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A novel silica catalysed stereoselective cyclic carbamate and carbonate rearrangement

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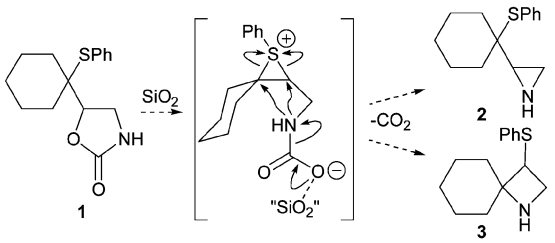
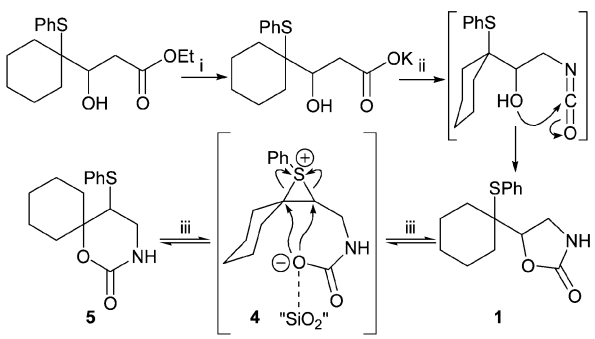
Phenylsulfanyl-containing five- and six-membered lactones, cyclic carbamates and carbonates stereospecifically interconvert in the presence of silica gel *via* thiiranium ions.

Pyrrolidines have been synthesised from six-membered-ring carbamates with stereospecific migration of a PhS group and loss of CO_2.[1,2] If a similar process were to occur with the five-membered-ring carbamate **1**, then the product would be either an aziridine **2** or an azetidine **3**, depending on the relative rates of these two competing ring-closing reactions (Scheme 1). Similar aziridine-forming reactions involve the opening of a bromonium[3] and iodonium ions.[4,5] Azetidines[6] and β-lactams can be made by the opening of bromonium[7,8] and sulfonium[9,10] ions.



Scheme 1

The synthesis of oxazolidinone **1** was achieved *via* an aldol reaction and a modified Curtius rearrangement in which the isocyanate is captured by the neighbouring hydroxyl group (Scheme 2). Treatment of this carbamate with silica gel in refluxing chloroform produced a 17 : 83 mixture of starting material and new compound that was neither of the cyclic amines **2** and **3**, but the six-membered-ring carbamate **5**. A rearrangement of the five-membered-ring carbamate had occurred without loss of CO_2. If the reaction occurred *via* an episulfonium ion intermediate **4** then the carbamate anion must be stable enough to reopen the episulfonium ion without decarboxylation and form the alternative carbamate **5** (Scheme 2). When the purified six-membered-ring carbamate **5** was resubjected to the rearrangement reaction procedure, five-membered-ring carbamate **1** was reformed, and after 32 hours, a similar (**1** : **5** 12 : 88) mixture was observed. The two carbamates are in equilibrium in these reaction conditions, and even after prolonged heating, no other products are observed. This isomerisation is similar to that observed for the non-cyclic carbamate previously reported, but there a true equilibrium was not established and both isomers ultimately reacted to form an allylic sulfide.[1]



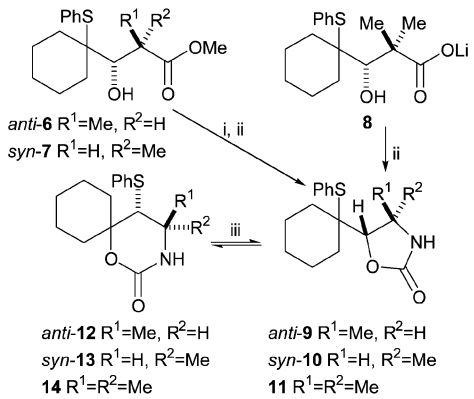
Scheme 2 *Reagents and conditions*: i, KOH, H_2O, THF; ii, $(PhO)_2PON_3$, t-BuOH, Δ, 70% (2 steps); iii, SiO_2, $CHCl_3$, Δ, see Table 1.

This reversible reaction was extended to more substituted compounds. Aldol products[11] **6,7** and **8** (aldol of isobutyric acid onto 1-phenylsulfanylcyclohexane carboxaldehyde[11]) were individually converted into oxazolidinones **9–11** which were heated in the presence of silica gel until equilibria with the six-membered-ring carbamates **12–14** were achieved (Table 1, Scheme 3). The configurations of compounds **10** and **13**, confirmed by X-ray crystallographic analysis, are consistent with the reaction occurring *via* a stereospecific episulfonium ion rearrangement with inversion at the secondary centre (Fig. 1).† In the least substituted case the oxazinone **5** is the more stable compound and 4,5-*cis*-substitution destabilises the near-planar oxazolidinones **10** and **11** with respect to their respective six-membered-ring isomers even more. The *trans*-relationship in carbamates **9** and **12** alone favours the five-membered-ring compound. Cyclisation of alkyl carbamates onto episulfonium,[12] episelenonium,[13,14] bromonium[12] and iodonium[13,14] ions also produce cyclic carbamates, but there is however no evidence in these cases that the cyclisations are reversible. The effect of changing the cyclohexane ring has not been investigated.

Table 1 The synthesis of 4-substituted oxazolidinones and their silica catalysed rearrangement to oxazinones (see Schemes 2 and 3)

R^1	R^2	Oxazolidinone yield from aldol	Oxazinone	Rearrangement equilibrium ratio
H	H	**1** (70%)	**5**	(**1** : **5**) 13 : 87
CH_3	H	*anti*-**9** (88%)	*anti*-**12**	(**9** : **12**) 64 : 36
H	CH_3	*syn*-**10** (84%)	*syn*-**13**	(**10** : **13**) 2 : 98
CH_3	CH_3	**11** (32%[a])	**14**	(**11** : **14**) 2 : 98

[a] Yield from isobutyric acid.



Scheme 3 *Reagents and conditions*: i, KOH, H_2O, THF; ii, $(PhO)_2PON_3$, t-BuOH, Δ; iii, SiO_2, $CHCl_3$, Δ; see Table 1 for yields.

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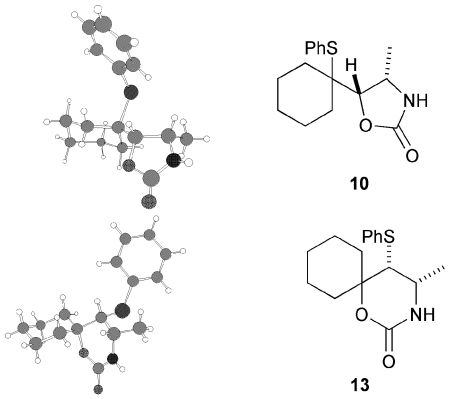
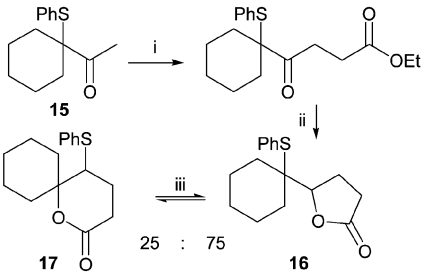


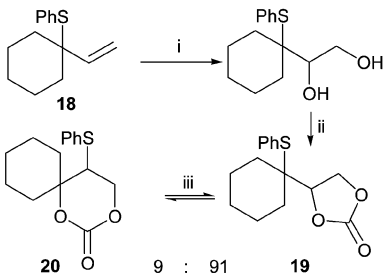
Fig. 1 Molecular structure of *syn*-carbamates **10** and **13** determined by X-ray analysis. Pictured is only one of the two enantiomers of **13** in the unit cell, each with a slightly different conformation.



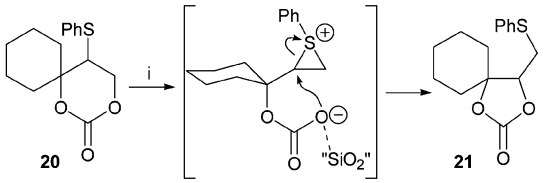
Scheme 4 *Reagents and conditions*: i, LDA, THF, −78 °C; $BrCH_2CO_2Et$, HMPA, 73%; ii, $NaBH_4$, THF, 0 °C, 18%; iii, SiO_2, $CHCl_3$, Δ.

Silica gel also catalyses the generation of episulfonium ions from esters and carbonates,[1] and we were interested to see whether this occurred with related lactones and cyclic carbonates. Five-membered-ring compounds **16** (Scheme 4) and **19** (Scheme 5) were made from known intermediates ketone[15] **15** and olefin[16] **18** respectively, and were treated with silica gel. In refluxing chloroform both compounds formed equilibrium mixtures with their six-membered-ring isomers **17** and **20** (**16** : **17** 75 : 25 and **19** : **20** 91 : 9), again without any loss of CO_2 from the carbonate. The position of equilibrium for the lactone favours the five-membered ring, a result in sharp contrast to the equivalent cyclic ethers where the THP is the only product in a thermodynamically controlled isomerisation,[17] so the inclusion of a carbonyl group stabilises the five-membered ring with respect to the six-membered ring. The additional oxygen atom in the carbonates **19** and **20** favours the five-membered ring even more. Five- and six-membered phenylseleno-lactones[18] have been shown to interconvert with strong acid or Lewis acid catalysis,[19] or on standing.[20] Silica gel also isomerises β- to γ-lactones *via* episulfonium[21] and episelenonium[21] ions. Phenylseleno-containing cyclic carbonates similar to compounds **19** and **20** also interconvert during silica column chromatography.[22]

When the mixture of carbonates **19** and **20** was heated in toluene at reflux a third identifiable carbonate was formed. In



Scheme 5 *Reagents and conditions*: i, $OsCl_3$, $K_3Fe(CN)_6$, K_2CO_3, quinuclidine, t-BuOH, H_2O; ii, CDI, CH_3CN, 40% (2 steps), iii, SiO_2, $CHCl_3$, Δ.



Scheme 6 *Reagents and conditions*: i, SiO_2, $PhCH_3$, Δ.

carbonate **20** the PhS group is adjacent to two similarly acylated carbons and the new product is the result of a further rearrangement to another five-membered-ring carbonate **21** (Scheme 6). This reaction is the first example of a PhS double migration in this type of rearrangement process.

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Notes and references

† *Crystal data* for **10**: $C_{16}H_{21}NO_2S$, M = 291.40, orthorhombic, space group $P2_12_12_1$ (no. 19), a = 6.7248(2), b = 13.1339(8), c = 16.6976(9) Å, U = 1474.8(2) Å^3, Z = 4, μ(Mo-Kα) = 0.221 mm^{-1}, 6257 reflections measured at 180(2) K using an Oxford Cryosystems Cryostream cooling apparatus, 2568 unique (R_{int} = 0.041); R_1 = 0.037, wR_2 = 0.085. Absolute structure parameter 0.04(8). The structure was solved with SHELXS-97[23] and refined with SHELXL-97.[23] CCDC 207751.

For **13**: $C_{16}H_{21}NO_2S$, M = 291.40, monoclinic, space group $P2_1/c$ (no. 14), a = 10.8413(3), b = 14.7036(9), c = 19.2137(11) Å, β = 90.201(3)°, U = 3062.8(3) Å^3, Z = 8, μ(Mo-Kα) = 0.213 mm^{-1}, 18109 reflections measured at 180(2) K using an Oxford Cryosystems Cryostream cooling apparatus, 5375 unique (R_{int} = 0.097); R_1 = 0.052, wR_2 = 0.095. The structure was solved with SHELXS-97[23] and refined with SHELXL-97.[23] CCDC 207752. See http://www.rsc.org/suppdata/cc/b3/b303791f/ for crystallographic data in CIF or other electronic format.

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