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Synthetic Routes to β-Lactams. Some Unexpected Hydrogen Atom Transfer Reactions

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Abstract: Appropriately substituted xanthate derivatives of N-ethenyl acetamides undergo radical cyclisation to give β-lactams with transfer of the xanthate group. In one case, a cascade of unexpected and unusual hydrogen transfer reactions occurred.

INTRODUCTION

A vast amount of work has been devoted over almost half a century to the synthesis of β-lactams.[1] This nucleus is the key feature in penicillins and cephalosporins, which constitute by far the most important family of antibiotics. The propensity of β-lactams to react with various nucleophiles appears to be at the heart of their biological activity; it has also been used to advantage in various synthetic applications.[2] So far, the construction of the central β-lactam unit has relied on ionic chemistry in the broadest sense. Radical reactions have only recently been found to allow, under certain circumstances, the formation of such a strained ring.[3] With the exception of studies from the group of Pattenden[3a-c] who has used organocobalt derivatives and a recent application by ourselves of the nickel / acetic acid reducing system,[4] essentially all the published work[3d-h] has involved tin hydride mediated radical cyclisations, with all the limitations imposed by such a system. In particular, it is usually necessary to operate under high dilution conditions (in general through slow addition of stannane) and to stabilise the radical created in the (relatively slow) cyclisation step with phenyl groups or sulfur substituents. As part of our work on the radical chemistry of xanthates, we have now found that it can be applied to the construction of β-lactams, thus usefully complementing existing methods.

RESULTS AND DISCUSSION

Over the past few years, we have shown that xanthates **1** were synthetically convenient sources of a wide variety of radicals, which can be generated and captured according to the general reaction manifold displayed in Scheme 1.[5] Several advantages are associated with such a system: (i) the radicals are created through initiation by organic peroxides or by light, without the intervention of heavy metals such as tin or mercury; (ii) although radical **2** can (and does) react with its precursor **1** to give adduct **3** (path **a**), this process is degenerate since breaking the O-Me (or O-Et) bond is quite difficult and fragmentation only leads back to radical **2** and starting xanthate **1**; because of this key property, radical **2** acquires a relatively long effective lifetime (by being continuously regenerated) allowing it to undergo difficult cyclisations or additions to unactivated olefins (path **b**); (iii) such a radical addition breaks the degeneracy of the system by producing intermediate **4** and eventually **5**, thus propagating a radical chain process; (iv) finally, product **5** is itself a xanthate which provides an entry into the rich chemistry of sulfur or, if desired, can be used in another radical sequence.

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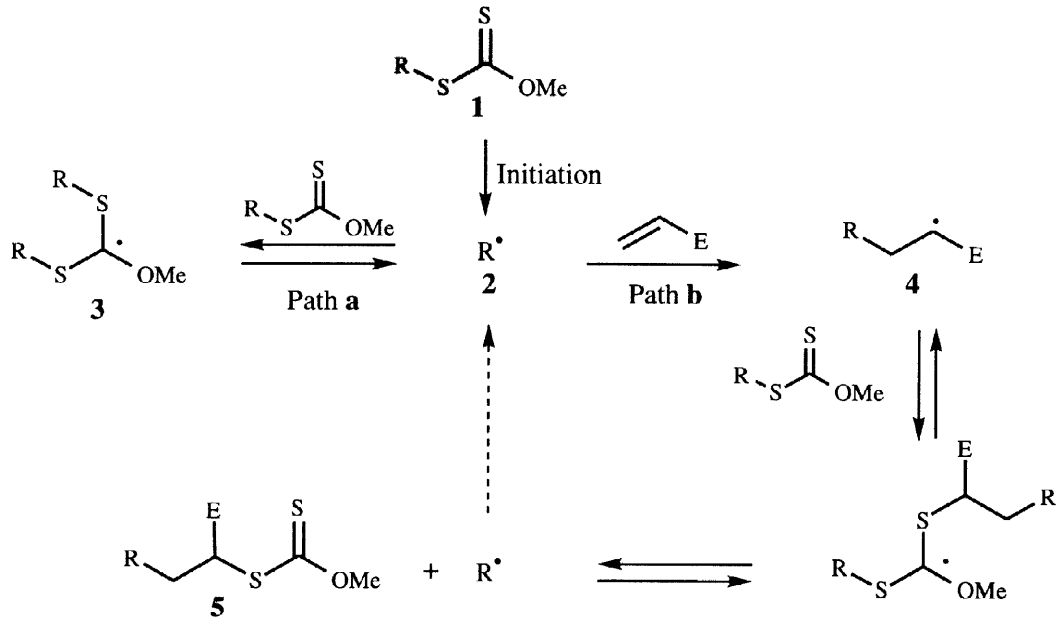
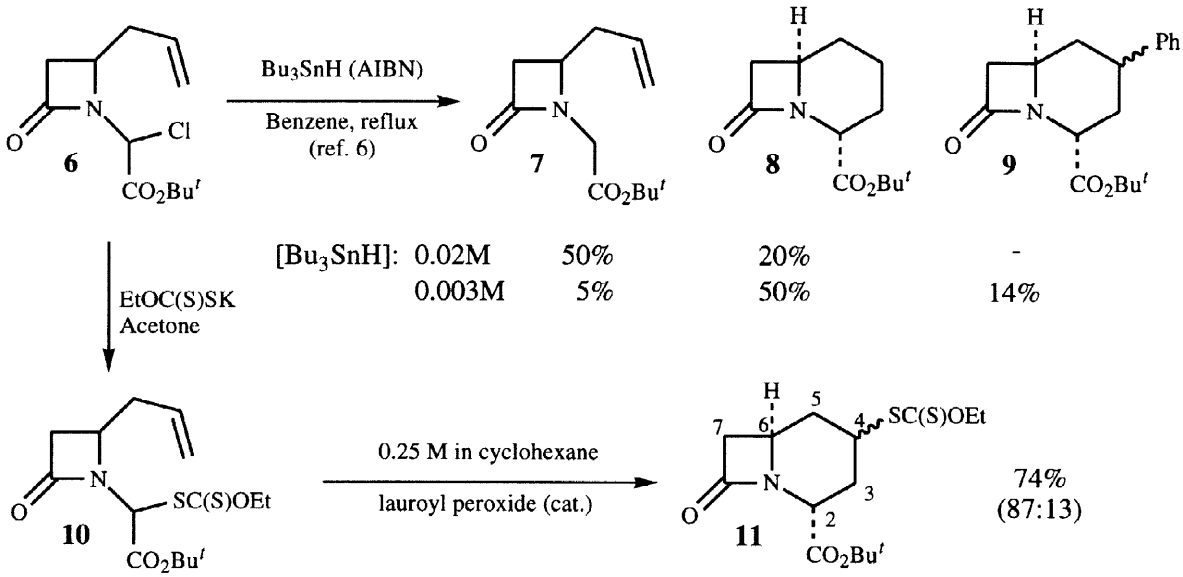


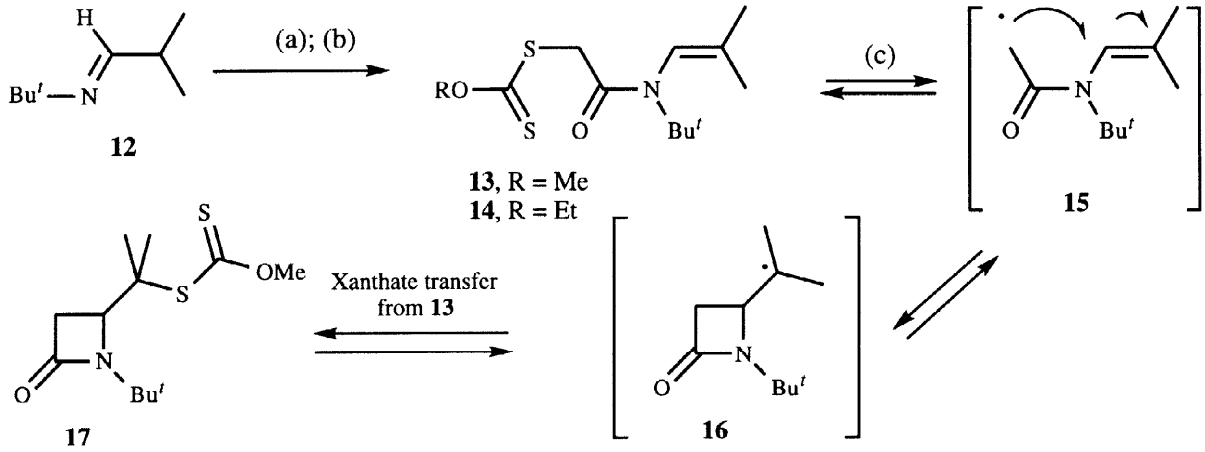
Scheme 1

One further consequence of the degeneracy of path **a**, in addition to allowing the use of relatively unreactive radical traps, is that the reactions can be run at a much higher concentration. These favourable features may be readily contrasted with those governing the radical chemistry of tributyltin hydride. This was accomplished in the first instance by comparing the construction of the adjacent ring to the β-lactam nucleus in a carbacepham. Thus, as summarised in Scheme 2, the radical cyclisation of chloride **6**, examined in a pioneering work by Bachi and co-workers[6] a decade ago, provides the 6-endo bicyclic β-lactam **8** in 20% yield, if the concentration of the medium is 0.02M in tributylstannane. The major side-product is, as would be expected, the reduced derivative **7**, isolated in 50% yield. If the concentration of the stannane is lowered to 0.003M, the yield of the desired bicylic β-lactam increases to 50% and that of the reduced compound **7** decreases to 5%. However, at such high dilution another side-product **9** (14%), arising from reaction of the intermediate radical with the solvent, benzene, becomes significant. This is clearly a slow cyclisation and high dilution is necessary if stannane is the radical generating reagent.



Scheme 2

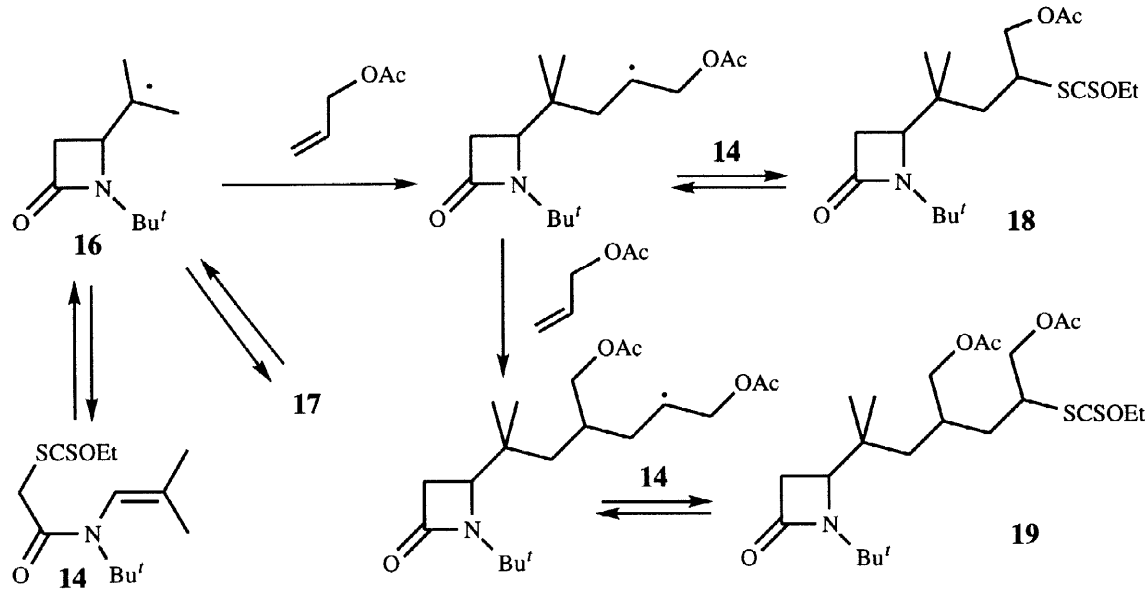
If, on the other hand, a 0.25M solution of the corresponding xanthate **10** in refluxing cyclohexane is treated with a small amount of lauroyl peroxide (20%), then a smooth reaction occurs to give β-lactam **11** in 74% yield as an 87:13 mixture of epimers. Xanthate **10** is made from the same chloride **6** by displacement with commercially available potassium ethyl xanthate. A better yield in cyclisation is therefore obtained at a concentration that is nearly a hundred-fold greater, with the added bonus that the product contains a xanthate group with all the attending synthetic opportunities.



Conditions : (a) $ClCH_2COCl$, cyclohexane, Et_3N ; (b) RO(CS)S K, ROH (R = Me or Et);
(c) Cyclohexane (reflux), cat. lauroyl peroxide

Scheme 3

For the construction of the β-lactam nucleus itself, our approach relies on the radical cyclisation starting from enamides such as **13**, prepared by the acylation of an imine with chloroacetyl chloride, followed by displacement of the chloride with a xanthate salt (Scheme 3).

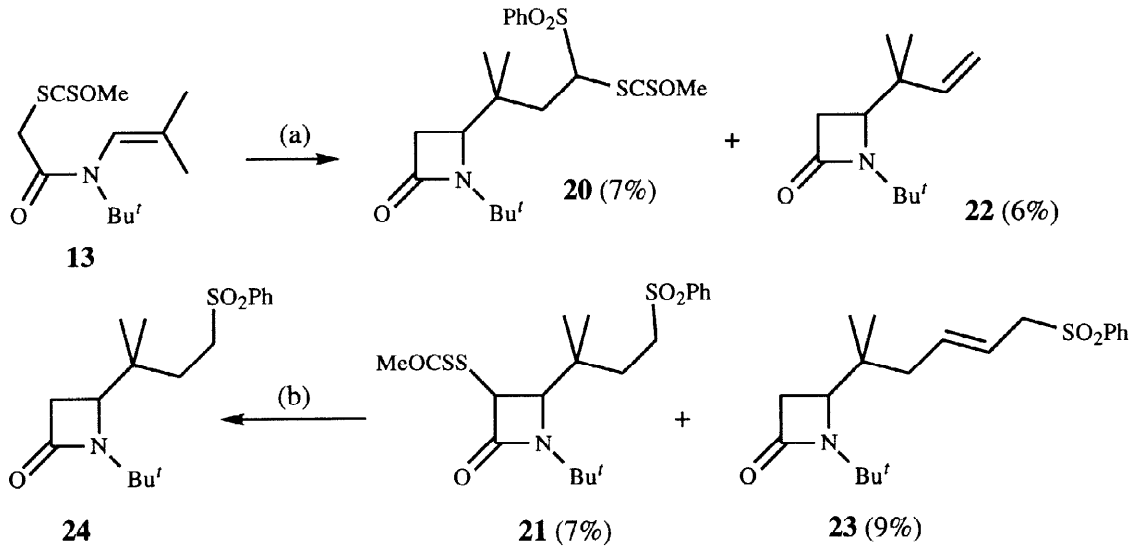


Conditions: allyl acetate (10 equiv.), cyclohexane (reflux), cat. lauroyl peroxide

Scheme 4

When xanthate **13** was subjected to the usual radical generating conditions (refluxing cyclohexane, catalytic lauroyl peroxide) no cyclised product **17** was isolated. Only starting material was recovered from the reaction. Even though we anticipated that intermediate radical had a sufficient lifetime in the medium to cyclise and capture a xanthate group to give ultimately **17**, our hopes seemed to be frustrated by the reversibility of both the cyclisation and the xanthate transfer steps. Radical **16** is apparently not sufficiently stabilised to shift the equilibrium towards the β-lactam structure, in contrast to the examples described in the literature[3d-h], and alluded to in the introduction above, where phenyl or phenylthiyl groups were used as stabilising substituents, but which constituted at the same time a limitation to the generality of such an approach.

In order to favour the formation of the β-lactam, it is therefore necessary to couple the cyclisation with an irreversible process. One simple expedient was to add an external olefinic trap which would preferentially and irreversibly react with radical **16**, giving concomitantly a more elaborated structure through the creation of one more carbon-carbon bond. This indeed turned out to be the case, as illustrated by the following example, delineated in Scheme 4 and involving the use of excess allyl acetate as the external olefin. Under these conditions, the cyclisation-addition product **18** (23%) along with lesser amounts of double addition derivative **19** (8%) were obtained, with 27% of the starting xanthate being recovered.

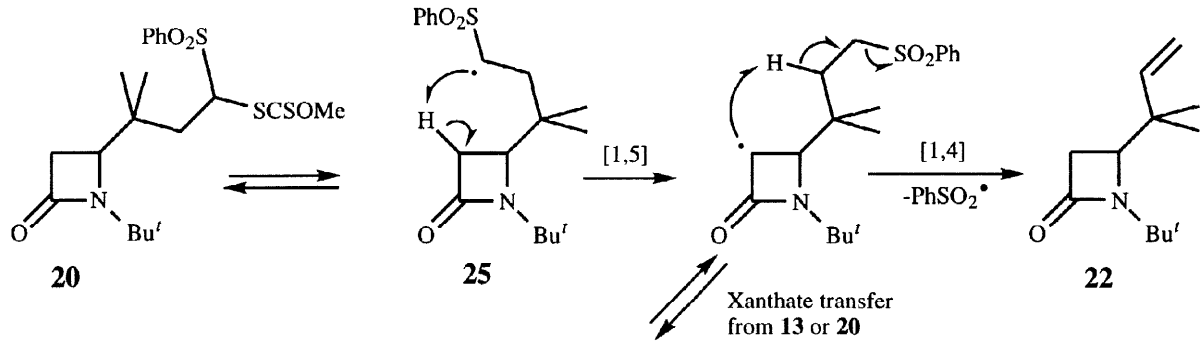


Conditions : (a) phenyl vinyl sulfone (1.5 equiv.), cyclohexane (reflux), cat. lauroyl peroxide;
(b) Bu_3SnH (1.9 equiv.), AIBN (0.6 equiv.), benzene, reflux

Scheme 5

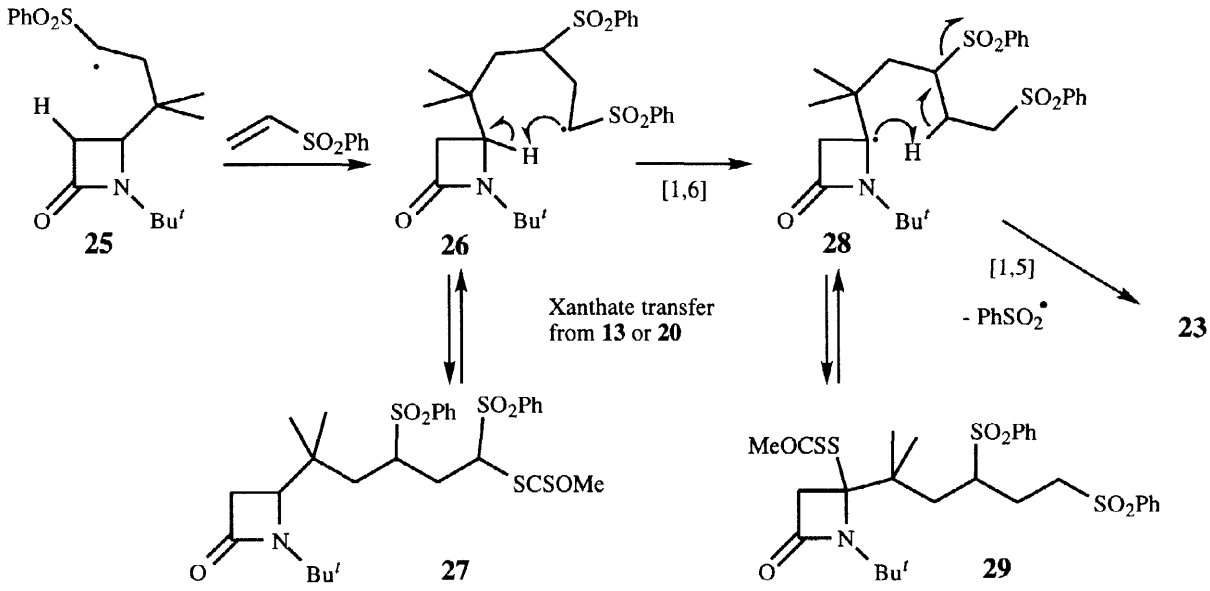
Allyl acetate is a poor radicophile. We therefore repeated the above experiment using phenyl vinyl sulfone which is a better trap and which could be used in smaller excess, thus eliminating perhaps the formation of double addition products. With 1.5 equiv. of phenyl vinyl sulfone, we were surprised by the sluggishness of the reaction and by the nature of the four products (Scheme 5) that were eventually isolated in poor yield and identified as **20** (7%), **21** (7%), **22** (6%), and **23** (9%), along with a large amount of unreacted starting material (65%). The first, **20**, is the expected product of the reaction, but the remaining three appear to arise by a remarkable sequence of transformations, permitted no doubt by the relatively long life of the intermediate radicals inherent to the xanthate system, as explained above, and maybe also by a favourable geometry imposed by the bulky *tert*-butyl group. For structural confirmation purposes, **21** was reduced by tributylstannane (Scheme 5) into the simpler derivative **24** (this compound is in fact also produced in small amounts in the main reaction and could be identified once an authentic sample was in hand).

The reaction manifold displayed in Scheme 6 provides a mechanistic rationale for the formation of **21** and **22**. The former arises through a 1,5-hydrogen shift, followed by a reversible transfer of the xanthate group. As for the latter, it appears necessary to invoke a 1,4-hydrogen shift, followed by β-elimination of a phenylsulfonyl radical. Unlike 1,5-hydrogen shifts[7] which are fairly common in radical chemistry, 1,4-hydrogen shifts are extremely rare[8]. The generation of phenylsulfonyl radicals in the medium explains the sluggishness of the reaction since these radicals are too stabilised to propagate the chain and act rather as inhibitors. Strong evidence for the proposed pathway in the present case was adduced by adding lauroyl peroxide (1.6 equiv.) portion-wise to a refluxing cyclohexane solution of pure **21** until its complete consumption. Under these conditions a good yield of **22** (70%) was obtained, demonstrating the remarkable efficiency of the 1,4-hydrogen translocation in the present case.



Scheme 6

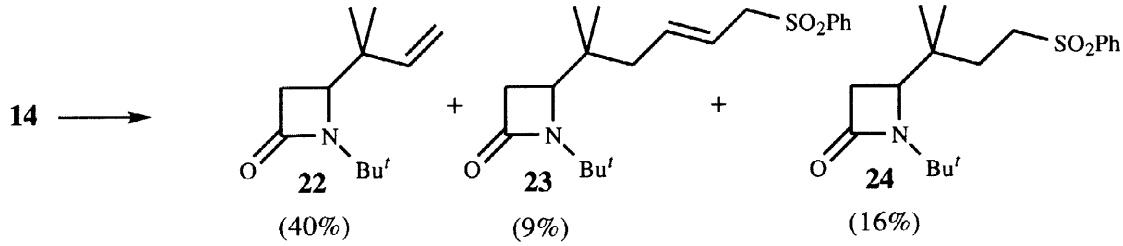
A probable path for the formation of compound **23** is outlined in Scheme 7. It implies an initial double addition to phenyl vinyl sulfone, followed by a 1,6- then a 1,5-hydrogen shifts, and finally a selective β-elimination of the secondary phenylsulfonyl group to give the more substituted olefin. Although 1,6- are rarer than 1,5-hydrogen shifts, they are much more common than 1,4-hydrogen shifts.[9] An alternative route would be a 1,7- (i. e.abstraction of H-7 instead of H-6 in **26**) followed by a 1,6-hydrogen shift, but this is perhaps less likely.



Scheme 7

Unfortunately, none of the xanthates **27** and **29** corresponding to the postulated intermediate radicals **26** and **28** could be isolated in this case to allow us to perform the same type of experiment as for **22**. This fact may be taken as an indication that the intervening steps are relatively fast, driven inexorably towards **23** by the final elimination of the phenylsulfonyl radical.

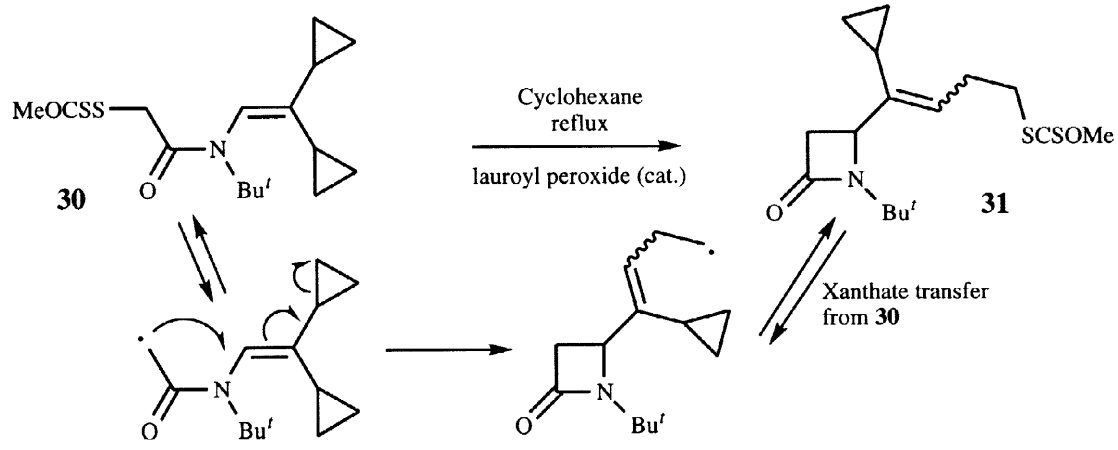
From a synthetic standpoint, we have exploited these mechanistic observations in order to improve the yield of compound **22** at the expense of the other products. As the formation of each molecule of **22** or **23** liberates a phenylsulfonyl radical which is too stabilised to propagate the chain, it is necessary to use lauroyl peroxide in stoichiometric amounts. This not only allows an essentially complete transformation of the starting material **14**, but has the added advantage of also inducing the conversion of intermediates **20** and **21** into elimination product **22**, since the presence of the xanthate group in these molecules provides a means to regenerate the radical precursors and thus re-enter the reaction manifold. Moreover, we hoped that a three-fold dilution of the reaction medium and batch-wise addition of phenyl vinyl sulfone (3 batches of 0.5 equiv. each) would limit the formation of compound **23** by diminishing the concentration of the external trap. Finally, we opted for 1,2-dichloroethane instead of cyclohexane because of its greater solubilising power. Under these modified conditions (Scheme 8), the yield of **22** rose to 40% but that of **23** did not change much (9%), whereas the reduced adduct **24** became more important (16%). Derivatives **20** and **21** were practically absent from the mixture. Although the yield of **22** might seem modest, its formation involves no less than five different radical species and, as far as we are aware, this is the first time that phenyl vinyl sulfone allows the introduction of a simple vinyl group under radical conditions.



Conditions : Phenyl vinyl sulfone (1.5 equiv.), 1,2-dichloroethane (reflux), lauroyl peroxide (1.3 equiv)

Scheme 8

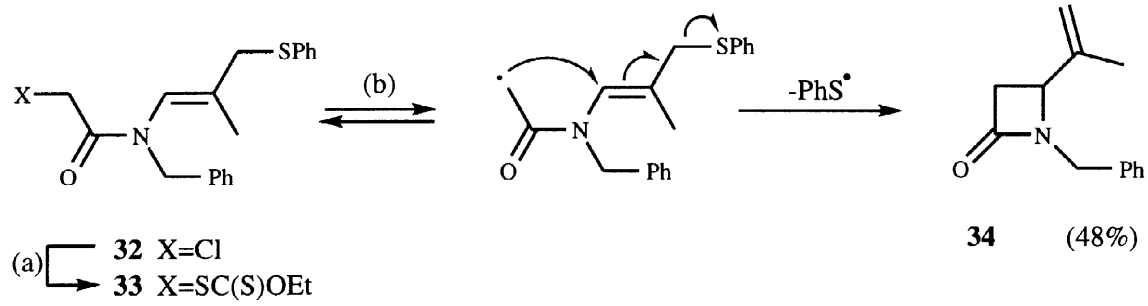
Another route to β-lactams was examined where the creation of the strained four-membered ring is coupled with the cleavage of an even more strained cyclopropane or the departure of a leaving group in the radical sense. The construction of strained rings by pulling an unfavourable equilibrium with the help of a fast but largely irreversible subsequent step has some precedent in the field of radical chemistry.[10] In our case, this approach had the advantage of having the loaded spring within the reacting molecule.



Scheme 9

One such precursor is xanthate **30**, prepared by the same route as above from dicyclopropylacetaldehyde. Indeed, upon exposure to catalytic amounts of lauroyl peroxide in cyclohexane, it was converted into β-lactam **31**, the logical product of the sequence depicted in Scheme 9, in an unoptimised 30% yield (60% based on recovered starting material). The opening of one of the cyclopropane rings is the driving force in this instance.

The second possibility is illustrated by the cyclisation of compound **33** with the concomitant expulsion of a phenylthiyl radical. The yield of the corresponding β-lactam **34** is 48% and a stoichiometric amount of lauroyl peroxide is needed since phenylthiyl radicals are incapable of propagating the chain. The fact that the olefinic bond in **34** is unsubstituted on one terminus makes the product vulnerable to further attack by radicals in the medium with opening of the four-membered ring and open chain amides arising from such a pathway appear to constitute the bulk of the side products.



Conditions : (a) $EtOC(S)S^- K^+$; ethanol; (b) Cyclohexane (reflux), lauroyl peroxide (1.3 equiv.)

Scheme 10

In summary, we have shown the utility of this new radical chemistry of xanthates in providing access to a variety of β-lactam structures, either by modification of an existing β-lactam ring or by forcing the formation of the azetidinone with the aid of fast, essentially irreversible steps. None of the yields has been optimised and room for improvement certainly exists.

Acknowledgement : We wish to thank Hoechst Marion Roussel for very generous financial support.

EXPERIMENTAL

Solvents and reagents were purified according to standard laboratory techniques. I.R. spectra are for neat films unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded on Bruker 200, 250, or 300 MHz in deuterated chloroform solutions with tetramethylsilane as internal standard (δ ppm); coupling constants are given in Hz. Mass spectra were recorded on AEI MS-50 (EI), AEI MS-9 (EC) or Kratos MS-80 (HRMS) spectrometer.

N-*tert*-Butyl-N-(2-methylpropenyl)-2-chloroacetamide. To *tert*-butylamine (2.6 ml, 25 mmol) in a separatory funnel, isobutyraldehyde (2.3 ml, 25 mmol) was slowly added at room temperature. The water formed during the reaction was removed. Potassium hydroxide pellets were added and the remaining water was taken off after 4 hours. The complete formation of imine **12** was confirmed by I.R. spectroscopy. A solution of the imine in dry cyclohexane (10 ml) was added dropwise over 4 hours under an inert atmosphere to chloroacetyl chloride (2.15 ml, 27 mmol) in cyclohexane (75 ml). To this mixture, a solution of triethylamine (10.4 ml, 75 mmol) in cyclohexane (20 ml) was added dropwise over 3 hours. The resulting precipitate was filtered off over celite, rinsed with ether and the filtrate concentrated under vacuum. After purification by silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1), the title compound (3.55g, 70%) was obtained as a colorless oil, ν_{max}/cm^{-1} 2978, 1677, 1656 (C=O), 1394, 1367, 1336 and 1200; δ_H (250 MHz; $CDCl_3$) 1.39 (9H, s, Bu^t), 1.67 (3H, d, *J* 1.4, $CMeCH_3$), 1.77 (3H, d, *J* 1.4, $CMeCH_3$), 3.88 (1H, d, J_{AB} 13.5, $ClCHH$), 4.04 (1H, d, J_{AB} 13.5, $ClCHH$) and 5.82 (1H, m, *H*C=C); δ_C (62 MHz; $CDCl_3$) 17.0 (CH_3), 21.0 (CH_3), 27.5 ($C(CH_3)_3$), 44.2 (CH_2Cl), 58.0 (CMe_3), 121.8 (*C*H=C), 137.5 (Me_2C=CH) and 165.3 (*C*=O).

N-*tert*-Butyl-N-(2,2-dicyclopropylethenyl)-2-chloroacetamide. To *tert*-butylamine (0.95 ml, 9 mmol) in a separatory funnel, 2,2-dicyclopropyl acetaldehyde[11] (1.12 g, 9 mmol) was slowly added at room temperature. The water formed during the reaction was removed. Potassium hydroxide pellets were added and the remaining water was taken off after 4 hours. The complete formation of the imine was confirmed by I.R. spectroscopy. A solution of the imine in dry cyclohexane (4 ml) was added dropwise over 4 hours under an inert atmosphere to chloroacetyl chloride (0.8 ml, 10 mmol) in cyclohexane (30 ml). To this mixture a solution of triethylamine (3.8 ml, 27 mmol) in cyclohexane (8 ml) was added dropwise over 3 hours. The resulting precipitate was filtered off over celite, rinsed with ether and the filtrate concentrated under vacuum. After purification by silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1), the title compound was obtained as a colorless oil, δ_H (200 MHz) 0.42-0.98 (9H, m, cyclopropyl: 1C*H*, 4CH_2), 1.40 (9H, s, Bu^t), 1.77-1.89 (1H, m, cyclopropyl C*H*), 4.02 (1H, d, J_{AB} 14, ClCH*H*), 4.10 (1H, d, J_{AB} 14, ClCH*H*) and 5.77 (1H, s, C*H*=C).

N-Benzyl-N-(2-methyl-3-phenylthiopropenyl)-2-chloroacetamide 32. 2-methyl-3-phenylsulfenyl-propionaldehyde was prepared by addition of thiophenol (5.13 ml, 50 mmol) to methacroleine (4.60 ml, 55 mmol) and with triethylamine (5.5 mmol; 10mol %) at room temperature, followed by evaporation of remaining methacroleine and triethylamine. This aldehyde was directly condensed with benzylamine (6.00 ml, 55 mmol) in a separatory funnel at room temperature. The water formed during the reaction was removed after 10 hours. The remaining water was azeotrppically removed by co-evaporation three times with toluene under vacuum. A solution of this imine in dry cyclohexane (20 ml) was added dropwise over 4 hours under an inert atmosphere to chloroacetyl chloride (4.38 ml, 55 mmol) in cyclohexane (150 ml). To this mixture a solution of triethylamine (20.9 ml, 150 mmol) in cyclohexane (40 ml) was added dropwise over 3 hours. The resulting precipitate was filtered off over celite, rinsed with ether, and the filtrate concentrated under vacuum. Purification by silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1) gave compound **32** (8.6 g, 50% from methacroleine) as a yellow oil, ν_{max}/cm^{-1} 3060, 1770, 1675 (C=O), 1657, 1438, 1407 and 1231; δ_H (250 MHz) 1.55 (3H, s, CH_3), 3.47 (2H, s, NCH_2), 3.54 (2H, s, CH_2S), 4.49 (2H, s, CH_2Cl), 5.80 (1H, br s, *H*C=C) and 7.11-7.38 (10H, m, 2Ph); δ_C (75 MHz; $CDCl_3$) 13.7 (*C*H$_3$), 38.9 (*C*H$_2$S), 41.3 (*C*H$_2$Cl), 50.4 (N*C*H$_2$), 124.2 (*C*H=C), 126.3 (*C*H, Ph), 126.6 (*C*H, Ph), 127.6 (2*C*H, Ph), 127.9 (2*C*H, Ph), 128.3 (2*C*H, Ph), 130.2 (2*C*H, Ph), 133.7 (*C*q), 135.6 (*C*q), 136.7 (*C*q) and 164.8 (*C*=O).

***tert*-Butyl (2-allyl-4-oxo-azetidin-1-yl)-ethoxythiocarbonylsulfenylacetate 10.** To a solution of chloride **6**[12] (1.9 mmol) in acetone (4 ml) was added portionwise potassium O-ethyl xanthate (455 mg, 2.85 mmol) at 10°C. The mixure was stirred for 3 hours at room temperature then concentrated under vacuum. The residue was dilluted in dichloromethane, then poured into water. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. Compound **10** (425 mg, 65%) was obtained as a pale yellow oil following silica gel column chromatography (eluent: heptane / ethyl acetate - 8 : 2); it was a mixture of two diastereomers (3 : 2). (Found: C, 52.15; H, 6.7. Calc. for $C_{15}H_{23}NO_4S_2$: C, 52.15; H, 6.7%); ν_{max}/cm^{-1} 2980, 1768 (C=O), 1740 (C=O), 1370, 1237 (O-CS), 1151, 1047 (C=S); δ_H (300 MHz) 1.44 (6/5H, t, *J* 7.0, OCH$_2$C*H*$_3$), 1.46 (9/5H, t, *J* 7.1, OCH$_2$C*H*$_3$), 1.48 (18/5H, s, Bu^t), 1.49 (27/5H, s, Bu^t), 2.26-2.42 (1H, m, CH*H*CH=CH$_2$), 2.56-2.80 (1H, m, CH*H*CH=CH$_2$), 2.66 (3/5H, dd, J_{AB} 15.1, J_{AX} 2.5, CH*H*CO), 2.70 (2/5H, dd, J_{AB} 15.0, J_{AX} 2.9, CH*H*CO), 2.98 (2/5H, dd, J_{AB} 15.0, J_{BX} 5.4, CH*H*CO), 3.04 (3/5H, dd, J_{AB} 14.9, J_{BX} 5.2, CH*H*CO), 3.77-3.86 (2/5H, m, NC*H*), 3.99-4.08 (3/5H, m, NC*H*), 4.67 (4/5H, q, *J* 7.1, OC*H*$_2$CH$_3$), 4.69 (6/5H, q, *J* 7.1, OC*H*$_2$CH$_3$), 5.06-5.21 (2H, m, CH=C*H*$_2$), 5.62-5.83 (1H, m, *H*C=CH$_2$), 6.16 (2/5H, s, SC*H*) and 6.23 (3/5H, s, NC*H*S); δ_C (62 MHz; $CDCl_3$) 13.5 (OCH$_2$*C*H$_3$), 27.6 (C(*C*H$_3$)$_3$), 37.1, 37.6 (*C*H$_2$), 41.3, 41.9 (*C*H$_2$), 51.1, 52.3 (N*C*HCH$_2$), 60.5, 60.6 (S*C*H), 70.6, 70.7 (O*C*H$_2$), 83.9 (*C*Me$_3$), 118.2, 118.4 (CH=*C*H$_2$), 132.2, 132.5 (*C*H=CH$_2$), 164.0, 164.5 (OC=O), 165.5, 166.3 (NC=O), 208.8, 209.5 (*C*=S).

N-*t*-Butyl-N-(2-methylpropenyl)-methoxythiocarbonylsulfenylacetamide 13. The same procedure was used with a solution of N-*tert*-Butyl-2-chloro-N-(2-methyl-propenyl)-acetamide (2.03 g, 10 mmol) in methanol (20 ml) and potassium O-methyl xanthate (2.2 g, 15 mmol). Xanthate **13** (2.52 g, 92%) was obtained as a pale yellow oil following silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1). (Found: C, 52.45; H, 7.7; N, 5.0. Calc. for $C_{12}H_{21}NO_2S_2$: C, 52.35; H, 7.7; N, 5.1%), ν_{max}/cm^{-1} 2976, 1651 (C=O), 1229 (O-CS) and 1069 (C=S); δ_H (250 MHz) 1.38 (9H, s, Bu^t), 1.71 (3H, d, *J* 1.1, CMeCH_3), 1.80 (3H, d, *J* 1.2, CMeCH_3), 3.79 (1H, d, J_{AB} 15.8, SCH*H*), 4.04 (1H, d, J_{AB} 15.8, SCH*H*), 4.15 (3H, s, OCH_3) and 5.90 (1H, m, C*H*=C); δ_C (62 MHz; $CDCl_3$) 17.7 (*C*H$_3$), 21.6 (*C*H$_3$), 28.1 (C(*C*H$_3$)$_3$), 42.6 (*C*H$_2$S), 58.6 (*C*Me$_3$), 60.1 (OCH$_3$), 122.9 (*C*H=C), 137.6 (Me$_2$*C*=CH), 166.3 (*C*=O), 215.2 (*C*=S), *m/z* (EI) 275 ($M^{+\bullet}$), 260, 218, 168 and 149.

N-*t*-Butyl-N-(2-methylpropenyl)-ethoxythiocarbonylsulfenylacetamide 14. To a solution of N-*tert*-butyl-N-(2-methylpropenyl)-2-chloro-acetamide (2.03 g, 10 mmol) in ethanol (20 ml) was slowly added potassium O-ethyl xanthate (2.4 g, 15 mmol). A white potassium chloride precipitate soon replaced the yellow potassium xanthate salt. The mixure was stirred for 2 hours at room temperature and poured into water, then extracted twice with a 7 : 3 pentane / ether mixture. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated. Xanthate **14** (2.65 g, 92%) was obtained as a pale yellow oil following silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1). (Found: C, 53.8; H, 8.05; N, 5.0. Calc. for

$C_{13}H_{23}NO_2S_2$: C, 53.95; H, 8.0; N, 4.85%); ν_{max}/cm^{-1} 2977, 1654 (C=O), 1227 (O-CS) and 1052 (C=S); δ_H (300 MHz) 1.38 (9H, s, Bu^t), 1.41 (3H, t, *J* 7.1, OCH_2CH_3), 1.71 (3H, d, *J* 1.3, $CMeCH_3$), 1.80 (3H, d, *J* 1.3, $CMeCH_3$), 3.78 (1H, d, J_{AB} 15.8, SCH*H*CO), 4.03 (1H, d, J_{AB} 15.8, SCH*H*CO), 4.64 (2H, q, *J* 7.1, OCH_2CH_3) and 5.90 (1H, m, C*H*=C); δ_C (62 MHz; $CDCl_3$) 13.5 (OCH_2CH_3), 17.9 (CH_3), 21.8 (CH_3), 28.4 ($C(CH_3)_3$), 42.5 (CH_2S), 58.9 (CMe_3), 78.2 (OCH_2Me), 123.2 (*C*H=C), 137.8 (Me_2C=CH), 166.6 (*C*=O) and 214.6 (*C*=S).

N-*t*-Butyl-N-(2,2-dicyclopropylethenyl)-methoxythiocarbonylsulfenylacetamide 30. The same procedure was used with a solution of N-*tert*-butyl-N-(2,2-dicyclopropylethenyl)-2-chloroacetamide (half of the material obtained above) in methanol (10 ml) and potassium O-methyl xanthate (1.0 g, 7 mmol). Xanthate **30** (955 mg, 65% from 2,2-dicyclopropyl acetaldehyde) was obtained as a yellow oil following silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1). (Found: EI, $MH^{+\bullet}$, 328.1406. Calc. for $C_{16}H_{26}NO_2S_2$: 328.1405); ν_{max}/cm^{-1} 2975, 1656 (C=O), 1361, 1226 (O-CS) and 1071 (C=S); δ_H (300 MHz) 0.2-1.0 (9H, m, cyclopropyl: 1C*H*, 2CH_2), 1.49 (9H, s, Bu^t), 1.6-1.9 (1H, m, cyclopropyl C*H*), 3.99 (1H, d, J_{AB} 15.8, CH*H*S), 4.04 (1H, d, J_{AB} 15.8, CH*H*S), 4.15 (3H, s, OCH_3) and 5.86 (1H, s, C*H*=C); δ_C (75 MHz; $CDCl_3$) 4.5, 5.0, 5.1 (4CH_2, cyclopropyl), 9.5 (cyclopropyl *C*H), 12.5 (cyclopropyl *C*H), 28.3 ($C(CH_3)_3$), 43.3 (CH_2S), 59.0 (CMe_3), 60.2 (OCH_3), 122.2 (*C*H=C), 144.9 (*C*=CH), 166.8 (*C*=O) and 215.5 (*C*=S); *m/z* (EI) 327 ($M^{+\bullet}$), 312, 252 and 219.

N-Benzyl-N-(2-methyl-3-phenylthiylpropenyl)-methoxythiocarbonylsulfenylacetamide 33. The same procedure was used with a solution of chloroacetamide **32** (3.46 g, 10 mmol) in ethanol (20 ml) and potassium O-ethyl xanthate (2.4 g, 15 mmol). Xanthate **33** (4.0 g, 93%) was obtained as a yellow oil following silica gel column chromatography (eluent: heptane / ethyl acetate - 9 : 1), (Found: C, 61.35; H, 5.9. Calc. for $C_{22}H_{25}NO_2S_3$: C, 61.2; H, 5.85%); ν_{max}/cm^{-1} 2959, 1672, 1654 (C=O), 1438, 1233 (O-CS) and 1052 (C=S); δ_H (300 MHz) 1.38 (3H, t, *J* 7.1, OCH_2CH_3), 1.62 (3H, d, *J* 1.3, CH_3), 3.51 (2H, s, NCH_2), 3.52 (2H, s, CH_2SPh), 4.50 (2H, s, CH_2CO), 4.60 (2H, q, *J* 7.1, OCH_2CH_3), 5.90 (1H, br s, *H*C=C) and 7.06-7.38 (10H, m, 2Ph); δ_C (75 MHz; $CDCl_3$) 13.3 (OCH_2CH_3), 14.5 (CH_3), 38.5 (CH_2S), 39.7 (CH_2S), 50.9 (NCH_2), 69.9 (OCH_2Me), 125.2 (*C*H=C), 126.7 (*C*H, Ph), 127.0 (*C*H, Ph), 127.9 (2*C*H, Ph), 128.3 (2*C*H, Ph), 128.6 (2*C*H, Ph), 130.6 (2*C*H, Ph), 134.1 (*C*q), 136.1 (*C*q), 136.7 (*C*q), 165.7 (*C*=O) and 213.0 (*C*=S).

***t*-Butyl 4-(ethoxythiocarbonylsulfanyl)-8-oxo-1-aza-bicyclo[4.2.0]octane-2-carboxylate 11.** This is a typical procedure which was used for the radical reactions of the various xanthates: a solution of xanthate **10** (323 g, 0.9 mmol) in dry cyclohexane (4 ml) was heated under reflux for 30 minutes in an inert atmosphere to deoxygenate the solution. Lauroyl peroxide (8 mg, 2%) was introduced every 2 hours through the reflux condenser to initiate the radical reaction which was monitored by TLC for completion. Thus, 0.2 equiv. of dilauryl peroxide (80 mg) were added over 20 hours. The solvent was removed under reduced pressure and the residue purified by silica gel column chromatogaphy (eluent: heptane / ethyl acetate - 95 : 5 to 4 : 6). Two diastereomers of **11** were in this way separated :

The first diastereomer (200mg, 65%) was obtained as white crystals mp 97-98°C (from CH_2Cl_2/pentane). (Found: C, 52.4; H, 6.9. Calc. for $C_{15}H_{23}NO_4S_2$: C, 52.15; H, 6.7%); ν_{max}/cm^{-1} 2979, 1760 (C=O), 1733 (C=O), 1393, 1369, 1221 (O-CS), 1157 and 1053 (C=S); δ_H (300 MHz) 1.25-1.51 (1H, m, C(5)H*H*), 1.41 (3H, t, *J* 7.2, OCH_2CH_3), 1.52 (9H, s, Bu^t), 1.76 (1H, ddd, J_{AB} 13.0, J_{AY} 13.0, J_{AX} 7.0, C(3)HH^{β}), 2.41-2.51 (1H, m, C(5)H*H*), 2.51 (1H, ddd, J_{AB} 13.3, J_{BY} 3.2, J_{BX} 1.4, C(3)HH^{α}), 2.66 (1H, dd, $J_{A'B'}$ 14.8, $J_{A'X'}$ 1.6, C(7)HH^{β}), 3.24 (1H, dd, $J_{A'B'}$ 14.7, $J_{B'X'}$ 4.5, C(7)HH^{α}), 3.75-3.94 (2H, m, C(4)H^{α}, C(6)H^{α}), 4.65 (1H, d, J_{AX} 7.0, C(2)H^{β}) and 4.65 (2H, q, *J* 7.1, OCH_2CH_3); δ_C (75 MHz; $CDCl_3$) 13.7 (OCH_2CH_3), 28.0 ($C(CH_3)_3$), 33.1 (*C*(3)H_2), 35.9 (*C*(5)H_2), 42.2 (*C*(4)H), 45.1 (*C*(7)H_2), 46.5 (*C*(6)H), 50.9 (*C*(2)H), 70.0 (OCH_2), 82.7 (CMe_3), 165.2 (*C*=O), 168.9 (*C*=O) and 212.2 (*C*=S).

The second diastereomer (28 mg, 9%) was obtained as a yellow oil, ν_{max}/cm^{-1} 2979, 2931, 1756 (C=O), 1394, 1369, 1253, 1223 (O-CS), 1155 and 1050 (C=S); δ_H (300 MHz) 1.41 (3H, t, *J* 7.1, OCH_2CH_3), 1.48 (9H, s, Bu^t), 1.77 (1H, ddd, J_{AB} 13.7, J_{AY} 11.0, J_{AZ} 4.0, C(5)H*H*), 2.16 (1H, ddd, J_{AB} 14.7, J_{AY} 7.9, J_{AZ} 4.0, C(3)H*H*), 2.38 (1H, ddd, J_{AB} 13.7, J_{AY} 3.7, J_{AZ} 3.7, C(5)H*H*), 2.65 (1H, dd, J_{AB} 14.7, J_{AY} 1.7, C(3)H*H*), 2.65 (1H, dd, J_{AB} 14.7, J_{AY} 1.7, C(7)H*H*), 3.26 (1H, dd, J_{AB} 14.7, J_{AY} 3.7, C(7)H*H*), 3.75-3.94 (2H, m, C(4)*H*, C(6)*H*), 4.24 (1H, dddd, J_{AW} =J_{AX} =J_{AY} =J_{AZ} =3.6, C(4)*H*), 4.46 (1H, d, 7.4, C(2)*H*) and 4.63 (2H, q, *J* 7.1, OCH_2CH_3); δ_C (75 MHz; $CDCl_3$) 13.9 (OCH_2CH_3), 27.9 ($C(CH_3)_3$), 30.2 (*C*(3)H_2), 34.8 (*C*(5)H_2), 43.5 (*C*(6)H), 43.7 (*C*(4)H), 45.1 (*C*(7)H_2), 48.8 (*C*(2)H), 70.1 (OCH_2), 82.6 (CMe_3), 165.8 (*C*=O), 169.4 (*C*=O) and 212.7 (*C*=S).

Reaction in the presence of allyl acetate. The same procedure was applied to a solution of **14** (0.29 g, 1 mmol) and allylacetate (1.00 g, 10 mmol) in dry benzene (5 ml),.and 0.25 equiv. of lauroyl peroxide was added overall (12 mg, 2.5% every 2 hours, i.e. 120 mg over 20 hours). After chromatography (eluent: petroleum ether / ethyl acetate - 3 : 1), 27% of the starting material was recovered, as well as the following products of simple and double addition :

1-*t*-Butyl-4-[4-acetoxy-1,1-dimethyl-3-(ethoxythiocarbonylsulfanyl)butyl]-azetidin-2-one 18. This compound was obtained as a pale yellow oil (90 mg, 23%) and as a 1:1 mixture of diastereoisomers. (Found: C, 55.6; H, 7.9; N, 3.5. Calc. for $C_{18}H_{31}NO_4S_2$: C, 55.5; H, 8.0; N, 3.6%); ν_{max}/cm^{-1} 2970, 1744 (C=O), 1226 (O-CS) and 1049 (C=S); δ_H (300 MHz) 1.00 (3/2H, s, CMeCH_3), 1.01 (3/2H, s, CMeCH_3), 1.02 (3/2H, s, CMeCH_3), 1.04 (3/2H, s, CMeCH_3), 1.32 (9H, s, Bu^t), 1.37 (3H, t, *J* 7.1, OCH_2CH_3), 1.52-1.61 (1H, m, CH*H*CMe$_2$), 1.63-1.70 (1H, m, CH*H*CMe$_2$), 1.99 (3H, s, CH_3CO_2), 2.36-2.43 (1H, m, CH*H*CO), 2.72-2.79 (1H, m, CH*H*CO), 3.50-3.55 (1H, m, NC*H*), 3.92-4.01 (1H, m, C*H*S), 4.03-4.18 (2H, m, CH_2OAc) and 4.59 (2H, q, *J* 7.1, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 13.7 (CH_3CH_2O), 20.8 (CH_3CO_2), 23.5, 23.7 (CH_3), 24.7, 25.1 (CH_3), 29.1 (C(CH_3)$_3$), 35.9 (CH_2CMe_2), 37.8 (CMe_2), 38.0 , 38.2 (CH_2CO), 44.8, 44.9 (CHS), 54.0 (CMe_3), 61.0, 61.2 (CHN), 66.9 (CH_2OAc), 70.3 (OCH_2Me), 167.9, 168.0 (NC=O), 170.5 ($MeCO_2$) and 212.7 (C=S); *m/z* (EI) 389 ($M^{+\bullet}$), 329, 300, 268, 263, 231, 226, 170, 161, 126, 84, 70, 57 and 43.

1-*t*-Butyl-4-[6-acetoxy-3-acetoxymethyl-1,1-dimethyl-5-(ethoxythiocarbonylsulfanyl)hexyl]-azetidin-2-one 19. This compound was obtained as a pale yellow oil (40 mg, 8%, mixture of diastereoisomers). (Found: CI, MH^+, 490.2296. Calc. for $C_{23}H_{40}NO_6S_2$: 490.2297); ν_{max}/cm^{-1} 2976, 1737 (C=O), 1232, 1048 (O-CS) and 737 (C=S); δ_H (300 MHz) 0.96-1.08 (6H, m, C(CH_3)$_2$), 1.18-1.37 (2H, m, $CH_2(CH_2)_2$), 1.39 (9H, s, Bu^t), 1.42 (1.5H, t, *J* 7.0, OCH_2CH_3), 1.44 (1.5H, t, *J* 7.0, OCH_2CH_3), 1.56-1.85 (2H, m, CH_2CMe_2), 1.92-2.11 (1H, m, CH(CH$_2$)$_3$), 2.07 (3H, s, CH_3CO_2), 2.08 (3H, s, CH_3CO_2), 2.41-2.54 (1H, m, CH*H*CO), 2.72-2.89 (1H, m, CH*H*CO), 3.47-3.57 (1H, m, NC*H*), 3.86-4.12 (3H, m, C*H*S, (CH)$_2$CHCH_2O), 4.17-4.35 (2H, m, SCHCH_2O), 4.64 (1H, q, *J* 7.0, OCH_2Me) and 4.66 (1H, q, *J* 7.0, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 13.8 (CH_3CH_2O), 20.9 (CH_3CO_2), 21.0 (CH_3CO_2), 23.2, 23.6, 23.8 (CH_3), 24.8, 25.2 (CH_3), 29.2 (C(CH_3)$_3$), 30.9, 31.1 (CH(CH$_2$)$_3$), 34.9, 35.2 (CH_2CMe_2), 35.9, 36.1 (CMe_2), 38.2 (CH_2CHS), 38.6, 38.8 (CH_2CO), 47.3, 47.7 (CHS), 54.2 (CMe_3), 61.7, 61.8, 62.0 (CHN), 65.7, 66.1 (CH_2OAc), 67.6, 68.1 (CH_2OAc), 70.4, 70.5 (OCH_2Me), 168.2 (NC=O), 170.7 ($MeCO_2$), 171.1 ($MeCO_2$) and 212.8 (C=S); *m/z* (EI) 474, 429, 368, 363, 326, 303, 215, 126, 84, 70, 59 and 43.

Reaction in the presence of phenyl vinylsulfone. The same procedure was applied to a solution of **13** (825 mg, 3 mmol) and phenyl vinyl sulfone (756 mg, 4.5 mmol) in cyclohexane (12 ml), and 0.2 equiv. of lauroyl peroxide was added overall (24 mg, 2% every 2 hours, i.e. 240 mg over 20 hours). After chromatography (eluent: heptane / ethyl acetate - 9 : 1 to 4 : 6), 65% of the starting material was recovered, as well as the following products :

1-*t*-Butyl-4-[1,1-dimethyl-3-(methoxythiocarbonylsulfanyl)-3-phenylsulfonylpropyl]-azetidin-2-one 20. Obtained as a yellow foam (95mg, 7%), and as a 1:1 mixture of diastereoisomers. (Found: C, 54.2; H, 6.4; N, 2.85. Calc. for $C_{20}H_{29}NO_4S_3$: C, 54.15; H, 6.6; N, 3.15%); ν_{max}/cm^{-1} 2974, 1739 (C=O), 1448, 1309, 1241 (O-CS), 1150 and 1062 (C=S); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.99 (3/2H, s, CMeCH_3), 1.01 (3/2H, s, CMeCH_3), 1.02 (3/2H, s, CMeCH_3), 1.05 (3/2H, s, CMeCH_3), 1.35 (9/2H, s, Bu^t), 1.37 (9/2H, s, Bu^t), 1.81 (1/2H, dd, J_{AB} 15.3, J_{AX} 9.8, CH*H*CMe$_2$), 1.83 (1/2H, dd, J_{AB} 15.2, J_{AX} 9.5, CH*H*CMe$_2$), 2.33-2.45 (2H, m, CH*H*CMe$_2$, CH*H*CO), 2.77 (1/2H, dd, $J_{A'B'}$ 14.9, $J_{B'X'}$ 5.7, CH*H*CO), 2.79 (1/2H, dd, $J_{A'B'}$ 14.9, $J_{B'X'}$ 5.7, CH*H*CO), 3.54 (1/2H, dd, $J_{B'X'}$ 5.8, $J_{A'X'}$ 2.3, NC*H*), 3.58 (1/2H, dd, $J_{B'X'}$ 5.8, $J_{A'X'}$ 2.3, NC*H*), 4.03 (3/2H, s, OCH_3), 4.04 (3/2H, s, OCH_3), 5.23 (3/2H, dd, J_{AX} 9.7, J_{BX} 1.5, SC*H*S), 5.26 (1/2H, dd, J_{AX} 9.5, J_{BX} 1.4, SC*H*S) and 7.51-8.08 (5H, m, Ph); δ_C (75 MHz; $CDCl_3$) 22.8, 23.1 (CH_3), 24.3, 24.7 (CH_3), 29.1 (C(CH_3)$_3$), 35.0, 35.3 (CH_2CMe_2), 36.2, 36.4 (CMe_2), 38.1, 38.4 (CH_2CO), 54.2, 54.4 (CMe_3), 60.5, 60.9 (NCH), 61.3, 61.4 (SCHS), 68.7 (OCH_3), 129.0 (2CH, Ph),130.2 (2CH, Ph), 134.3 (CH, Ph), 136.0 (Cq, Ph), 167.8 (C=O) and 210.7 (C=S).

1-*t*-Butyl-4-(1,1-dimethyl-3-phenylsulfonyl)propyl)-3-methoxythiocarbonylsulfanyl-azetidin-2one 21. Obtained as a yellow syrup (90 mg, 7%), ν_{max}/cm^{-1} 2972, 1751 (C=O), 1447, 1305, 1236 (O-CS), 1150 and 1065 (C=S); δ_H (300 MHz) 0.98 (3H, s, CMeCH_3), 1.02 (3H, s, CMeCH_3), 1.31 (9H, s, Bu^t), 1.72-1.80 (2H, m, CH_2CMe_2), 3.09-3.18 (2H, m, CH_2SO_2), 3.45 (1H, d, *J* 2.7, NC*H*), 4.20 (3H, s, OCH_3), 4.45 (1H, d, *J* 2.7, SC*H*) and 7.51-7.93 (5H, m, Ph); δ_C (75 MHz; $CDCl_3$) 23.1 (CH_3), 23.9 (CH_3), 29.0 (C(CH_3)$_3$), 31.9 (CH_2CMe_2), 35.5 (CMe_2), 52.0 (CH_2SO_2), 52.7 (NCH), 55.2 (CMe_3), 60.8 (OCH_3), 67.6 (SCHCO), 128.1 (2CH, Ph), 129.5 (2CH, Ph), 133.9 (CH, Ph), 138.7 (Cq, Ph), 165.1 (C=O) and 210.7 (C=S).

1-*tert*-Butyl-4-(1,1-dimethyl-2-propenyl)-azetidin-2-one 22. Obtained as a yellow oil (37 mg, 6%), (Found: CI, MH^+, 196.1704. Calc. for $C_{12}H_{22}NO$: 196.1701); ν_{max}/cm^{-1} 2967, 2927, 2855, 1743 (C=O), 1368, 1231 and 1150; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.03 (3H, s, CMeCH_3), 1.08 (3H, s, CMeCH_3), 1.35 (9H, s, Bu^t), 2.47 (1H, dd, J_{AB} 14.7, J_{AX} 2.3, CH*H*CO), 2.78 (1H, dd, J_{AB} 14.7, J_{BX} 5.6, CH*H*CO), 3.58 (1H, dd, J_{BX} 5.6, J_{AX} 2.3, NC*H*), 5.06 (1H, dd, J_1 17.7, J_2 1.0, CH=CH*H*), 5.07 (1H, dd, J_3 10.5, J_2 1.0, CH=CH*H*) and 5.89 (1H, dd, J_1 17.7, J_3 10.5, *H*C=CH$_2$); δ_C (75 MHz; $CDCl_3$) 20.9 (CH_3), 25.9 (CH_3), 29.1 (C(CH_3)$_3$), 38.4 (CH_2CO), 39.1 (CMe_2), 55.3 (CMe_3), 60.4 (NCH), 112.8 (CH=CH_2), 145.9 (CH=CH_2) and 168.1 (C=O); *m/z* (EI) 126, 84, 70, 57 and 41.

1-*t*-Butyl-4-(1,1-dimethyl-5-phenylsulfonyl-3-pentenyl)-azetidin-2-one 23 Obtained as a yellow oil (95 mg, 9%), (Found: CI, MH^+, 364.1963. Calc. for $C_{20}H_{30}NO_3S$: 364.1946); ν_{max}/cm^{-1} 2971, 1732 (C=O), 1448, 1307, 1148,

1086, 733 and 690; δ_H (300 MHz) 0.84 (3H, s, CMeCH_3), 0.90 (3H, s, CMeCH_3), 1.36 (9H, s, Bu^t), 2.00 (2H, d, J 7.4, CMe$_2$CH_2), 2.42 (1H, dd, J_{AB} 14.7, J_{AX} 2.3, CHHCO), 2.73 (1H, dd, J_{AB} 14.7, J_{BX} 5.7, CHHCO), 3.44 (1H, dd, J_{AX} 2.3, J_{BX} 5.7, NCH), 3.81 (2H, d, J 7.3, CH_2SO$_2$), 5.42 (1H, dt, J_d 15.2, J_t 7.3, CHCH$_2$CMe$_2$), 5.62 (1H, dt, J_d 15.2, J_t 7.45, CHCH$_2$SO$_2$) and 7.52-7.95 (5H, m, Ph); δ_C (75 MHz; CDCl$_3$) 22.9 (CH$_3$), 24.7 (CH$_3$), 29.1 (C(CH$_3$)$_3$), 35.9 (CMe$_2$), 37.9 (CH$_2$CO), 42.5 (CH$_2$CMe$_2$), 54.0 (CMe$_3$), 60.0 (CH$_2$SO$_2$), 60.5 (NCH), 119.1 (CHCH$_2$CMe$_2$), 128.3 (2CH, Ph), 129.2 (2CH, Ph), 133.7 (CH, Ph), 137.1 (CHCH$_2$SO$_2$), 138.7 (Cq, Ph) and 168.0 (C=O); *m/z* (EI) 348, 222, 180, 166, 141, 126, 77, 57 and 41.

The same procedure was applied to a solution of **13** (825 mg, 3 mmol) and phenyl vinyl sulfone (252 mg, 1.5 mmol) in 1,2-dichloroethane (36 ml). 1.3 Equiv. of lauroyl peroxide were added overall (60 mg, 5% every 2 hours, i.e. 1560 mg over 52 hours), until the disappearance of compounds **13**, **20** or **21**. After the addition of 30% and 70% lauroyl peroxide, extra batches of phenylvinylsulfone (252 mg, 1.5 mmol) were added to the mixture. After chromatography (eluent: heptane / ethyl acetate - 9 : 1 to 4 : 6), **22** (232, 40%) , **23** (98 mg, 9%) and **25** (190 mg, 19%) were obtained.

Conversion of 21 into 22. The same procedure was applied to a solution of **21** (70 mg, 0.16 mmol) in benzene (5 ml). 1.6 equiv. of lauroyl peroxide was overall added (6 mg, 10% every hour, i.e. 96 mg over 16 hours). The chromatography (eluent: heptane / ethyl acetate - 8 : 2) gave the same elimination product **22** (22 mg, 70%).

1-*t*-Butyl-4-[1-cyclopropyl-4-(methoxythiocarbonylsulfanyl)-1-butenyl]-azetidin-2-one 31. The same procedure was applied to a solution of **30** (327 mg, 1 mmol) in cyclohexane (4 ml). 0.16 equiv. of lauroyl peroxide was overall added (8 mg, 2% every 2 hours, i.e. 64 mg over 16 hours). After chromatography (eluent: heptane / ethyl acetate - 9 : 1), 50% of the starting material was recovered in addition to compound **31** which was obtained as a yellow oil (100 mg, 30%) and as a 3:2 mixture of isomers. (Found: EI, MH$^{+\bullet}$, 328.1404. Calc. for $C_{16}H_{26}NO_2S_2$: 328.1405); ν_{max}/cm^{-1} 2861, 1735 (C=O), 1368, 1232 (O-CS) and 1076 (C=S); δ_H (400 MHz) 0.30-0.37 (3/5H, m, cyclopropyl), 0.42-0.48 (2/5H, m, cyclopropyl), 0.56-0.64 (1H, m, cyclopropyl), 0.70-0.89 (2H, m, cyclopropyl), 1.31 (18/5H, s, Bu^t), 1.33 (27/5H, s, Bu^t), 1.38-1.49 (1H, m, cyclopropyl CH), 2.45 (2/5H, dd, $J_{1'}$ 14.2, $J_{2'}$ 2.3, CHHCO), 2.53 (6/5H, td, J_{A2X2} J_{B2X2} 7.4, J_5 7.5, CH_2CH$_2$S), 2.58-2.68 (4/5H, m, CH_2CH$_2$S), 2.84 (3/5H, dd, J_{A1B1} 14.5, J_{A1X1} 2.7, CHHCO), 2.92 (3/5H, dd, J_{A1B1} 14.5, J_{B1X1} 5.2, CHHCO), 2.93 (2/5H, dd, $J_{1'}$ 14.2, $J_{3'}$ 5.4, CHHCO), 3.09 (3/5H, dt, J_{A2B2} 13.3, J_{A2X2} 7.4Hz, CHHS), 3.17 (3/5H, dt, J_{A2B2} 13.3, J_{B2X2} 7.4, CHHS), 3.21 (4/5H, t, $J_{4'}$ 7.3, CH_2S), 3.80 (2/5H, dd, $J_{3'}$ 5.3, $J_{2'}$ 2.2, NCH), 4.18 (3H, s, OCH_3), 4.65 (3/5H, dd, J_{B1X1} 5.1, J_{A1X1} 2.6, NCH), 5.01 (3/5H, t, J_5 7.6, C=CH) and 5.71 (2/5H, t, $J_{5'}$ 7.3, C=CH); δ_C (75 MHz; CDCl$_3$) 4.4, 5.0, 6.1, 10.4 (2CH$_2$, cyclopropyl), 9.5 (CH, cyclopropyl), 26.2, 26.5 (CH$_2$CH$_2$S), 27.9, 28.0 (C(CH$_3$)$_3$), 36.0 (CH$_2$CO), 40.5, 44.7 (CH$_2$S), 48.6, 51.7 (NCH), 54.4, 54.5 (CMe$_3$), 60.2, 60.3 (OCH$_3$), 120.1, 124.9 (C=CH), 140.8, 142.1 (C=CH), 168.0, 168.1 (C=O) and 215.5 (C=S); *m/z* (EI) 327 (M$^{+\bullet}$), 294, 238, 220, 120, 105, 84, 75, 57 and 41.

1-Benzyl-4-(1-methylethenyl)-azetidin-2-one 34. The same procedure was applied to a solution of **33** (862 mg, 2 mmol) in cyclohexane (24 ml). 1.3 equiv. of lauroyl peroxide was added overall (80 mg, 10% every 2 hours, over 8 hours, then 40 mg, 5% every 2 hours, over 36 hours, i.e. 1040 mg over 44 hours). Purification by column chromatography (eluent: heptane to heptane / ethyl acetate - 1 : 1) gave the elimination product **34** as a colorless oil (315 mg, 48%), (Found: C, 77.6; H, 7.65. Calc. for $C_{13}H_{15}NO$: C, 77.6; H, 7.5%); ν_{max}/cm^{-1} 2917, 1752 (C=O), 1391 and 907; δ_H (300 MHz) 1.64 (3H, s, CH_3), 2.74 (1H, dd, J_{AB} 14.6, J_{AX} 2.1, CHHCO), 3.05 (1H, dd, J_{AB} 14.6, J_{BX} 5.2, CHHCO), 3.88 (1H, d, $J_{A'B'}$ 15.1, CHHPh), 3.90 (1H, dd, J_{AX} 2.1, J_{BX} 5.1, NCH), 4.70 (1H, d, $J_{A'B'}$ 14.9, CHHPh), 4.94-4.99 (2H, m, C=CH_2) and 7.19-7.38 (5H, m, Ph); δ_C (75 MHz, CDCl$_3$) 16.6 (CH$_3$), 42.4 (CH$_2$CO), 45.2 (CH$_2$Ph), 55.4 (NCH), 115.0 (C=CH$_2$), 127.7 (CH, Ph), 128.6 (2CH, Ph), 128.8 (2CH, Ph), 135.8 (Cq, Ph), 141.8 (C=CH$_2$), 167.0 (C=O).

1-*t*-Butyl-4-(1,1-dimethyl-3-phenylsulfonylpropyl)-azetidin-2-one 24. A solution of **21** (36 mg, 0.08 mmol), tributyltin hydride (0.04 ml, 0.15 mmol) and AIBN (8 mg, 0.05 mmol) in benzene (6 ml) was stirred under reflux in an inert atmosphere for 15 minutes. Chloroform (0.8 ml) was then added and the reaction mixture was refluxed for 10 minutes to destroy excess hydride. The solvent was then evaporated under reduced pressure and the residue taken up in acetonitile, washed twice with pentane to remove tin compounds, and purified by preparative TLC (eluent: petroleum ether / ethyl acetate - 2 : 3) to give **24** as a colorless oil (35 mg, 70%). (Found: CI, MH$^+$, 338.1784. Calc. for $C_{18}H_{28}NO_3S$: 338.1790); ν_{max}/cm^{-1} 2972, 1731 (C=O), 1298, 1230, 1149, 1087, 736 and 690; δ_H (300 MHz) 0.90 (3H, s, CMeCH_3), 0.94 (3H, s, CMeCH_3), 1.30 (9H, s, Bu^t), 1.66-1.74 (2H, m, CH_2CMe$_2$), 2.38 (1H, dd, J_{AB} 14.9, J_{AX} 2.3, CHHCO), 2.75 (1H, dd, J_{AB} 14.9, J_{BX} 5.7, CHHCO), 3.04-3.14 (2H, m, CH_2SO$_2$), 3.48 (1H, dd, J_{BX} 5.7, J_{AX} 2.3, NCH) and 7.55-7.96 (5H, m, Ph); δ_C (75 MHz; CDCl$_3$) 23.1 (CH$_3$), 23.7 (CH$_3$), 29.1 (C(CH$_3$)$_3$), 31.9 (CH$_2$CMe$_2$), 35.1 (CMe$_2$), 38.1 (CH$_2$CO), 52.2 (CH$_2$SO$_2$), 54.2 (CMe$_3$), 60.5 (NCH), 128.2 (2CH, Ph),129.5 (2CH, Ph), 134.0 (CH, Ph), 139.0 (Cq, Ph) and 167.9 (C=O); *m/z* (EI) 337 (M$^{+\bullet}$), 322, 280, 268, 196, 143 and 126.

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