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Assessing the scope of the tandem Michael/intramolecular aldol reaction mediated by secondary amines, thiols and phosphines

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Abstract—The outcome of a tandem Michael/intramolecular aldol reaction which is mediated by secondary amines, thiols and phosphines has been found to be highly substrate dependent, with the best results being obtained for the formation of 5 and 6-membered rings using thiol or thiolate nucleophiles. Amine and phosphine mediated cyclisations were found to be problematic in several cases but were still effective methods for the formation of 5–7 membered rings.

1. Introduction

In our preliminary communications,[1] we described the ability of a range of nucleophiles, including secondary amines, thiols and phosphines to effect a tandem intramolecular Michael/aldol cyclisation of enones **1** leading to either the adducts **2** or the eliminated Baylis–Hillman type product **3**[1] (Scheme 1).

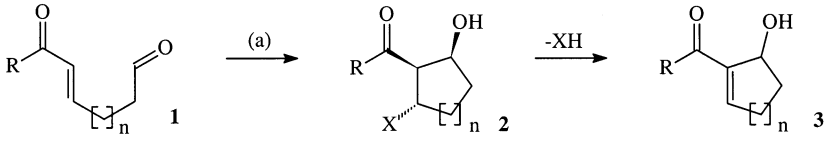
Following these preliminary studies we were keen to assess the scope of this reaction taking into account such variables as the nature of the nucleophile and the group R and the potential for variations in the ring size of the product formed. We were also interested in studying the mechanistic aspects of this reaction and this paper brings together our preliminary findings on these matters and our further studies on the process.

2. Preparation of aldehydes 1

The substrates (**1a–j**) for the investigation were prepared by reaction of a suitable phosphorus ylid with a dialdehyde prepared by either hydrolysis of 2,5-dimethoxytetrahydrofuran in the case of succinaldehyde (method A),[2] ozonolysis of a cycloalkene (method B) or using an aqueous solution of glutaraldehyde (method C) (Table 1). The crude products are purified by column chromatography and a *bis*-enone, obtained by double Wittig reaction on the dialdehyde, is generally obtained as a by-product of the reaction[3] which can lead to diminished yield. In the case of reactions in aqueous media, the yields are generally low and the *Z*-alkene isomers are also isolated in significant amounts (Scheme 2).

3. Reactions involving secondary amines

Our preliminary investigation stemmed from the observations that a suitable catalyst for effecting the conversion of the substrate **1a** into the cyclised product **3a** was the secondary amine piperidine. We thus performed a preliminary study of the reaction of other amines and it was apparent that piperidine was by far the superior choice of catalyst for effecting this transformation. The results in Table 2 illustrate that, with the exception of the hindered amine 2,6-dimethylpiperidine, all the secondary amines gave the expected cyclised product, however none of the



Scheme 1. (a) X=R_2N, R_3P^+, PhS; *n*=1,2; R=Alkyl, Ph.

Keywords: tandem Michael/intramolecular aldol reaction; secondary amine; thiols; phosphines.
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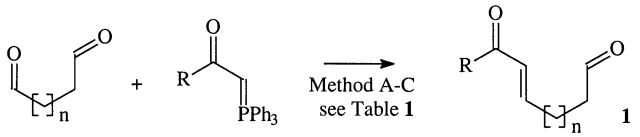


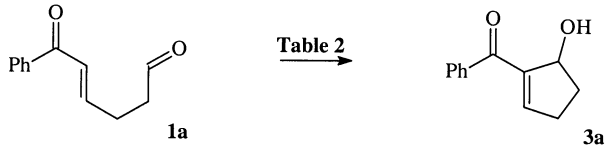
Scheme 2.

Table 1.

Entry	R	*n*	Method	Yield (%)
1a	Ph	1	A	48
1b	Ph	2	B/C	70/73
1c	Ph	3	B	41
1d	Ph	4	B	47
1e	Ph	5	B	49
1f	OEt	1	A	58
1g	OEt	2	C	*E*-41, *Z*-23
1h	OEt	3	B	38
1i	STol	1	A	46
1j	STol	2	C	32

Method A: $RCOCHPPh_3$, 2.0 equiv. succinaldehyde, CH_2Cl_2. Method B: (i) 10–20 equiv. cycloalkene, O_3, CH_2Cl_2, −78°C, (ii) PPh_3, −78°C, (iii) 1 equiv. $RCOCHPPh_3$. Method C: 20 equiv. glutaric dialdehyde (25% w/v in H_2O), EtOH, rt, $RCOCHPPh_3$.

catalysts showed an improvement in yield compared to piperidine. In addition, a trend was observed in the series piperidine, 2-methylpiperidine and 2,6-dimethylpiperidine, in that the yield of product decreases as steric bulk of the amine increases. To further investigate this reaction, we performed a series of experiments in which the concentration of substrate **1a** was varied. The previous experiments were all performed at a concentration of 0.35 M, on repeating at 0.18 and 0.09 M a slight increase in yield (ca. 5% for 0.09 M) was observed for the formation of **3a**, however reaction time was increased for both reactions (10 and 15 days for 95% conversion, respectively) (Scheme 3).



Scheme 3.

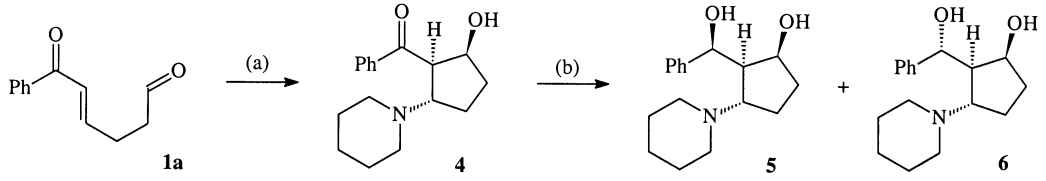
These observations suggest that the reaction for the formation of **3a** is concentration dependent, however on closer inspection of the NMR data for these reactions, it was apparent that the reaction was proceeding through a long-lived and fairly stable intermediate which we presumed to be the product of 1,4-addition and intramolecular aldol condensation (**4**). This was indeed shown to be true, as treatment of aldehyde **1a** with an excess of piperidine in chloroform effected a complete transformation of the starting material to the intermediate **4** (together with a small amount of **3a**). In addition, **4** was stable for long periods of time (>7 days) in chloroform solution and very little further conversion to **3a** was observed. Furthermore, evaporation of the chloroform, followed by treatment of a methanolic solution of **4** with sodium borohydride gave a separable 1:1.3 mixture of the diols **5** and **6** in 67% overall yield, the former providing crystals suitable for X-ray analysis[1b] which confirmed the relative stereochemistry of the intermediate **4**, as that depicted (Scheme 4).

We repeated this reaction using the enone **1b** and found that the adduct **8** was formed very rapidly. The presence of signals at δ 3.2 (1H, ddd, J=3, 12, 12 Hz), 3.6 (1H, dd, J=2.0, 12 Hz) and 4.2 (1H, m), indicated that the relative stereochemistry of **8** is as illustrated. In addition, it was apparent that the reaction leading to **8** was proceeding via an intermediate enol, possibly of structure **7**, as indicated by signals at δ 4.3 (1H, dt, J=14, 7.5 Hz) and 5.8 (1H, d, J=14 Hz). Again, **8** was found to be stable in solution for prolonged periods of time with only ca. ~10% conversion

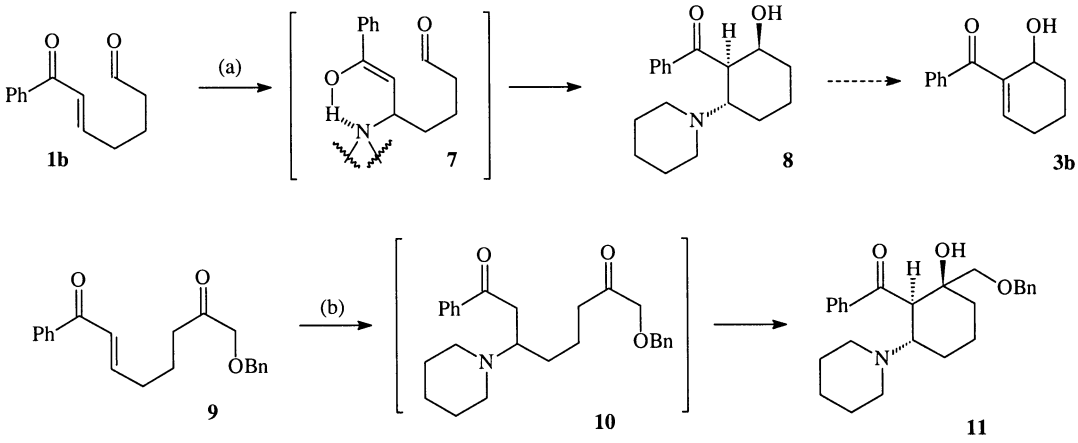
Table 2.

Amine[a]	% Conversion	% **3a**[b]	% Recovery	% Dec.
Piperidine	93	55 (50)	7	38
2-Methylpiperidine	97	30 (26)	3	67
2,6-Dimethylpiperidine[c]	63	0	37	63
Morpholine	74	16	39	45
Piperazine	94	28	9	63
N-Methylpiperazine	83	21	25	54
Pyrrolidine	82	15	18	67
Di-*n*-butylamine	100	15	0	85

[a] Conditions: catalyst (30 mol%), $CDCl_3$ (0.35 M), rt, 7 days.
[b] Yields are calculated from ^1H NMR data, with yields in brackets being isolated yields.
[c] A mixture of the *cis*- and *trans*-amines was used.



Scheme 4. (a) 1.3 equiv. piperidine, $CHCl_3$, 10 min, rt, (b) $NaBH_4$, MeOH, 0°C.

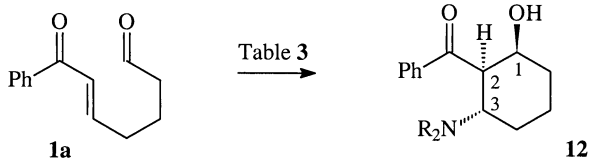


Scheme 5. (a) 1.3 equiv. piperidine, $CHCl_3$, (b) 1.3 equiv. piperidine, $CHCl_3$; 60%.

to the cyclohexenol **3b** being observed over 28 days. We were also able to isolate the adduct **11** which arose from the addition of piperidine to ketone **9**[4] and found that this compound gave suitable crystal for X-ray structure determination which confirmed the stereochemistry as that shown below.[1b] Interestingly, this cyclisation took considerably longer to effect than the previous case, requiring six days for complete reaction, possibly reflecting the lower reactivity of ketones. We were also able to observe (NMR) the intermediate conjugate adduct **10** in the reaction mixture and, as in other cases, the Michael/aldol sequence proceeded to give a single diastereoisomer by NMR and as yet we have been unable to isolate any minor diastereomeric products (Scheme 5).

As it was apparent that the intermediates **4**, **8** and **11** are easily formed, we decided to investigate their presence in the reactions of a variety of amines (Table 3). Reaction of **1b** with a 1.3 molar excess of the amine, whilst following the reaction by NMR and observing the signals in the intermediate **12** for H_1, H_2 and H_3, illustrated that again piperidine was the best base for effecting this transformation (Scheme 6).

As can be seen, the only amines leading to the intermediate adduct **12** in a good yield are the 6-membered cyclic amines piperidine and 1-methylpiperazine. The 4-, 5- and 7-membered cyclic amines together with dibenzylamine predominantly gave products of decomposition arising from self-aldol condensations of the substrate **1b**. The reason for the success of the reaction only with 6-membered amines is unclear but it is unlikely to be differences in basicity owing to the similarity in structure of the amines employed. As previously stated, it is likely that the reaction is proceeding via an intermediate enol similar in structure to **7** and it may be that the propensity to form this moiety is the key to the success or failure of the reactions. It is possible that changes in the structure of the base have a significant influence on the stability of this intermediate or even its ability to be formed. Whatever this reason might be, it is obvious that the reaction is susceptible to changes in structure of the amine and it is likely that progress with this methodology is best focused on the development of further 6-membered cyclic amine systems.



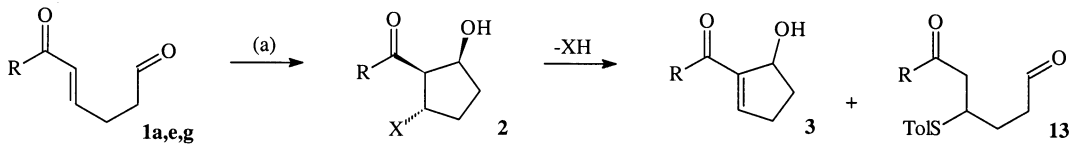
Scheme 6. (a) 1.3 equiv. $R_2NH/CDCl_3$, 0–7 days.

4. Systematic modification of substrates and catalyst

With these preliminary studies in hand, we next embarked upon a systematic study of the cyclisation process and chose to investigate the use of different electron withdrawing groups in the Michael substrate and to couple these modifications with variation in ring size and the use of other nucleophiles. This decision was based upon literature reports that metal thiolates and selenates,[6] or metallated amines[7] can be used in tandem Michael-aldol reactions, including some cyclisations,[8] and that phosphines can catalyse intramolecular Baylis–Hillman reactions,[9] albeit in poor isolated yield. Our first area of investigation focused on the formation of the 5-membered adducts **2** or the corresponding cyclopentenols **3** using either the

Table 3.

Amine	Time	**12** (%)	Decomp. (%)	H_1 (J)	H_2 (J)	H_3 (J)
Azetidine	2 h	0	100	–	–	–
Pyrrolidine	24 h	~25	~75	4.18 (br m)	3.57 (dd, 2, 11)	3.47 (ddd, *J*=3, 11, 11)
Piperidine	10–15 min	>90	<10	4.20 (br m)	3.60 (dd, 2, 12)	3.20 (ddd, *J*=3, 12, 12)
1-Methylpiperazine	3 h	>85	<15	4.14 (br m)	3.68 (dd, 2, 11)	3.47 (ddd, *J*=3, 12, 12)
Homopiperidine	24 h	~5	~95	4.17 (br m)	3.58 (dd, 2, 11)	3.30 (obscured)
Dibenzylamine	7 days	Trace	>95	–	–	–



Scheme 7.

Table 4.

Entry	Substrate	R	Method	X	2[a]	3	13[a]
1	**1a**	Ph	1.3 equiv. piperidine, $CDCl_3$, 10 min	Piperidyl	**4**, 90%[b]	–	–
2	**1a**	Ph	0.3 equiv. piperidine, $CDCl_3$, 144 h	Piperidyl	–	**3a**, 50%	–
3	**1a**	Ph	1.3 equiv. TolSH, $CHCl_3$, 16 h	TolS	**2aT**, 77%	–	Trace
4	**1a**	Ph	0.2 equiv. *n*-Bu_3P, $CDCl_3$, 17 h	–	–	**3a**, 20%	–
5	**1f**	OEt	1.3 equiv. piperidine, $CDCl_3$ 2 days	Piperidyl	Dec[c]	–	–
6	**1f**	OEt	0.3 equiv. piperidine, $CDCl_3$ 2 days	Piperidyl	Dec[c]	–	–
7	**1f**	OEt	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	**2fT**, 72%	–	**13fT**, 10%
8	**1f**	OEt	0.4 equiv. *n*-Bu_3P, $CDCl_3$, 28 days	–	–	**3f,** 40%	–
9	**1i**	STol	1.3 equiv. piperidine, $CDCl_3$, 2 days	Piperidyl	**2iP**, 10%[b]	–	–
10	**1i**	STol	0.3 equiv. piperidine, $CDCl_3$, 2 days	Piperidyl	Dec[c]	–	–
11	**1i**	STol	3 equiv. TolSH, Δ, $CHCl_3$, 12 h	TolS	**2iT**, 56%	–	Trace
12	**1i**	STol	0.4 equiv. *n*-Bu_3P, $CDCl_3$, 1 h	–	Dec[d]	–	–

[a] **P** refers to adducts derived from piperidine, **T** from *p*-TolSH.
[b] As observed by NMR of the progress of the reaction.
[c] Largely composed of products derived from aldol condensation.
[d] Unidentified decomposition products.

piperidine-based methodology described earlier, or by the use of thiolate or phosphine-based catalyst; these results are summarised in Table 4 (Scheme 7).

Our investigations on the 5-membered series focused on the use of an aryl ketone (**1a**), ester (**1f**) or thiolester (**1i**) acceptor group and the reactions with piperidine were attempted first. Reaction of the ketone **1a** gave, as previously noted, the adduct **4** with excess piperidine (entry 1) and the cyclised product **3a** with 0.3 equiv. (entry 2). However, application of these conditions (entries 5 and 6) to the ester-containing substrate **1f** gave only products derived from aldol condensation of the aldehyde function, possibly reflecting the lower reactivity of α,β-unsaturated esters towards Michael reactions. Similar reactions of the thiolester-containing substrate **1i** with piperidine (entries 9 and 10) were also complicated by considerable decomposition, including some evidence of amide formation (by displacement of the thiotolyl group) and aldol reaction processes, and only a low yield (10%) of the intermediate adduct **2iP** was observed to be formed.

Turning our attention to the use of a thiol as the nucleophile in the reaction, we were pleased to observe that the addition of an excess of *p*-TolSH to a chloroform solution of **1a** at room temperature effected the cyclisation to the adduct **2aT** in 77% isolated yield (entry 3). Careful analysis of the NMR of the crude reaction mixture failed to show the presence of any other isomeric compounds. Similar treatment of the ester-substituted **1e** failed to effect this transformation even at reflux in chloroform. However, if the reaction was performed with 2 equiv. of *p*-TolSH and a catalytic quantity of *p*-TolSNa[10], the adduct **2fT** was obtained in 72% yield (entry 7) as well as the addition product **13fT** in 10% yield. We were able to grow crystals of **2fT** which were suitable for X-ray analysis[11] and this confirmed the structure to be as illustrated in Fig. 1. Cyclisation of the thiolester substrate **1i** did not require the use of sodium thiolate as a catalyst, however refluxing the reaction for 12 h was essential to

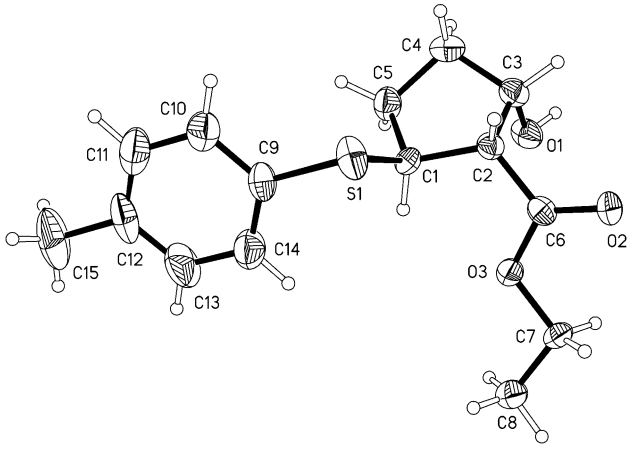


Figure 1. X-Ray structure of **2fT**.

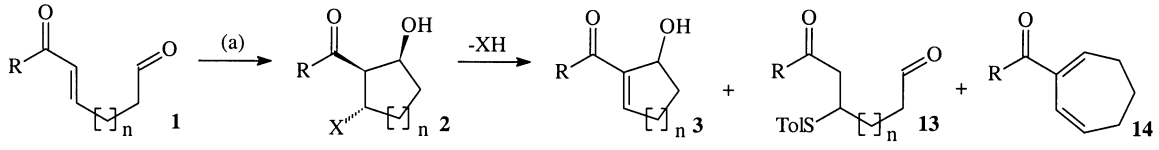
effect the formation of the adduct **2iT** in 56% yield (entry 11). Again, careful analysis of the NMR of the crude reaction mixture seemed to suggest that the reaction gave essentially a single product.

We next investigated the use of phosphines and found that treatment of a solution of enone **1a** in chloroform with a catalytic amount of *n*-Bu_3P led to the formation of the previously prepared enone **3a** in a mediocre 20% yield (entry 4) and similar treatment of **1f** led to the formation of **3f** in 40% yield, however a prolonged reaction time was required (entry 8). Not surprisingly, treatment of thiolester **1i** under these conditions led to a rapid complete decomposition.

We turned our attention to the reactions of enone substrate **1b**, the ester **1g** and the thioester **1j** which, on cyclisation, would lead to 6-membered adducts **2** or cyclohexenes **3**. The results of these investigations together with the results of our cyclisation attempts to give 7- and 9-membered ring systems are reported in Table 5 (Scheme 8).

As previously reported,[1] reaction of the ketone **1b** with excess piperidine gave the adduct **2bP** (entry 1) and the cyclised product **3b** using 0.3 equiv. (entry 2). However, as with the 5-membered series, application of these conditions (entries 5 and 6) to the ester-containing substrate ***E*-1g** gave only products derived from aldol condensation of the aldehyde function. Similarly, reaction of the thiolester-containing substrate **1j** with piperidine (entries 10 and 11) was complicated by considerable decomposition, including amide formation and aldol condensations with only a low yield (ca. 5%) of the intermediate adduct **2jP** being observed by NMR.

The use of a thiol as the nucleophile in the reaction was again very successful and we were pleased to observe that the addition of an excess of *p*-TolSH to a chloroform solution of **1b** at room temperature effected the cyclisation to the adduct **2bT** in 93% isolated yield as the sole cyclisation product (entry 3). A similar treatment of the ester-substituted ***E*-1g** failed to effect the transformation even at reflux in chloroform, however, if the reaction was



Scheme 8.

Table 5.

Entry	Substrate	R	*n*	Method[a]	X	2[b]	3	13	14
1	**1b**	Ph	2	1.3 equiv. piperidine, 10 min	Piperidyl	**2bP**, 90%[c]	–	–	–
2	**1b**	Ph	2	0.3 equiv. piperidine, 14–28 days	Piperidyl	–	**3b**, 24–30%	–	–
3	**1b**	Ph	2	1.3 equiv. TolSH, 16 h rt	TolS	**2bT**, 93%	–	Trace	
4	**1b**	Ph	2	0.2 equiv. nBu_3P, 2 h	–	–	**3b**, 75%	–	–
5	***E*-1g**	OEt	2	1.3 equiv. piperidine	Piperidyl	Dec[d]	–	–	–
6	***E*-1g**	OEt	2	0.3 equiv. piperidine	Piperidyl	Dec[d]	–	–	–
7	***E*-1g**	OEt	2	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	**2gT**,[e] 75%	–	Trace	–
8	***E*-1g**	OEt	2	0.2 equiv. *n*-Bu_3P, 24 h	–	–	**3g**, 50%	–	–
9	***Z*-1g**	OEt	2	0.2 equiv. *n*-Bu_3P, 24 h	–	–	**3g**, 70%	–	–
10	**1j**	STol	2	1.3 equiv. piperidine, 2 days	Piperidyl	**2jP**,[c] ca. 5%	–	–	–
11	**1j**	STol	2	0.3 equiv. piperidine, 2 days	Piperidyl	**2jP**,[c] ca. 5%	–	–	–
12	**1j**	STol	2	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	**2jT**,[e] 60%	–	Trace	–
13	**1j**	STol	2	0.4 equiv. *n*-Bu_3P, 17 h	–	Rapid dec[f]	–	–	–
14	**1c**	Ph	3	1.3 equiv. piperidine	Piperidyl	Dec[d]	–	–	–
15	**1c**	Ph	3	0.3 equiv. piperidine	Piperidyl	Dec[d]	–	–	–
16	**1e**	Ph	5	1.3 equiv. piperidine	Piperidyl	Dec[d]	–	–	–
17	**1e**	Ph	5	0.3 equiv. piperidine	Piperidyl	Dec[d]	–	–	–
18	**1c**	Ph	3	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	–	–	**13cT**, 79%	–
19	**1e**	Ph	5	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	–	–	**13eT**, 79%	–
20	**1c**	Ph	3	0.2 equiv. *n*-Bu_3P, 2 days	–	Trace[c]	–	–	**14c**, 77%
21	**1c**	Ph	3	0.2 equiv. nBu_3P, 2 days, C_6D_6	–	Trace[c]	–	–	**14c**, 46%
22	**1d**	Ph	4	0.2 equiv. *n*-Bu_3P, 6 days	–	No reaction	–	–	–
23	**1e**	Ph	5	0.2 equiv. *n*-Bu_3P, 6 days	–	No reaction	–	–	–
24	**1h**	OEt	3	0.2 equiv. *n*-Bu_3P, 6 days	–	Trace[c]	**3h**, 16%	–	**14h**, 10%

[a] All reactions performed in $CHCl_3$ or $CDCl_3$ at rt unless specified.
[b] **P** refers to adducts from piperidine, **T** from *p*-TolSH.
[c] As observed by NMR of the progress of the reaction.
[d] Largely composed of products derived from aldol condensation.
[e] Major isomer; see text.
[f] Unidentified decomposition products.

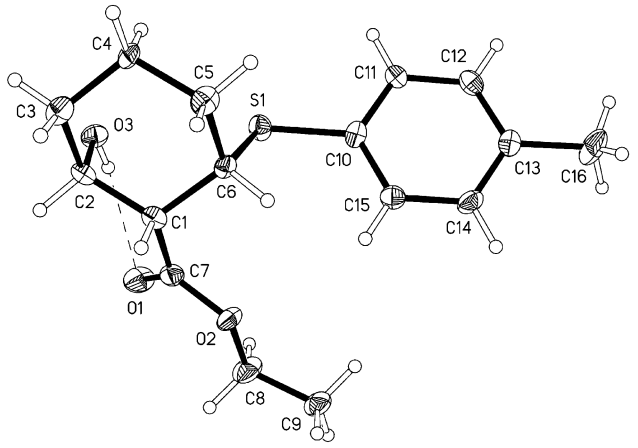


Figure 2. X-Ray structure of **2gTb**.

performed with 2 equiv. of *p*-TolSH and a catalytic quantity of *p*-TolSNa,[12] the adduct **2gT** was obtained in 75% yield (entry 7). Interestingly, we were able to isolate two further compounds **2gTa** and **2gTb** from this reaction in 7 and 5% yield, respectively. The stereochemistry of **2gTa** was determined by proton NMR, as the C-2 methine proton displayed two large *trans*-diaxial coupling constants (δ=2.33 ppm, J=11.5, 12 Hz) whilst the stereochemistry of **2gTb** was assigned using X-Ray analysis[11] (Fig. 2). Similarly, treatment of the thiolester-containing substrate **1j** under identical conditions led to the formation of the adduct **2jT** in 60% yield (entry 11). Again, two minor by-products **2jTa** and **2jTb** were isolated in 7 and 6% yield, respectively. The stereochemistry of **2jTa** was again determined from proton NMR as the C-2 methine proton displayed two large *trans*-diaxial coupling constants (δ=2.69 ppm, J=11.5, 9.7 Hz) whilst the stereochemistry of **2jTb** was tentatively assigned, based on the signal for the C-2 methine proton (δ=3.04 ppm, J=4.3, 9.4 Hz) (Scheme 9).

We next investigated the use of phosphines and found that treatment of a solution of enone **1b** in chloroform with a catalytic amount of *n*-Bu_3P led to the formation of the previously prepared enone **3b** in an excellent (75%) yield (entry 4). We also found that treatment of ***E*-1g** gave the cyclised product **3g** in 50% yield (entry 8) and the corresponding compound ***Z*-1g** gave the same compound in an improved 70% yield; the exact reason for this higher yield is unclear. Again, unsurprisingly, treatment of thiolester **1j** under these conditions led to a rapid complete decomposition.

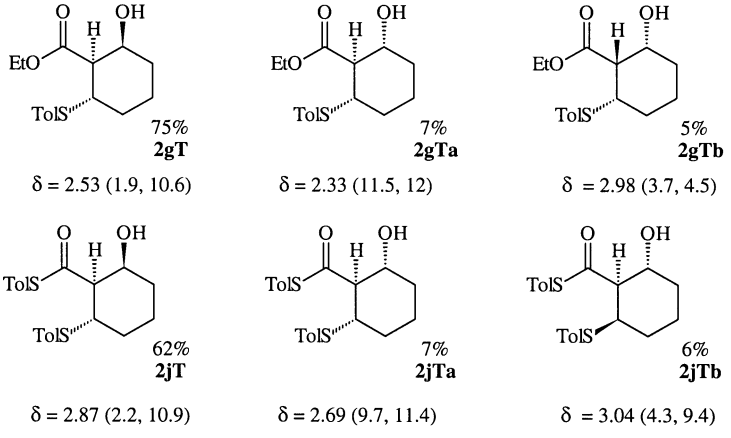
With these results in hand, we decided to investigate the formation of medium ring carbocycles using the substrates **1c** and **1e**. We firstly treated the substrates **1c** and **1e** with both stoichiometric and catalytic amounts of piperidine at differing concentrations (entries 14–17) and it was apparent from these reactions that intermediate adducts **2c** and **2e** or cycloalkenols **3c** and **3e** were not formed, even on prolonged reaction time. Again the formation of aldol related products was the major reaction pathway. Reaction of **1c** and **1e** with *p*-TolSH and *p*-TolSNa under the previously detailed conditions led to the formation of the Michael adducts **13c** and **13e** as the only products even on reflux for long periods (entries 18, 19).

More success was obtained with the use of phosphines and treatment of **1c** with 0.2 equiv. of *n*-Bu_3P for 48 h led to the formation of a trace amount of the cycloheptenol **3c**, as evidenced by NMR, together with the cycloheptadiene **14c** as the major product in 77% isolated yield (entry 20). This product was unexpected and similar products were not observed in any previous *n*-Bu_3P catalysed cyclisation reaction. In order to determine if this elimination was occurring due to an interaction between the phosphine and the deuterochloroform, we repeated the reaction in D_6-benzene with comparable results (entry 21). Treatment of the substrates **1d** and **1e** under identical conditions failed to give the corresponding cycloocta- or cyclononadienes or indeed any reaction product (entry 22, 23).

Treatment of the ester-containing substrate **1h** under these conditions also led to the formation of the cycloheptadiene **14h** but in much lower yield, in this case however, the expected Baylis–Hillman product **3h** was also obtained in low yield (entry 24).

5. Conclusion

It is apparent from these results that the amine catalysed



Scheme 9.

cyclisations are limited in scope to the 5- and 6-membered cyclisations with enones as the Michael acceptors; yields for the tandem processes being high in both cases. Yields for the formation of the eliminated products using a catalytic amount of piperidine are satisfactory with enone substrates, however, enoate and thioenoate examples lead only to decomposition. The phosphine mediated cyclisations work best for the 6- and 7-membered enones and for the 6-membered enoate substrates leading to the Baylis–Hillman products or the eliminated cycloheptadiene **14c** in high yield. Less success was observed with the 5-membered enone and enoate substrates, whilst the thioenoates were totally unsuitable for this reaction. In contrast, the thiol and thiolate mediated cyclisations were by far the most successful reactions proceeding for all the 5- and 6-membered substrates in 56–93% yield for the formation of the major adduct with excellent stereoselectivity which is comparable with stoichiometric methods such as those using dimethylaluminiumthiophenylates[8a] or lithium thiophenoxide.[8b] We are currently investigating synthetic applications of these reactions and will report our findings in due course.

6. Experimental

Reagents: All reagents were obtained from commercial suppliers and were used without further purification.

Solvents: Solvents were purified when necessary using standard methods, in particular, dichloromethane (DCM) was distilled over calcium hydride. Petrol refers to the fraction of petroleum spirit boiling in the range 40–60°C. *Chromatography:* The purity of compounds was assessed by thin layer chromatography (TLC). Unless otherwise stated, all new compounds were homogeneous as indicated by TLC. TLC was performed on BDH glass silica plates coated with Kieselgel 60 F254 (Art. 5554, Merck). Compounds were visualised by examination under ultraviolet light or staining by contact with a solution of phosphomolybdic acid (PMA) in ethanol and heating to 180°C. Column chromatography was performed using Merck 7736 silica gel under medium pressure with the eluting solvent specified in each case.

Analytical methods: Melting points were determined using a Gallenkamp capillary apparatus and are uncorrected. Infrared (IR) spectra were recorded as thin films on NaCl plates (oils) or KBr discs (solids) using a Perkin–Elmer 1600 FTIR spectrometer. Microanalyses were obtained using a Carbo–Erba Model 1106 CHN analyser. Electron impact (EI), chemical ionisation (CI), fast atom bombardment and high resolution mass spectra were recorded using a VG Masslab Model 12/253 spectrometer by the EPSRC Mass Spectrometry Service at Swansea. Proton NMR spectra were recorded at 250 MHz using a Bruker AC250 spectrometer. Carbon NMR spectra were recorded using the Bruker AC250 spectrometer at 62.9 MHz and were broadband-decoupled. All spectra were recorded in $CDCl_3$ unless otherwise stated. Chemical shifts are reported as δ values relative to tetramethylsilane.

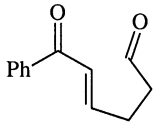
6.1. General conditions for the Wittig reaction with dialdehydes

Method A: The required phosphorane (1 equiv.) was dissolved in dry DCM (10 ml per gram of phosphorane) and added dropwise to a solution of succinaldehyde (4 equiv.) as a cooled (0°C) solution in DCM (3×the volume employed for the phosphorane) and the resulting solution stirred for 48 h. The solution was then washed with a large volume of water (typically 3×250 ml for each 100 ml of reaction solvent) and after drying and evaporation of the solvent, the resulting solid mass was triturated with ether (ca. 50–100 ml) then diluted with petrol (ca. 25–50 ml) and the supernatant liquid decanted with filtration. After repeating this process a further three times, the combined filtrates were dried ($MgSO_4$), evaporated and subjected to chromatography (ether/petrol) to yield the products **1**.

Method B: The cycloalkene (10–20 equiv.) was dissolved in dry dichloromethane (15 ml per g) and cooled to −78°C whereupon ozone was bubbled in the flask until the solution became blue in colour and at this point, the reaction was flushed with nitrogen gas and triphenylphosphine (equivalent to the amount of cycloalkene) was added in one portion and the reaction stirred until it dissolved and for a further 30 min. The phosphorane (1 equiv.) was then added and the reaction stirred to room temperature overnight. The reaction solvent was evaporated and the solid mass remaining was triturated with ether (ca. 3×100 ml). The triturates were then filtered, combined and washed with a large volume of water (ca. 3×250 ml), then dried ($MgSO_4$) and evaporated. Silica gel chromatography (ether/petrol) gave the products **1**.

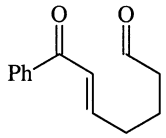
Method C: The required phosphorane (1 equiv.) was dissolved in EtOH (20 ml per g of phosphorane) at room temperature whereupon aqueous glutaric dialdehyde solution (20 equiv.) was added and the reaction stirred overnight at room temperature. Water (ca. 50 ml per g of phosphorane) was added and the reaction extracted with ether (typically 3×200 ml) and the combined ether extracts washed with aqueous HCl solution (0.2 M, ca. 3×300 ml), followed by brine (ca. 3×50 ml). After drying ($MgSO_4$) and evaporation, silica gel chromatography (ether/petrol) gave the products **1**.

6.1.1. *E*-6-Phenyl-6-oxohex-4-enal (1a).



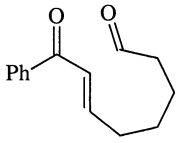
Method A: Phosphorane (3.55 g; 9.4 mmol) gave 840 mg, 48%; 20–50% ether in petrol, R_f=0.29 (50% ether in petrol). ^{1}H NMR: δ=2.65 (4H, m, 2×CH_2), 6.90–7.10 (2H, m, 2×CH), 7.6–8.0 (5H, m, Ph), 9.82 (1H, s, CHO). ^{13}C NMR: δ=24.97 (CH_2), 41.92 (CH_2), 126.74 (CH), 128.48 (CH), 128.54 (CH), 132.78 (CH), 137.64 (C), 146.67 (CH), 190.33 (C=O), 200.37 (CHO). IR: ν_{max}=3058, 2897, 2826, (C–H), 2725 (CHO), 1722 (C=O), 1670 (C=O), 1621 (C=C) cm^{-1}. MS (CI): 206 (100%, $[M+NH_4]^+$), 189 (70%, $[M+H]^+$). HRMS: $C_{12}H_{13}O_2$ ($[M+H]^+$) requires 189.0916, found 189.0916.

6.1.2. *E*-7-Phenyl-7-oxohept-5-enal (1b).



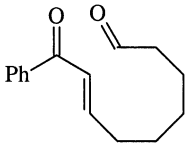
Method B: Cyclopentene (8.9 g, 0.13 mol) and phosphorane (5.0 g; 13.2 mmol) gave 1.87 g, 70%. Method C: Phosphorane (4.02 g; 10.6 mmol) gave 1.54 g, 73%; 30% ether in petrol, R_f=0.10 (30% ether in petrol). ^{1}H NMR: δ=1.90 (2H, quintet, J=7.3 Hz, CH_2), 2.37 (2H, dt, J=6.7, 7.3 Hz, CH_2), 2.50 (2H, dt, J=0.8, 7.3 Hz, CH_2), 6.70–7.10 (2H, m, 2×CH), 7.40–8.00 (5H, m, Ph), 9.80 (1H, t, J=0.8 Hz, CHO). ^{13}C NMR: δ=20.49 (CH_2), 31.83 (CH_2), 42.99 (CH_2), 126.64 (2×CH), 128.49 (2×CH), 128.52 (CH), 132.72 (CH), 137.77 (C), 147.97 (CH), 190.55 (C=O), 201.55 (CHO). IR: ν_{max}=3056, 2930 (C–H), 2726 (CHO), 1722 (C=O), 1669 (C=O), 1620 (C=C) cm^{-1}. MS (CI): 220 (80%, $[M+NH_4]^+$), 203 (100%, $[M+H]^+$). HRMS: $C_{13}H_{15}O_2$ ($[M+H]^+$) requires 203.1072, found 203.1072.

6.1.3. *E*-8-Phenyl-8-oxo-6-octenal (1c).



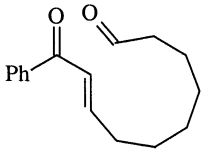
Method B: Cyclohexene (16.4 g, 200 mmol) and phosphorane (3.88 g, 10 mmol) gave 0.878 g, 41%; 20% ether in petrol, R_f=0.17 (20% ether in petrol). ^{1}H NMR: δ=1.50–1.70 (4H, m, 2×CH_2), 2.37 (2H, app q, J=6.4 Hz, CH_2), 2.49 (2H, dt, J=1.5, 7.0 Hz, CH_2), 6.90 (1H, d, J=14.5 Hz, CH), 7.03 (1H, dd, J=6.4, 14.5 Hz, CH), 7.43–7.95 (5H, m, Ph), 9.78 (1H, d, J=1.5 Hz, CHO). ^{13}C NMR: δ=21.58 (CH_2), 27.61 (CH_2), 32.49 (CH_2), 43.58 (CH_2), 126.24, 128.51, 132.67 (6×CH), 137.85 (C), 148.88 (CH) 190.26 (C=O), 202.15 (CHO). IR: ν_{max}=2935 (C–H), 2724 (CHO), 1722 (C=O), 1668 (C=O), 1619 (C=C) cm^{-1}. MS (CI): 234 (100%, $[M+NH_4]^+$), 217 (70%, $[M+H]^+$). HRMS: $C_{14}H_{17}O_2$ ($[M+H]^+$) requires 217.1229, found 217.1226.

6.1.4. *E*-9-Phenyl-9-oxo-7-nonenal (1d).



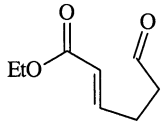
Method B: Cycloheptene (4.81 g, 50 mmol) and phosphorane (3.04 g, 8.0 mmol) gave 0.858 g, 47%; 20% ether in petrol, R_f=0.16 (20% ether in petrol). ^{1}H NMR: δ=1.30–1.80 (6H, m, 3×CH_2), 2.34 (2H, app q, J=7.0 Hz, CH_2), 2.46 (2H, t, J=7.3 Hz, CH_2), 6.88 (1H, d, J=16.5 Hz, CH), 7.05 (1H, m, CH), 7.45–7.95 (5H, m, Ph), 9.78 (1H, s, CHO). ^{13}C NMR: δ=21.78 (CH_2), 27.92 (CH_2), 28.69 (CH_2), 32.54 (CH_2), 43.73 (CH_2), 126.08, 128.51, 132.63 (6×CH), 138.00 (C), 149.40, (CH) 190.81 (C=O), 202.44 (CHO). IR: ν_{max}=2930 (C–H), 2721 (CHO), 1721 (C=O), 1668 (C=O), 1618 (C=C) cm^{-1}. MS (CI): 248 (100%, $[M+NH_4]^+$), 231 (55%, $[M+H]^+$). HRMS: $C_{15}H_{19}O_2$ ($[M+H]^+$) requires 231.1385, found 231.1385.

6.1.5. *E*-10-Phenyl-10-oxo-8-decenal (1e).



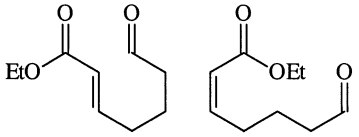
Method B: Cyclooctene (11.0 g, 0.10 mol) and phosphorane (3.82 g, 10.0 mmol) gave 1.19 g, 49%; 25% ether in petrol, R_f=0.16 (25% ether in petrol). ^{1}H NMR: δ=1.30–1.70 (8H, m, 4×CH_2), 2.32 (2H, app q, J=7.0 Hz, CH_2), 2.45 (2H, dt, J=1.0, 6.7 Hz, CH_2), 6.85 (1H, d, J=15.3 Hz, CH), 7.06 (1H, dd, J=7.0, 15.3 Hz, CH), 7.40–7.95 (5H, m, Ph), 9.75 (1H, d, J=1.0 Hz, CHO). ^{13}C NMR: δ=21.90 (CH_2), 27.94 (CH_2) 28.90 (CH_2), 28.93 (CH_2), 32.70 (CH_2), 43.80 (CH_2), 125.99, 128.50, 132.60 (6×CH), 137.96 (C), 149.71 (CH) 190.87 (C=O), 202.65 (CHO). IR: ν_{max}=2931, 2856 (C–H), 2720 (CHO), 1722 (C=O), 1669 (C=O), 1619 (C=C) cm^{-1}. MS (CI): 262 (100%, $[M+NH_4]^+$), 245 (80%, $[M+H]^+$. HRMS: $C_{16}H_{21}O_2$ ($[M+H]^+$) requires 245.1542, found 245.1542.

6.1.6. *E*-6-Ethoxy-6-oxo-4-hexenal (1f).



Method A: Phosphorane (2.84 g; 8.1 mmol) gave 730 mg, 58 %; 50% ether in petrol, R_f=0.30 (50% ether in petrol). ^{1}H NMR: 1.30 (3H, t, J=7.1 Hz, CH_3), 2.50–2.70 (4H, m, 2×CH_2), 4.19 (2H, q, J=7.1 Hz, CH_2), 5.85 (1H, d, J=15.7 Hz, CH), 6.94 (1H, dd, J=6.4, 15.7 Hz, CH), 9.7 (1H, d, J=0.7 Hz, CHO). ^{13}C NMR: δ=14.23 (CH_3), 24.41 (CH_2), 41.83 (CH_2), 60.34 (CH_2), 122.46 (CH), 146.26 (CH), 166.26 (C=O), 200.33 (CHO). IR: ν_{max}=2981, 2832 (C–H), 2727 (CHO), 1721 (C=O), 1657 (C=C) cm^{-1}. MS (CI): 174 (100%, $[M+NH_4]^+$). HRMS: $C_8H_{16}NO_3$ ($[M+NH_4]^+$) requires 174.1130, found 174.1129.

6.1.7. *E*- and *Z*-7-Ethoxy-7-oxo-5-heptenal (*E*-1g and *Z*-1g).



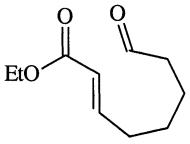
Method C: Phosphorane (3.66 g, 10.5 mmol) gave ***Z*-1g**, 410 mg, 23% and ***E*-1g**, 737 mg, 41%; 10% ether in petrol, R_f=0.14 and 0.07 (10% ether in petrol).

Data for ***Z*-1g**. ^{1}H NMR: 1.18 (3H, t, J=7.1 Hz, CH_3), 1.70 (2H, app quintet, J=7.3 Hz, CH_2), 2.40 (2H, t, J=7.2 Hz, CH_2), 2.60 (2H, app q, J=7.4 Hz, CH_2), 4.05 (2H, q, J=7.1 Hz, CH_2), 5.72 (1H, d, J=11.4 Hz, CH), 6.11 (1H, dd, J=7.4, 11.4 Hz, CH) 9.28 (1H, s, CHO). ^{13}C NMR: δ=14.12 (CH_3), 21.17 (CH_2), 27.98 (CH_2), 43.05 (CH_2), 59.73 (CH_2), 120.67 (CH), 148.44 (CH), 166.05 (C=O),

201.83 (CHO). IR: ν_{max}=3038, 2982, 2937, 2826 (C–H), 2724 (CHO), 1722 (C=O), 1644 (C=C) cm^{-1}. MS (CI): 188 (100%, $[M+NH_4]^+$), 171 (30%, $[M+H]^+$). HRMS: $C_9H_{15}O_3$ ($[M+H]^+$) requires 171.1021, found 171.1018.

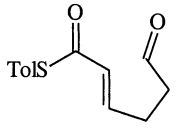
Data for ***E*-1g**. ^{1}H NMR: 1.05 (3H, t, J=7.1 Hz, CH_3), 1.57 (2H, app quintet, J=7.3 Hz, CH_2), 2.05 (2H, app q, J=7.1 Hz, CH_2), 2.27 (2H, t, J=7.0 Hz, CH_2), 3.93 (2H, q, J=7.1 Hz, CH_2), 5.61 (1H, d, J=15.6 Hz, CH), 6.69 (1H, dd, J=6.8, 15.6 Hz, CH), 9.54 (1H, s, CHO). ^{13}C NMR: δ=14.24 (CH_3), 20.30 (CH_2), 31.22 (CH_2), 42.93 (CH_2), 60.27 (CH_2), 122.25 (CH), 147.53 (CH) 167.50 (C=O), 201.62 (CHO). IR: ν_{max}=2982, 2938 (C–H), 2724 (CHO), 1716 (C=O), 1653 (C=C) cm^{-1}. MS (CI): 188 (100%, $[M+NH_4]^+$), 171 (25%, $[M+H]^+$). HRMS: $C_9H_{15}O_3$ ($[M+H]^+$) requires 171.1021, found 171.1023.

6.1.8. *E*-8-Ethoxy-8-oxo-6-octenal (1h).



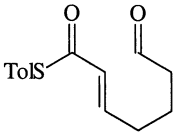
Method B: Cycloheptene (16.4 g, 171 mmol) and phosphorane (3.48 g, 10.0 mmol) gave 700 mg, 38%; 40% ether in petrol, R_f=0.22 (40% ether in petrol). ^{1}H NMR: 1.29 (3H, t, J=7.0 Hz, CH_3), 1.48–1.70 (4H, m, 2×CH_2), 2.23 (2H, app q, J=7.0 Hz, CH_2), 2.47 (2H, t, J=7.0 Hz, CH_2), 4.19 (2H, q, J=7.0 Hz, CH_2), 5.83 (1H, d, J=15.9 Hz, CH), 6.92 (1H, dd, J=6.7, 15.9 Hz, CH), 9.78 (1H, s, CHO). ^{13}C NMR: δ=14.24 (CH_3), 21.47 (CH_2), 27.45 (CH_2), 31.83 (CH_2), 43.56 (CH_2), 60.20 (CH_2), 121.79 (CH), 148.25 (CH), 166.56 (C=O), 202.11 (CHO). IR: ν_{max}=2981, 2937, 2862 (C–H), 2721 (CHO), 1719 (C=O), 1654 (C=C) cm^{-1}. MS (CI): 202 (100%, $[M+NH_4]^+$). HRMS: $C_{10}H_{20}NO_3$ ($[M+NH_4]^+$) requires 202.1443, found 202.1444.

6.1.9. 6-(*S*-*p*-Tolyl)-6-oxohept-4-enal (1i).



Method A: Phosphorane[12] (2.14 g; 5.02 mmol) gave 540 mg, 46% yield; 25–30% ether in petrol, R_f=0.22 (30% ether in petrol), mp 31–33°C. ^{1}H NMR: δ=2.42 (3H, s, CH_3), 2.50–2.62 (4H, m, 2×CH_2), 6.22 (1H, dt, J=15.5, 1.5 Hz, CH), 6.95 (1H, dt, J=15.5, 6.5 Hz, CH), 7.2–7.4 (4H, m, Ph), 9.85 (1H, t, J=0.8 Hz, CHO). IR: ν_{max}=3035, 2942, 2872 (C–H), 2756 (CHO), 1709 (C=O), 1680 (C=O), 1634 (C=C) cm^{-1}. MS (CI): 252 (50%, $[M+NH_4]^+$), 235 (40%, $[M+H]^+$). HRMS (EI): $C_{13}H_{14}O_2S$ ($[M]^+$) requires 234.0715, found 234.0716.

6.1.10. 7-(*S*-*p*-Tolyl)-7-oxohept-5-enal (1j).

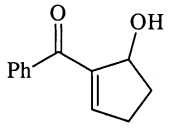


Method B: Phosphorane[12] (4.47 g; 10.5 mmol), gave 840 mg, 32%; 30% ether in petrol, R_f=0.16 (30% ether in petrol), mp 32–34°C. ^{1}H NMR: δ=1.84 (2H, app quintet, J=7.3 Hz, CH_2), 2.30 (2H, ddt, J=7.3, 6.9, 1.4 Hz, CH_2), 2.39 (3H, s, CH_3), 2.52 (2H, dt, J=7.3, 1.3 Hz, CH_2CHO), 6.20 (1H, dt, J=15.5, 1.4 Hz, CH), 6.90 (1H, dt, J=15.5, 6.9 Hz, CH), 7.25 (4H, AA′BB′, J=8.0 Hz, tolyl), 9.75 (1H, t, J=1.3 Hz, CHO). IR: ν_{max}=2976, 2952, 2857 (C–H), 2738 (CHO), 1715 (C=O), 1680 (C=O), 1633 (C=C) cm^{-1}. MS (CI): 266 (100%, $[M+NH_4]^+$), 249 (40%, $[M+H]^+$). HRMS (EI): $C_{14}H_{16}O_2S$ ($[M]^+$) requires 248.0871, found 248.0861. Microanalysis: found C=67.86; H=6.38, $C_{14}H_{16}O_2S$ requires C=67.71; H=6.49.

6.2. General conditions for the addition reactions of secondary amines

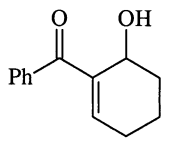
The aldehyde (typically 100 mg) was placed into a NMR tube and diluted to the correct concentration with $CDCl_3$. The required amine (0.3 or 1.3 equiv.) was then added (either neat or as a solution in $CDCl_3$) and the tube agitated. The reaction was followed by NMR and on completion (to ca. 95%) the solvent was removed and the cyclisation products isolated by chromatography (ether/petrol). For larger scale reactions, chloroform was employed as the solvent and the reaction was carried out in a round bottom flask. For yields, see Tables 4 and 5.

6.2.1. 2-Benzoyl-1-hydroxycyclopent-2-ene (3a).



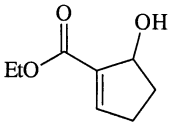
Column solvent: 35% ether in petrol, R_f=0.10 (50% ether in petrol). ^{1}H NMR: δ=1.94 (1H, m, CH_aH$_b$), 2.30–2.85 (3H, m, CH$_a$$H_b$+C$H_2$), 3.33 (1H, br s, OH), 5.30 (1H, m, CHOH), 6.71 (1H, t, J=1.5 Hz, CH), 7.42–7.78 (5H, m, Ph). ^{13}C NMR: δ=31.40 (CH_2), 31.74 (CH_2), 76.51 (CH), 128.35 (2×CH), 128.92 (2×CH), 132.44 (CH), 138.13 (C), 144.54 (C), 149.05 (CH), 194.86 (C=O). IR: ν_{max}=3460 (O–H) 3058, 2940 (C–H), 1639 (C=O) cm^{-1}. MS (CI): 206 (45%, $[M+NH_4]^+$), 189 (100%, $[M+H]^+$). HRMS: $C_{12}H_{13}O_2$ ($[M+H]^+$) requires 189.0916, found 189.0916.

6.2.2. 2-Benzoyl-1-hydroxycyclohex-2-ene (3b).



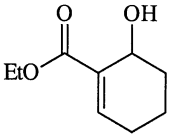
Column solvent: 20% ether in petrol, R_f=0.11 (25% ether in petrol). ^{1}H NMR: δ=1.67 (1H, m, CH_aH$_b$), 1.90 (3H, m, CH$_a$$H_b$+C$H_2$), 2.31 (2H, m, CH$_aH_b$), 3.53 (1H, br s, OH), 4.75 (1H, m, CHOH), 6.73 (1H, t, J=4.0 Hz, CH), 7.40–7.68 (5H, m, Ph). ^{13}C NMR: δ=17.29 (CH_2), 26.23 (CH_2), 29.60 (CH_2), 63.83 (CH), 128.03 (2×CH), 129.10 (2×CH), 131.77 (CH), 137.69 (C), 140.00 (C), 146.79 (CH), 199.38 (C=O). IR: ν_{max}=3436 (O–H) 3058, 2938, 2864 (C–H), 1636 (C=O) cm^{-1}. MS (CI): 220 (15%, $[M+NH_4]^+$), 203 (100%, $[M+H]^+$), 202 (35%, $[M]^+$). HRMS: $C_{13}H_{15}O_2$ ($[M+H]^+$) requires 203.1072, found 203.1072.

6.2.3. 2-Carboethoxy-1-hydroxycyclopent-2-ene (3f).



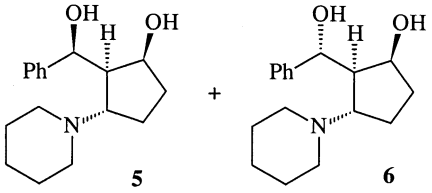
Column solvent: 20% ether in petrol, R_f=0.04 (20% ether in petrol). ^{1}H NMR: δ=1.36, (3H, t, J=7.1 Hz, CH_3), 1.89 (1H, m, CH_aH$_b$), 2.27–2.67 (3H, m, CH$_a$$H_b$+C$H_2$), 2.85 (1H, br s, OH), 4.24 (2H, q, J=7.1 Hz, CH_2), 5.08 (1H, m, CHOH), 6.71 (1H, t, J=2.5 Hz, CH). ^{13}C NMR: δ=14.25 (CH_3), 31.80 (CH_2), 31.78 (CH_2), 60.46 (CH_2), 75.54 (CH), 138.00 (C), 146.24 (CH), 165.06 (C=O). IR: ν_{max}=3583/3440 (O–H), 2924 (C–H), 1713 (C=O), 1634 (C=C) cm^{-1}. MS (CI): 174 (60%, [M+NH$_4$]$^+$) HRMS: $C_8H_{16}NO_3$ ([M+NH$_4$]$^+$) requires 174.1130, found 174.1130.

6.2.4. 2-Carboethoxy-1-hydroxycyclohex-2-ene (3g).



Column solvent: 30% ether in petrol, R_f=0.10 (30% ether in petrol). ^{1}H NMR: δ=1.31, (3H, t, J=7.1 Hz, CH_3), 1.43–1.85 (5H, m, 2×CH_2+OH), 2.09–2.32 (2H, m, CH$_a$H$_b$), 4.23 (2H, q, J=7.1 Hz, CH_2), 4.55 (1H, m, CHOH), 7.11 (1H, t, J=2.0 Hz, CH). ^{13}C NMR: δ=14.19 (CH_3), 17.42 (CH_2), 26.05 (CH_2), 29.82 (CH_2), 60.55 (CH_2), 63.41 (CH), 132.37 (C), 142.78 (CH), 167.31 (C=O). IR: ν_{max}=3460 (O–H), 2971, 2938, 2867 (C–H), 1712 (C=O), 1646 (C=C) cm^{-1}. MS (CI): 188 (70%, [M+NH$_4$]$^+$), 171 (100%, [M+H]$^+$). HRMS: $C_9H_{15}O_3$ ([M+H]$^+$) requires 171.1021, found 171.1020.

6.2.5. Preparation of 5 and 6 from 6-phenyl-6-oxo-4-hexen-1-al (1a).

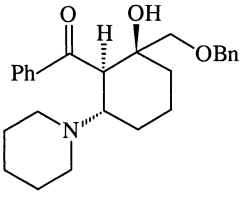


The enone **1a** (200 mg; 1.064 mmol) was dissolved in chloroform (3 ml), cooled (0°C) and piperidine (118 mg; 1.38 mmol) was added to the solution with stirring. After 10 min a solution of sodium borohydride (202 mg; 5.32 mmol) in methanol (5 ml) was added to the mixture and stirring continued for 1 h. The reaction was evaporated to dryness and the solid mass which resulted was triturated with chloroform and the triturates filtered through a cotton wool plug. On evaporation, silica gel chromatography (methanol in ethyl acetate 1–10%) gave **5** and **6** as crystalline solids.

Data for ***5***: Yield: 0.083 g, 29%. Mp 180–183°C (ethyl acetate); R_f=0.12 (10% methanol in ethyl acetate). ^{1}H NMR: δ=1.24 (1H, d, J=3.4 Hz, CH_aH$_b$), 1.49–1.79 (11H, m, 4×CH_2+2×CH$_a$$H_b$+2×OH), 1.99 (1H, ddd, J=4.7, 9.8, 10.6 Hz, CH), 2.57 (2H, m, 2×CH_aH$_b$N), 2.73 (2H, m, 2×CH$_a$$H_b$N), 3.59 (1H, m, C$H$N), 3.76 (1H, m, C$H$OH), 5.00 (1H, d, J=9.8 Hz, PhCHOH), 7.24–7.50 (5H, m, Ph). ^{13}C NMR: δ=17.98, 20.28, 24.63, 26.31, 32.75 (7×CH_2), 51.37 (CH), 69.47 (CH), 71.70 (CH), 75.72 (CH), 126.60, 127.43, 128.36 (5×CH), 143.93 (C). IR: ν_{max}=3407 (O–H) 3018, 2932 (C–H) cm^{-1}. MS (CI): 276 (40%, [M+H]$^+$), 86 (100%, [C_5H_{12}N]$^+$). HRMS: $C_{17}H_{26}NO_2$ ([M+H]$^+$) requires 276.1964, found 276.1964.

Data for ***6***: Yield: 0.110 g, 38%. Mp 77–80°C (ethyl acetate), R_f=0.07 (10% methanol in ethyl acetate). ^{1}H NMR: δ=1.46–2.09 (13H, m, 5×CH_2+CH+2×OH), 2.54 (2H, m, 2×CH_aH$_b$N), 2.79 (2H, m, 2×CH$_a$$H_b$N), 2.98 (1H, m, C$H$N), 3.81 (1H, ddd, J=5.0, 6.7, 8.0, CHOH), 4.61 (1H, d, J=9.6 Hz, PhCHOH), 7.28–7.45 (5H, m, Ph). ^{13}C NMR: δ=19.16, 24.54, 26.27, 26.30, 31.04 (7×CH_2), 54.75 (CH), 71.84 (CH), 72.02 (CH), 80.16 (CH), 126.68, 128.17, 128.90 (5×CH), 143.80 (C). IR: ν_{max}=3372 (O–H) 3017, 2935 (C–H) cm^{-1}. MS (CI): 276 (100%, [M+H]$^+$). HRMS: $C_{17}H_{26}NO_2$ ([M+H]$^+$) requires 276.1964, found 276.1964.

6.2.6. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-2-Benzoyl-1-benzyloxymethyl-3-(*N*-piperidyl)cyclohexan-1-ol (11).

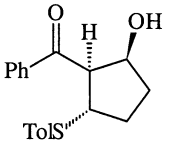


Enone **9** (81.4 mg, 0.253 mmol) in $CDCl_3$ (0.5 ml) with piperidine (25.8 mg; 0.303 mmol) after 6 days gave **11** (61.5 mg, 60%, 15% ether in petrol, R_f=0.12 (15% ether in petrol)). Mp 154°C (petrol). ^{1}H NMR: δ=0.73–1.87 (12H, m, 6×CH_2), 2.24 (2H, m, 2×CH_aH$_b$N), 2.47 (2H, m, CH$_a$$H_b$N), 3.26 (3H, m, C$H$N+C$H_2$O), 3.86 (1H, d, J=11.6 Hz, CH), 4.33 (2H, s, OCH_2Ph), 5.00 (1H, br s, CHOH), 7.14–7.94 (10H, m, Ph). ^{13}C NMR: δ=19.72 (CH_2), 23.62 (CH_2), 24.57 (CH_2), 25.71 (CH_2), 29.63 (CH_2), 49.23 (CH_2), 49.23 (CH), 50.07 (CH_2), 65.73 (CH), 73.39 (CH_2), 74.58 (C), 77.87 (CH_2), 125.96–128.50 (9×CH), 132.44 (CH), 137.82 (C), 139.87 (C), 210.09 (C=O). IR: ν_{max}=3451 (O–H), 2926, 2851, 2801 (C–H), 1646.4 (C=O) cm^{-1}. MS (CI): 409 (2%, [M+H]$^+$), 408 (5%, [M]$^+$), 86 (100%, [C_5H_{12}N]$^+$). HRMS: $C_{26}H_{33}O_3N$ ([M]$^+$) requires 407.2460, found 407.2464. Microanalysis: found C=76.33; H=8.47; N=3.43, $C_{26}H_{33}O_3N$ requires C=76.62; H=8.16; N=3.57.

6.3. General method for thiol and thiolates reactions

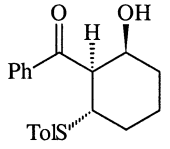
The aldehyde (typically 100–250 mg) was placed in either a RBF in the case of reactions that were heated to reflux or into an NMR tube and diluted with $CHCl_3$ or $CDCl_3$. The TolSH (1.3–2 equiv. either neat or as a solution in $CHCl_3$/$CDCl_3$) and the catalyst, TolSNa (0.2 equiv.) were then added. The reaction was followed to completion by NMR or TLC at which point the solvent was removed and the products were obtained by chromatography. For specific conditions, see Tables 4 and 5.

6.3.1. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-2-Benzoyl-1-(*S*-tolyl)cyclopentan-3-ol (2aT).



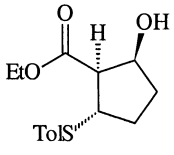
Enone **1a** (100 mg; 0.53 mmol) and TolSH (85 mg; 0.69 mmol) gave the product **57** (127.6 mg, 77%) after chromatography in 15% EtOAc in petrol (R_f=0.2) as an oil. ^{1}H NMR: δ=1.86 (2H, m, CH_2), 2.13 (1H, m, CH_aH_b), 2.26 (3H, s, CH_3), 2.48 (1H, m, CH_aH_b), 2.69 (1H, br s, OH), 3.89 (1H, dd, J=5.3, 8.3 Hz, CH), 4.19 (1H, ddd, J=6.3, 8.3, 8.3 Hz, CH), 4.59 (1H, m, CH), 6.96–7.88 (9H, m, 9×ArCH). ^{13}C NMR: δ=20.85 (CH_3), 30.88 (CH_2), 34.93 (CH_2), 48.28 (CH), 57.79 (CH), 75.15 (CH), 128.20, 128.38, 129.44, 132.44, 133.28 (9×ArCH), 130.77 (C), 137.10 (C), 137.19 (C), 200.76 (C). IR: ν_{max}=3372 (O–H), 2920 (C–H), 1677 (C=O) cm^{-1}. MS (CI): 330 (3%, $[M+NH_4]^+$), 313 (10%, $[M+H]^+$). HRMS (EI): $C_{19}H_{20}O_2S$ ($[M]^+$) requires 312.1184, found 312.1171.

6.3.2. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-2-Benzoyl-1-(*S*-tolyl)cyclohexan-3-ol (2bT).



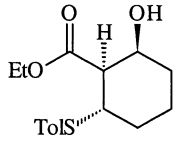
Enone **1b** (60 mg; 0.297 mmol) and TolSH (40 mg; 0.322 mmol) gave the product (89.6 mg 93%) after chromatography in 10% EtOAc in petrol (R_f=0.13) as an oil. ^{1}H NMR (C_6D_6): δ=1.35 (1H, m, CH_aH_b), 1.59 (2H, m, CH_2), 1.73 (1H, m, CH_aH_b), 2.18 (1H, m, CH_aH_b), 2.25 (3H, s, CH_3), 2.43 (1H, s, CH_aH_b), 3.77 (1H, dd, J=11.5, 2.5 Hz, CH), 3.93 (1H, br s, CHOH), 4.20 (1H, m, CH), 4.22 (1H, ddd, J=4.0, 11.5, 11.5 Hz, CHS), 7.03 (2H, d, J=8.2 Hz, 2×CH), 7.25–7.57 (5H, m, Ph), 8.18 (2H, d, J=8.2 Hz, 2×CH). ^{13}C NMR: δ=19.57 (CH_2), 20.94 (CH_3), 31.10 (CH_2), 33.54 (CH_2), 44.97 (CH), 52.13 (CH), 67.11 (CH), 128.48, 128.57, 129.39, 133.51, 133.61 (9×ArCH), 129.60, 137.00, 137.50 (3×ArC), 204.50 (C). IR: ν_{max}=3475 (O–H), 2950, 2900 (C–H), 1663 (C=O) cm^{-1}. MS (EI): 326 (10%, $[M]^+$). HRMS: $C_{20}H_{22}O_2S$ ($[M]^+$) requires 326.1341, found 326.1325.

6.3.3. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-2-Carboethoxy-1-(*S*-tolyl)cyclopentan-3-ol (2fT).



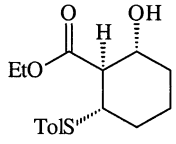
Enone **1f** (206.6 mg; 1.324 mmol), TolSH (328 mg; 2.70 mmol) and TolSNa (40 mg, 0.27 mmol) gave the product **57** (283 mg, 72%) after chromatography in 30% ether in petrol (R_f=0.06) as crystals. Mp 39–42°C (ether/petrol). ^{1}H NMR: δ=1.23 (3H, t, J=7.1 Hz, CH_3), 1.60–2.00 (3H, m, CH_2+CH_aH_b), 2.33 (3H, s, CH_3), 2.36 (1H, m, CH_aH_b), 2.76 (1H, dd, J=5.0, 9.0 Hz, CH), 2.86 (1H, br s, CHOH), 3.97 (1H, m, CH), 4.10 (2H, m, CH_2), 4.47 (1H, m, CH), 7.10 (2H, d, J=8.0 Hz, 2×CH), 7.33 (2H, d, J=8.0 Hz, 2×CH). ^{13}C NMR: δ=14.08 (CH_3), 21.05 (CH_3), 30.84 (CH_2), 33.64 (CH_2), 47.30 (CH), 56.41 (CH), 61.05 (CH_2), 74.10 (CH), 129.56 (2×CH), 130.9 (CH), 132.7 (2×CH), 137.4 (C), 173.40 (C). IR: ν_{max}=3429 (O–H), 2973, 2927 (C–H), 1735 (C=O) cm^{-1}. MS (CI): 298 (20%, $[M+NH_4]^+$), 281 (10%, $[M+H]^+$). HRMS: $C_{15}H_{21}O_3S$ ($[M+H]^+$) requires 281.1211, found 281.1212.

6.3.4. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-2-Carboethoxy-1-(*S*-tolyl)cyclohexan-3-ol (2gT).



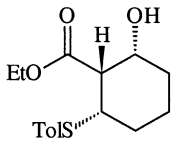
Enone ***E*-1g** (213 mg; 1.253 mmol) and TolSH (314 mg, 2.51 mmol) and TolSNa (37 mg, 0.25 mmol) gave the product (276 mg, 75%) after chromatography in 20% ether in petrol (R_f=0.17) as an oil. ^{1}H NMR: δ=1.28 (2H, m, CH_2), 1.34 (3H, t, J=7.0 Hz, CH_3), 1.52 (1H, m, CH_aH_b), 1.83 (2H, m, CH_2), 2.30 (1H, m, CH_aH_b), 2.35 (3H, s, CH_3), 2.53 (1H, dd, J=1.9, 10.6 Hz, CH), 3.35 (1H, br s, CHOH), 3.48 (1H, ddd, J=4.0, 11.3, 11.3 Hz, SCH), 4.18 (1H, m, CHOH), 4.23 (2H, m, CH_2), 7.12 (2H, d, J=8.0 Hz, 2×CH), 7.38 (2H, d, J=8.0 Hz, 2×CH). ^{13}C NMR: δ=14.16 (CH_3), 19.76 (CH_2), 21.11 (CH_3), 30.75 (CH_2), 32.68 (CH_2), 44.13 (CH), 52.54 (CH), 61.12 (CH_2), 67.23 (CH), 129.02 (C), 129.57 (2×CH), 134.28 (2×CH), 137.90 (C), 174.72 (C=O). IR: ν_{max}=3508 (O–H), 2977, 2936, 2864 (C–H), 1724 (C=O) cm^{-1}. MS (CI): 312 (100%, $[M+NH_4]^+$), 295 (45%, $[M+H]^+$). HRMS: $C_{16}H_{23}O_3S$ ($[M+H]^+$) requires 295.1368, found 295.1375.

6.3.5. 1*S*,2*R*,3*R*/1*R*,2*S*,3*S*-2-Carboethoxy-1-(*S*-tolyl)cyclohexan-3-ol (2gTa).



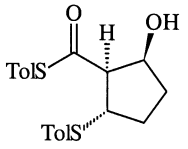
A small quantity of **2gTa** (25.8 mg, 7%) was isolated as an oil by careful chromatography of the recovered column residues of the reaction to prepare **2gT**. ^{1}H NMR: δ=1.22 (2H, m, CH_2), 1.35 (3H, t, J=7.0 Hz, CH_3), 1.74 (2H, m, CH_2), 1.98 (2H, m, CH_2), 2.33 (1H, dd, J=11.5, 12.0 Hz, CH), 2.35 (3H, s, CH_3), 3.01 (1H, ddd, J=3.6, 12.0, 12.0 Hz, SCH), 3.80 (1H, ddd, J=4.3, 11,5, 11.5 Hz, CHOH), 4.26 (2H, m, CH_2), 7.13 (2H, d, J=8.0 Hz, 2×CH), 7.40 (2H, d, J=8.0 Hz, 2×CH). ^{13}C NMR: δ=14.27 (CH_3), 21.14 (CH_3), 23.19 (CH_2), 32.41 (CH_2), 33.85 (CH_2), 47.31 (CH), 57.91 (CH), 60.88 (CH_2), 72.53 (CH), 128.48 (C), 129.55 (2×CH), 134.97 (2×CH), 138.20 (C), 173.46 (C=O). IR: ν_{max}=3442 (O–H), 2924, 2853 (C–H), 1732 (C=O) cm^{-1}. MS (CI): 312 (100%, $[M+NH_4]^+$), 295 (10%, $[M+H]^+$). HRMS: $C_{16}H_{23}O_3S$ ($[M+H]^+$) requires 295.1368, found 295.1367.

6.3.6. 1*S*,2*S*,3*R*/1*R*,2*R*,3*S*-2-Carboethoxy-1-(*S*-tolyl)cyclohexan-3-ol (2gTb).



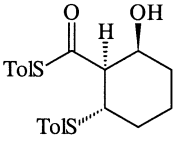
A small quantity of **2gTb** (18.5 mg, 5%) was isolated as a solid by careful chromatography of the recovered column residues of the reaction to prepare **2gT**. Mp 63–68°C. ^{1}H NMR: δ=1.20–1.70 (3H, m, CH_2+CH_aH_b), 1.27 (3H, t, J=7.0 Hz), 1.85–2.20 (3H, m, CH_2+CH_aH_b), 2.29 (3H, s, CH_3), 2.92 (1H, br s, CHOH), 2.98 (1H, dd, J=3.7, 4.5 Hz, CH), 3.44 (1H, m, CHS), 4.08 (1H, m, CHOH), 4.22 (2H, m, CH_2), 7.07 (2H, d, J=8.0 Hz, 2×CH), 7.30 (2H, d, J=8.0 Hz, 2×CH). ^{13}C NMR: δ=14.24 (CH_3), 18.14 (CH_2), 21.05 (CH_3), 29.98 (CH_2), 30.56 (CH_2), 48.04 (CH), 50.57 (CH), 60.89 (CH_2), 67.72 (CH), 129.57 (C), 129.63 (2×CH), 132.40 (2×CH), 137.19 (C), 174.00 (C=O). IR: ν_{max}=3436 (O–H), 2927, 2855 (C–H), 1730 (C=O) cm^{-1}. MS (CI): 312 (75%, $[M+NH_4]^+$), 295 (35%, $[M+H]^+$). HRMS: $C_{16}H_{23}O_3S$ ($[M+H]^+$) requires 295.1368, found 295.1365.

6.3.7. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-1-(*S*-Tolyl)-2-(*S*-tolylthiocarboxy)cyclopentan-3-ol (2iT).



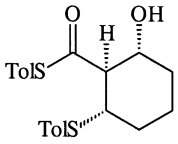
Enone **1i** (149.1 mg; 0.637 mmol) and TolSH (232 mg, 1.91 mmol) gave the product (128 mg, 56%) after chromatography in 30% ether in petrol (R_f=0.04) as an oil which solidified on standing. Mp 63–69°C. ^{1}H NMR: δ=1.68–2.16 (4H, m, 2×CH_2), 2.35 (3H, s, CH_3), 2.38 (3H, s, CH_3), 2.86 (1H, br s, CHOH), 3.14 (1H, dd, J=4.8, 8.8 Hz, CH), 4.04 (1H, ddd, J=8.8, 8.8, 6.2 Hz, CHS), 4.55 (1H, m, CHOH), 7.00–7.40 (8H, m, 8×CH). ^{13}C NMR: δ=21.15 (CH_3), 21.36 (CH_3), 30.86 (CH_2), 33.83 (CH_2), 47.64 (CH), 64.52 (CH), 75.19 (CH), 123.52 (C), 128.52 (2×CH), 129.79 (2×CH), 130.61 (C), 132.91 (2×CH), 134.34 (2×CH), 137.57 (C), 139.98 (C), 199.09 (C). IR: ν_{max}=3349 (O–H), 2920 (C–H), 1711 (C=O) cm^{-1}. MS (CI): 376 (100%, $[M+H]^+$), 359 (30%, $[M+NH_4]^+$). HRMS: $C_{20}H_{23}O_2S_2$ ($[M+H]^+$) requires 359.1139, found 359.1140.

6.3.8. 1*S*,2*R*,3*S*/1*R*,2*S*,3*R*-2-(*S*-Tolylthiocarboxy)-1-(*S*-tolyl)cyclohexan-3-ol (2jT).



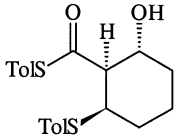
Enone **1j** (72.3 mg; 0.292 mmol) and TolSH (73.4 mg, 0.58 mmol) and TolSNa (8.6 mg, 0.06 mmol) gave the product (69 mg, 60%) after chromatography in 20% ether in petrol (R_f=0.16) as an oil. ^{1}H NMR: δ=1.22–2.21 (6H, m, 3×CH_2), 2.36 (3H, s, CH_3), 2.40 (3H, s, CH_3), 2.87 (1H, dd, J=2.2, 10.9 Hz, CH), 2.88 (1H, br s, OH), 3.60 (1H, ddd, J=4.0, 10.9, 11.7 Hz, CHS), 4.30 (1H, m, CHOH), 7.11–7.42 (8H, m, 8×CH). ^{13}C NMR: δ=19.62 (CH_2), 21.14 (CH_3), 21.37 (CH_3), 30.93 (CH_2), 33.15 (CH_2), 43.96 (CH), 60.49 (CH), 67.86 (CH), 123.56 (C), 129.57 (2×CH), 130.10 (2×CH), 133.84 (2×CH), 134.27 (2×CH) 137.80 (C), 140.08 (2×C), 201.35 (C=O). IR: ν_{max}=3520 (O–H), 3021, 2937, 2864 (C–H), 1706/1679 (C=O) cm^{-1}. MS (CI): 390 (100%, $[M+NH_4]^+$), 373 (20%, $[M+H]^+$). HRMS: $C_{21}H_{25}O_2S_2$ ($[M+H]^+$) requires 373.1296, found 373.1295.

6.3.9. 1*S*,2*R*,3*R*/1*R*,2*S*,3*S*-2-(*S*-Tolylthiocarboxy)-1-(*S*-tolyl)cyclohexan-3-ol (2jTa).



A small quantity of **2jTa** (8 mg, 7%) was isolated as an oil by careful chromatography of the recovered column residues of the reaction to prepare **2jT**. ^{1}H NMR: δ=1.20–2.10 (7H, m, 3×CH_2+OH), 2.35 (3H, s, CH_3) 2.39 (3H, s, CH_3) 2.69 (1H, dd, J=9.7, 11.4 Hz, CH), 3.14 (1H, ddd, J=2.5, 11.4, 11.6 Hz, CHS), 3.88 (1H, ddd, J=4.0, 9.0, 9.8 Hz, CHOH), 7.0–7.55 (8H, m, 8×CH). IR: ν_{max}=3440 (O–H), 2921, 2844 (C–H), 1703 (C=O) cm^{-1}. MS (CI): 390 (50%, $[M+NH_4]^+$), 373 (5%, $[M+H]^+$). HRMS: $C_{21}H_{28}NO_2S_2$ ($[M+NH_4]^+$) requires 390.1561, found 390.1562.

6.3.10. 1*R*,2*R*,3*R*/1*S*,2*S*,3*S*-2-(*S*-Tolylthiocarboxy)-1-(*S*-tolyl)cyclohexan-3-ol (2jTb).

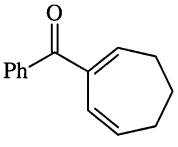


A small quantity of **2jTb** (ca. 7 mg, ca. 6%) contaminated with **2jT** was isolated by chromatography of the recovered column residues of the reaction to prepare **2jT**. Selected data: ^{1}H NMR: δ=3.04 (1H, dd, J=4.3, 9.4 Hz, CH), 3.95 (1H, br m, CHS), 4.22 (1H, m, CHOH).

6.4. General method for phosphine reactions

The aldehyde (typically 100 mg) was weighed into an NMR tube and diluted to the correct concentration with $CDCl_3$. The tri-*n*-butylphosphine (0.05–0.4 equiv.) was then added neat and the tube agitated. The reaction was followed by NMR and on completion (to ca. 95%), the solvent was removed and the products were obtained by column chromatography. For specific conditions, see Tables 4 and 5.

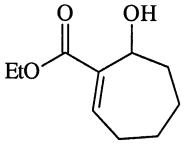
6.4.1. 2-Benzoylcyclo-1,3-heptadiene (14c).



Column solvent: 20% ether in petrol, R_f=0.13. ^{1}H NMR: δ=1.94 (2H, m, CH_2), 2.37–2.53 (4H, m, 2×CH_2), 6.06

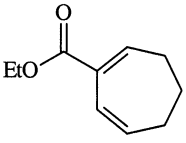
(1H, dt, J=5.2, 11.9 Hz, CH), 6.33 (1H, dd, J=1.2, 11.9 Hz, CH), 6.57 (1H, br t, J=5.2 Hz, CH), 7.38–7.58 (3H, m, Ph), 7.66–7.76 (2H, m, Ph). ^{13}C NMR: δ=25.70 (CH_2), 30.98 (CH_2), 31.71 (CH_2), 123.29 (CH), 128.04 (2×CH), 129.58 (2×CH), 131.75 (CH), 135.33 (CH), 137.89 (C), 138.21 (C), 145.34 (CH), 198.22. (C=O). IR: ν_{max}=3027, 2926, 2881 (C–H), 1651 (C=O/C=C) cm^{-1}. MS (CI): 216 (100%, $[M+NH_4]^+$), 199 (70%, $[M+H]^+$). HRMS: $C_{14}H_{15}O$ ($[M+H]^+$) requires 199.1123, found 199.1122.

6.4.2. 2-Carboethoxy-1-hydroxycyclohept-2-ene (3h).



Column solvent: 10% ether in petrol, R_f=0.05. ^{1}H NMR: δ=1.31 (3H, t, J=7.3 Hz, CH_3), 1.50–2.10 (6H, m, 3×CH_2), 2.20–2.55 (2H, m, CH_2), 3.13 (1H, br s, CHO*H*), 4.22 (2H, q, J=7.3 Hz, CH_2), 4.81 (1H, m, C*H*OH), 7.11 (1H, t, J=6.4 Hz, CH). ^{13}C NMR: δ=14.19 (CH_3), 23.50 (CH_2), 25.66 (CH_2), 27.28 (CH_2), 32.36 (CH_2), 60.82 (CH_2), 68.70 (CH), 136.77 (C), 145.17 (CH), 168.40 (C=O). IR: ν_{max}=3450 (O–H), 2981, 2930, 2857 (C–H), 1702 (C=O), 1642 (C=C) cm^{-1}. MS (CI): 202 (90%, $[M+NH_4]^+$), 185 (100%, $[M+H]^+$). HRMS: $C_{10}H_{17}O_3$ ($[M+H]^+$) requires 185.1178, found 185.1179.

6.4.3. 2-Carboethoxy-1,3-heptadiene (14h).



Column solvent: 5% ether in petrol, R_f=0.48 (20% ether in petrol). ^{1}H NMR: δ=1.30 (3H, t, J=7.0 Hz, CH_3), 1.90 (2H, m, CH_2), 2.35 (2H, m, CH_2), 2.45 (2H, m, CH_2), 4.23 (2H, q, J=7.0 Hz, CH_2), 5.98 (1H, dt, J=5.4, 11.6 Hz, CH), 6.38 (1H, br d, J=1.5, 11.6 Hz, CH), 7.14 (1H, t, J=5.5 Hz, CH). ^{13}C NMR: δ=14.21 (CH_3), 25.89 (CH_2), 30.62 (CH_2), 31.39 (CH_2), 60.67 (CH_2), 122.88 (CH), 128.39 (C), 134.66 (CH), 143.61 (CH), 167.72 (C=O). IR: ν_{max}=3023, 2981, 2932 (C–H), 1708 (C=O), 1607 (C=C) cm^{-1}. MS (CI): 184 (70%, $[M+NH_4]^+$). HRMS: $C_{10}H_{18}NO_2$ ($[M+NH_4]^+$) requires 184.1338, found 184.1339.

Acknowledgements

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4. This material was prepared from cyclopent-1-ene-1-methanol[5] which was benzylated (NaH, BnBr, TBAI, THF; 69%), ozonised (O_3, −78°C, then PPh_3) and treated with benzoylmethylenetriphenylphosphorane (1.3 equiv., DCM, rt, 24 h, 97%).
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11. *X-ray structure determination*. The intensity data were collected on a Nonius Kappa CCD area-detector diffractometer at the window of a rotating anode FR591 generator (Mo-Kα radiation, =0.71073 Å). There structure was solved by direct methods and refined on F^2 by full-matrix least-squares refinements. Full details have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 150272 for **2eT** and CCDC 150990 for **2fTb**. **2eT**: $C_{15}H_{20}O_3S$. T=150 K, M=280.37, monoclinic space group $P2_1$, Z=2, a=8.9143(6) Å, b=4.9923(3) Å, c=16.7387(15) Å, β=95.936(2)°, V=740.93(9) Å^3, D_c=1.257 Mg m^{-3}, μ(Mo-Kα)=0.22 mm^{-1}. Colourless needle, crystal size 0.70×0.03×0.03 mm, range: 2.0–25.2°, 2475 unique data and 190 parameters, $R1[F^2 > 2\sigma(F^2)] = 0.049$, $wR2$(all data) = 0.096, Flack parameter=0.05(9). **2fTb**: $C_{16}H_{22}O_3S$. T=150 K, M=294.40, orthorhombic space group $Pca2_1$, Z=8, a=15.8301(2) Å, b=5.62760(10) Å, c=33.8340(6) Å, V=3014.12(8) Å^3, D_c=1.298 Mg m^{-3}, μ(Mo-Kα)=0.22 mm^{-1}. Colourless prism, crystal size 0.10×0.07×0.07 mm, range: 2.0–25.1°, 5060 unique data and 408

parameters, $R1[F^2 > 2\sigma(F^2)] = 0.043$, $wR2$(all data) = 0.069, Flack parameter=0.05(12).

12. The ylid TolSCOCHPPh$_3$ was prepared by coupling bromoacetic acid with toluene-4-thiol (DCC, DMAP, DCM, 0°C, 3 h) followed by reaction of the crude product thus obtained with triphenylphosphine (toluene, 48 h). This was followed by reaction of a DCM solution of the phosphonium salt formed with excess aqueous sodium carbonate solution followed by separation, drying and precipitation of the phosphorane with hexane; 69% Yield, mp 179°C. ^{1}H NMR: δ=2.30 (3H, s, CH_3), 3.64 (1H, d, J_{P-H}=22 Hz, CH), 7.12 (2H, d, J=7.9 Hz, 2×CH), 7.40–7.70 (17H, m, 3×Ph and 2×CH).