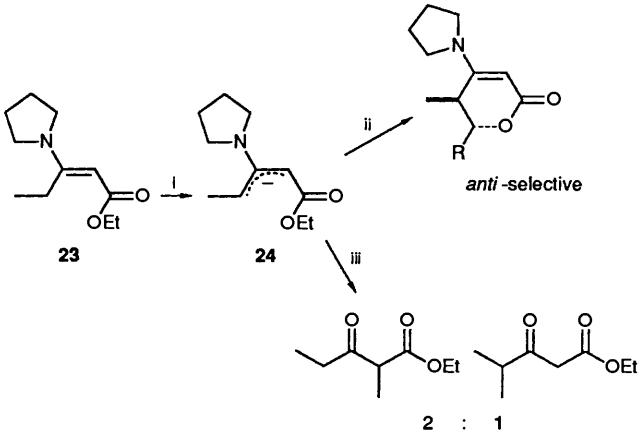
Furthermore, the cyclopentyl and cycloheptyl derivatives behaved in a similar fashion (Table 2) to those enolates incorporating a cyclohexyl framework (Table 1) and it is reasonable to conclude that the observation of exclusive α-alkylation should be general for constrained anions of this type. It is, however, interesting to compare the reactivity of the 'endocyclic' enolates **2** with results that have been reported for structurally similar systems. Enolate **20**, where the carbonyl function is also incorporated in the ring, undergoes alkylation at the γ-site.[8] However, in this and related cases there is also the possibility of reactions resulting from deprotonation of α′ which has been shown to be favoured under kinetically controlled conditions.[8c]



20 **21** **22**

Another cyclic variant, the quinolizidine-based enolate **21**, has been shown to react with alkylating agents (1-bromo-3-chloropropane) to give the α-adduct as the major product (α:γ = 7:1).[9] It is also of interest to compare the reactivity of the 'endocyclic' enolates **2** with those generated from enamines derived from acyclic β-keto esters. Enolate **22** (from the enamine of methyl acetoacetate) may be generated using either KH or LDA and has been shown to undergo methylation and silylation at the γ-site exclusively.[8b,10]

Some of the most significant contributions to this area have been made by Schlessinger and co-workers who have developed the synthetic utility of the enolate **24** derived from enamine **23**.[11] Aldehydes react with this species at the γ-site with a high degree of both regioselectivity and either *anti*- or *syn*-diastereoselectivity (depending on the nature of the secondary amine component). Furthermore, good levels of asymmetric induction may be achieved by incorporation of an appropriate secondary amine into **24**.[12] Given the difficulties that we had encountered with aldol-type reactions of enolates **4**, we were interested to probe the regioselectivity exhibited by **24** towards alkyl halides.

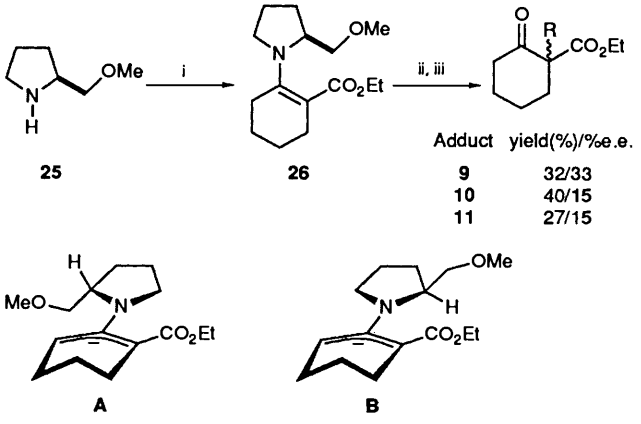


23 **24**

Scheme 4 *Reagents and conditions:* i, LDA, THF, −78 °C; ii, RCHO (ref. 11); iii, Mel, then H_3O^+

Quenching enolate **24**[11] with methyl iodide followed by hydrolysis of the crude reaction mixture gave a 2:1 mixture (^{1}H NMR) of the α- and γ-adducts in quantitative yield (Scheme 4). Clearly, the regioselectivity observed in anions of this type depends, not surprisingly, on the nature of the electrophile (RX *vs.* RCHO) and the need for a much more thorough appreciation of solution structure of the reactive species has been recognised.[13]

Asymmetric Alkylation Studies.—The development of the asymmetric variation of the chemistry shown in Scheme 3 was our longer term goal. Schlessinger has shown that the incorporation of a chiral secondary amine into the acyclic enamine **23** provides an efficient mechanism for asymmetric induction and this approach was obviously applicable to the cyclic variants, such as **2**. Our initial effort focused on the use of readily available (*S*)-2-methoxymethylpyrrolidine **25**[14] as a chiral auxiliary (Scheme 5).



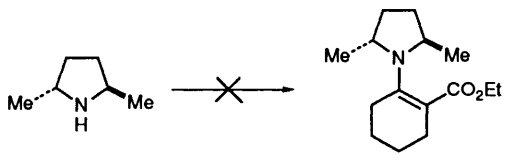
25 **26**

A **B**

Scheme 5 *Reagents and conditions:* i, 2-Ethoxycarbonylcyclohexanone, $TolSO_3H$ (cat), C_6H_6, reflux (66%); ii, LDA, THF, −78 °C, then R–X (see Table 1); iii, H_3O^+

Condensation of 2-ethoxycarbonylcyclohexanone with this amine gave the corresponding enamine **26** (66% yield) which was isolated as a 9:1 mixture with the 'conjugated' form (as shown) predominating. Alkylation of **26** was carried out under standard conditions (LDA, THF, −78 °C, then R–X) and the initially-formed adduct was hydrolysed *in situ* and the corresponding substituted β-keto ester was isolated in the yield shown.* The level of asymmetric induction in the alkylated products was evaluated by chiral shift ^{1}H NMR spectroscopy using Eu(hfc)$_3$ and this method of analysis was validated by using the corresponding racemates as standards. The results of this study are shown in Scheme 5, but in the best case—alkylation of **26** using methyl iodide—the level of asymmetric induction was modest (33% e.e). This is presumed to be a consequence for a preference for conformer **A** over conformer **B** which would lead to a minimization of the interactions between the methoxymethyl residue and ethoxycarbonyl function. Conformer **B** would, however, provide a much higher level of diastereofacial selectivity in the alkylation step but presumably the rate of isomerisation (**A** ⇌ **B**) is slow compared to the rate of alkylation. This problem has been recognised by Whitesell who observed: 'Clearly, what is needed is an amine with a C_2 axis of symmetry.'[15] C_2-Symmetric amines have, as a result, been studied widely, finding applications in a

* See footnote on p. 2171.



27 28

29 30

number of asymmetric processes and we focused on the use of *trans*-2,5-dimethylpyrrolidine **27** as a suitable auxiliary. This amine, first used by Whitesell[15] in the asymmetric alkylation of more conventional enamines, was prepared as the (2*R*,5*R*) enantiomer by the methods described by Masamune.[16]

We have, however, been unable to achieve the synthesis of the target enamine **28**. Although amine **27** is available, the synthetic routes described to date for its preparation do require a significant effort and the conventional methods of enamine synthesis which would rely on the use of an excess of this volatile amine were not considered attractive for obvious reasons. We then examined a number of alternative procedures for enamine generation[17] based on other dehydrating agents and Lewis acids, but were unable to prepare enamine **28** under a variety of conditions. The presence of the flanking methyl residues in **27** clearly reduces the nucleophilicity of nitrogen and it appears that this steric hindrance, combined with a less reactive ketone function, are responsible for this failure. Weinreb has reported that *N*-silylation of volatile amines promotes enamine formation.[18] While this method worked well for the synthesis of enamine **4a** (75% yield), reaction of 2-ethoxycarbonylcyclohexanone with *N*-trimethylsilylpiperidine (a less nucleophilic amine and a reasonable model for reactions involving the more valuable C_2-symmetric amine **27**) gave only the corresponding silyl enol ether and no trace of **4b** was observed (by GC).

A similar lack of reactivity was observed in all attempts to generate enamines from 2-ethoxycarbonylcyclohexanone and racemic *trans*-2,5-(dimethoxymethyl)pyrrolidine **29**[19] and (−)-**30** and this approach to the asymmetric synthesis of substituted β-keto esters has been abandoned. The results shown in Scheme 5 are promising but the basic problem in this area has been redefined with the major hurdle being the incorporation of a suitable amine auxiliary rather than the alkylation sequence. We are currently examining alternative approaches to this problem of enamine synthesis but the limitations of methods that rely on C_2-symmetric monoamines are significant and the practical value of these systems in stoichiometric processes must be very carfully evaluated. Schlessinger[13] has, in a recent and very elegant study, addressed these limitations within the context of the acyclic derivative **23** and the development of an efficient and general asymmetric alkylation of β-keto esters remains an attractive objective.

Experimental

General.—IR spectra were recorded using a Perkin-Elmer 1310 grating spectrophotometer. Routine mass spectra from electron ionisation (EI, 70 eV), chemical ionisation (CI, isobutane) and high resolution accurate mass determination were recorded with a VG Analytical 7070E instrument with a VG2000 data system and using the SERC MS Service Centre at Swansea. ^{1}H NMR (270 MHz) and ^{13}C NMR (68 MHz) spectra were recorded in $CDCl_3$ at 270 MHz on a JEOL GNM GX FT 270 spectrometer. Elemental microanalyses were carried out using a Carlo Erba 1106 Elemental Analyser. Gas chromatography (GC) was carried out using a AI 93 gas chromatograph with a 0.2 mm × 25 m OV-1 capillary column and helium as carrier gas with a temperature gradient (50–150 °C).

General Procedure for the Deprotonation and Alkylation of Enamines.—The β-keto ester enamine (1 mmol) in THF (2 cm^3) was added dropwise to a solution of LDA (1.1 mol equiv.) in THF (5 cm^3) at −78 °C and the resulting solution was stirred for 1 h. The alkyl halide (2–5 mol equiv.) was then added and after 0.5 h, the solution was allowed to warm to room temperature and stirred until the reaction was judged to be complete by GC. Hydrochloric acid (5 cm^3; 2 mol dm^{-3}) was added and the mixture stirred vigorously overnight to effect hydrolysis. Ethyl acetate was then added to this mixture and the organic layer separated. The aqueous phase was further extracted with ethyl acetate and the combined organic phases were washed with saturated aqueous $NaHCO_3$ and then brine. The extracts were dried ($MgSO_4$) and removal of solvents under reduced pressure gave the crude product as an oil which was analysed by ^{1}H NMR spectroscopy and GC. The purified products were then isolated following flash column chromatography (silica gel) using ethyl acetate–light petroleum as eluent.

When DMPU was used as a co-solvent, this reagent (2 cm^3 on the scale described above) was added to the pre-formed solution of LDA prior to addition of the enamine.

Using literature procedures, based on the alkylation of ethyl 2-oxocyclohexanecarboxylate using either NaOEt or NaH, authentic samples of **9**,[20] **10**,[21] **12**,[22] **13**,[23] **14**,[24] **16**,[25] **17**[26] and **18**[21] were prepared. Ethyl 3-methyl-2-oxocyclohexanecarboxylate **8** (R = Me) was prepared using the procedure described by Huckin and Weiler.[6] In all cases physical and spectroscopic data obtained for the substituted β-keto esters was consistent for the required structure and in agreement with that described previously.

Ethyl 1-(3-*Bromo*-2-*methylprop*-2-*enyl*)-2-*oxocyclohexanecarboxylate* **11**.—Prepared by alkylation of the enolate derived from **4b** or by alkylation of ethyl 2-oxocyclohexanecarboxylate with 1,3-dibromo-2-methylpropene using sodium ethoxide (in 70% yield). (Found: M$^+$ + 1, 303.059. $C_{13}H_{19}BrO_3$ + 1 requires *M*, 303.059); ν_{max}(film)/cm^{-1} 2920, 1720 and 1640; δ_H(270 MHz; $CDCl_3$) (2 : 1 mixture of *E*/*Z*-isomers) 5.95 (1 H, m, =CHBr), 4.15 (2 H, m, CO_2CH_2Me), 2.60–2.20 (6 H, m), 1.78 (2 H, d, *J* 1, =CCH$_3$), 1.77 (1 H, d, *J* 1, =CCH$_3$), 1.70–1.54 (4 H, m) and 1.1 (3 H, m, $CO_2CH_2CH_3$); δ_C (68 MHz; $CDCl_3$) 174.8 (C), 173 (C), 138.7 (C), 103/102.5 (CH), 60.1 (CH_2), 54.0 (CH), 40.9 (CH_2), 33.8 (CH_2), 31.4 (CH_2), 26.5 (CH_2), 22.0 (CH_2), 22.0/18.6 (CH_3) and 14.0 (CH_3); *m*/*z* (CI) 305/303 (M$^+$ + H, 5%) and 171 (100).

Ethyl 1-(3-*Bromo*-2-*methylprop*-2-*enyl*)-2-*oxocyclopentanecarboxylate* **15**.—Prepared by alkylation of the enolate derived from enamine **5a** and 1,3-dibromo-2-methylpropene in 16% isolated yield (Found: M$^+$ − Br, 209.120. $C_{12}H_{17}O_3$ requires *M* − Br, 209.118); ν_{max}(film)/cm^{-1} 2960, 1720 and 1625; δ_H (270 MHz; $CDCl_3$) (2:1 mixture of *E*/*Z*-isomers) 6.00 (1 H, s, =CHBr), 4.10 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 2.60-1.80 (8 H, m), 1.78 (1 H, d, *J* 1.2, =CCH$_3$), 1.73 (2 H, d, *J* 1.2, =CCH$_3$) and 1.20 (3 H, t, *J* 7, OCH_2CH_3); δ_C(68 MHz; $CDCl_3$) CO (not observed), 170 (C), 137.5 (C), 105.5 (CH), 61.7 (C), 41.5 (CH_2), 37.5 (CH_3), 32 (CH_3), 20.1 (CH_2), 19.4 (CH_2), 17 (CH_2) and 14 (CH_2); *m*/*z* (CI) 291 (MH$^+$, 55%) and 289 (MH$^+$, 60); *m*/*z* (EI) 209 (M$^+$ − Br, 100).

Ethyl 2-[(S)-2-*Methoxymethylpyrrolidin*-1-*yl*]*cyclohexenecarboxylate* **26**.—A solution of ethyl 2-oxocyclohexanecarboxylate (4.0 g, 26 mmol) and (*S*)-2-methoxymethylpyrrolidine **25** (3.0 g, 26 mmol) in benzene (50 cm^3) containing a catalytic amount of toluene-*p*-sulfonic acid was heated to reflux under Dean and Stark conditions for 3 d. After this time the solvent was removed under reduced pressure and the residue was purified by bulb to bulb distillation to yield *enamine* **26** (4.7 g, 68%) as a colourless oil b.p. (bulb to bulb) 150 °C/0.04 mmHg. (Found: M^+, 267.1835. $C_{15}H_{25}NO_3$ requires *M*, 267.1833); ν_{max}(film)/cm^{-1} 2934, 1737, 1679 and 1217; δ_H(270 MHz; $CDCl_3$) 4.2 (2 H, m, $CO_2CH_2CH_3$), 3.4–3.2 (4 H, m, NCH, OCH_2, NCH_2), 3.3 (3 H, s, OMe), 2.95 (1 H, m), 2.6–1.4 (12 H, m, CH_2) and 1.3 (3 H, m, $CO_2CH_2CH_3$); δ_C(68 MHz; $CDCl_3$) 168 (C), 164.7 (C), 140 (C), 74.9 (CH_2), 59 (CH), 58.8 (CH_3), 57.2 (CH_2), 53.2 (CH_2), 41.8 (CH_2), 29.9 (CH_2), 27.7 (CH_2), 27.1 (CH_2), 25.2 (CH_2), 23.2 (CH_2) and 14.2 (CH_3); *m*/*z* (EI) 267 (M^+, 10%), 222 (60%), 170 (40%) and 124 (100%).

Approximately 10% of the unconjugated form of this enamine was observed in the ^1H NMR spectrum: δ_H 4.6 (0.1 H, m, C=CH).

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