Synthesis of (±)-Thienamycin based on a New Approach to β-Lactams *via* 4-*Exo-trig* Cyclisation of Carbamoylcobalt Salophens

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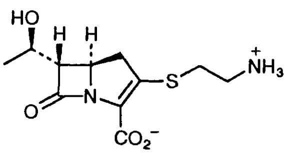
A series of *N*-propenyl substituted *N*-benzylcarbamoylcobalt(III) salophens, *i.e.* **11**, **20** and **30**, have been prepared, and have been shown to be useful precursors in a new approach to β-lactams (*viz.* **12–16**, **21** and **31**), *via* 4-*exo-trig* modes of cyclisation of the corresponding intermediate carbamoyl radicals. A new formal synthesis of (±)-thienamycin **1** from the *trans*-disubstituted azetidin-2-one **31** produced in one step by heating the carbamoylcobalt salophen **30** in toluene, is also described.

The novel antibiotic substance thienamycin **1** produced by *Streptomyces cattleya*[1] has been the focal point of many ingenious synthetic studies. Indeed, the first total synthesis of (±)-thienamycin was reported as early as 1978,[2] and a stereocontrolled synthesis of natural (+)-thienamycin was described in 1980.[3] Since this time more than 40 publications describing partial, formal and total syntheses of this intriguing β-lactam have testified to its prominence in contemporary organic synthesis.[4] A synthetic design to the β-lactam moiety in thienamycin, and related antibiotics, that has received scant attention however is one which uses a cyclisation involving the amide carbonyl and C-3 in an acyclic precursor molecule, *i.e.* disconnection **2**→**3**.[5]



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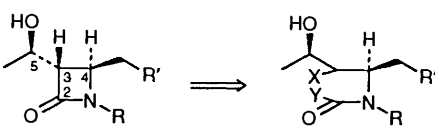

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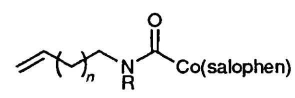
In studies of the scope for homolytic reactions involving organocobalt reagents in the generation of carbon-centred radical intermediates, we have earlier described the synthesis of several unsaturated carbamoylcobalt salophen reagents **4** and illustrated their potential as precursors for novel carbamoyl radical intermediates, *viz.* **5**.[6] Furthermore, we have shown that under appropriate conditions the intermediates **5** undergo facile cyclisation accompanied by trapping [e.g. with cobalt(II) species or 2,2,6,6-tetramethylpiperidin-1-yloxyl (TEMPO) radical] or by dehydrocobaltation leading to functionalised β-, γ- or δ-lactams, *i.e.* **6** and **7**. In this paper we describe how the principles and the chemistry developed in these earlier studies can be applied to a new and concise synthetic route to (±)-thienamycin **1**.[7]

We began our approach towards a new synthesis of thienamycin based on the disconnection **2**→**3**, by first examining the specificity of the 4-*exo-trig* cyclisation and dehydrocobaltation from the product radical centre in the carbamoylcobalt substrate **11**. The substrate **11** provided the extra methyl group at C-5 required for elaboration to the crucial 3-(1′-



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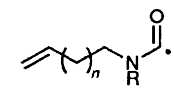

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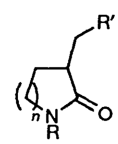

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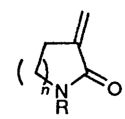

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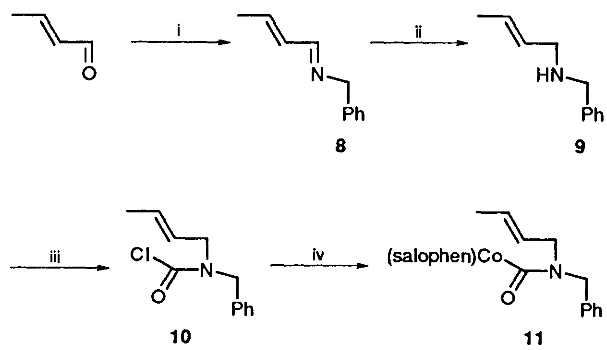
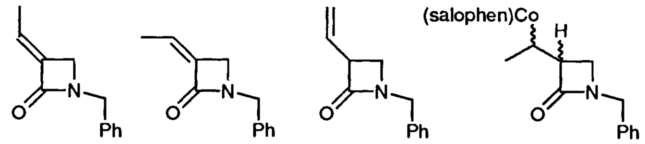
hydroxyethyl) side chain in the natural product. Thus, the carbamoylcobalt salophen reagent **11** was first prepared starting from the imine **8** derived from but-2-enal and benzylamine, and using methodology which we had already developed in our model studies (Scheme 1).[6] When a solution of the carba-



Scheme 1 *Reagents:* i, $PhCH_2NH_2$, 3 Å, CH_2Cl_2; ii, $NaBH_4$, MeOH; iii, $Cl_3C(CO)O(CO)CCl_3$; iv, NaCo^I salophen

moylcobalt salophen **11** in toluene was heated in an inert atmosphere for 24 h it was found to undergo homolytic cleavage, 4-*exo-trig* cyclisation and simultaneous dehydrocobaltation producing a 1:1:2 mixture of the isomeric β-lactams **12**, **13** and **14**, respectively, in a combined yield of 40%; none of the presumed intermediate organocobalt salophen **15**, between **11** and **12–14** was detected amongst the reaction products. Unperturbed, we next attempted to produce the hydroxylamine **16** in one step from **11** by homolysing the cobalt salophen in the presence of TEMPO. In the event, however, the major product isolated from this reaction was the carbamate **17** (86%), only small amounts (~6%) of the substituted β-lactam **16** being produced.

Based on the outcome of our studies with **11** we next



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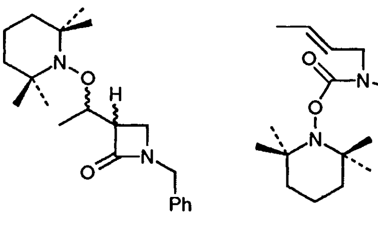

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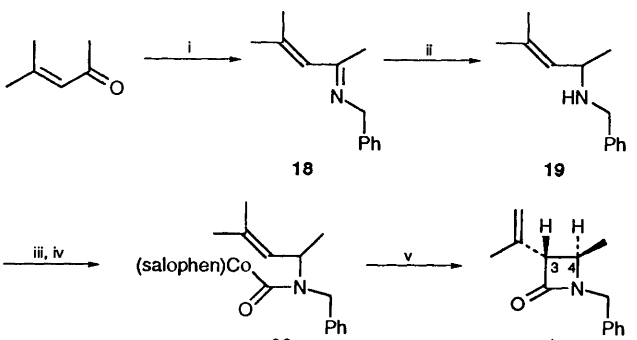
investigated the radical cyclisation of the 1,3-dimethylallyl substituted carbamoylcobalt salophen **20** which was produced in four simple steps starting from mesityl oxide (Scheme 2). To our delight when **20** was heated in toluene the carbamoyl radical intermediate was found to undergo stereoselective 4-*exo-trig* cyclisation and regioselective dehydrocobaltation from the product radical, leading to the *trans*-β-lactam **21** containing an allyl substituent at C-3, in a modest 30% yield. The *trans*-stereochemistry in **21** followed exclusively from the magnitude of the vicinal coupling ($J_{3,4}$ 2.3 Hz) between 3-CH and 4-CH in the ^{1}H NMR spectrum; *cf.* $J_{3,4}$ 5.9 Hz for the corresponding *cis*-stereochemistry in **21**.[5]



Scheme 2 *Reagents:* i, $PhCH_2NH_2$, 3 Å, CH_2Cl; ii, $NaBH_4$, MeOH; iii, $Cl_3C(CO)O(CO)CCl_3$; iv, $NaCo^I$ salophen; v, heat, $PhCH_3$

With the encouraging model study of the synthesis of *trans*-substituted β-lactams from cyclisation of appropriate alkene substituted carbamoylcobalt reagents complete, we now turned to a synthesis of the substituted *N*-allylcarbamoylcobalt **30** as a precursor to the **31** en route to thienamycin **1**. The carbamoylcobalt(III) salophen **30** was prepared first therefore, starting from *N*-BOC-protected (±)-α-amino-γ-butyrolactone **22**. Thus, reduction of the lactone **22** with diisobutylaluminium hydride at −78 °C first provided the lactol **23** as a white crystalline solid in 83% yield, whose formation was accompanied by small amounts of the diol **24** as a by-product. The lactol **23** was found to be remarkably stable and unreactive towards nucleophiles, and only after considerable experimentation were we able to promote its reaction with the ylide obtained from isopropyltriphenylphosphonium bromide and sodamide, leading to the unsaturated amino alcohol **25** (54%).

Treatment of the alcohol **25** with 2 equiv. of sodium hydride and benzyl bromide next led to the dibenzyl derivative **26**. The dibenzyl derivative was then converted into the free amine **28**, following reaction with toluene-*p*-sulfonic acid[8] to produce the amine salt **27**, and treatment of **27** with aqueous sodium

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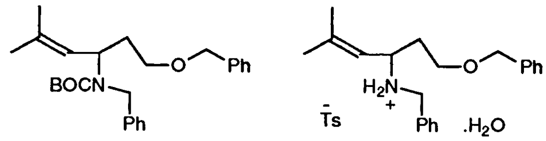

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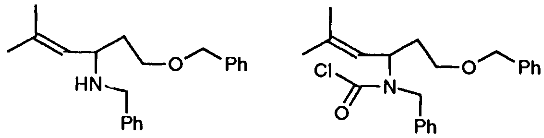

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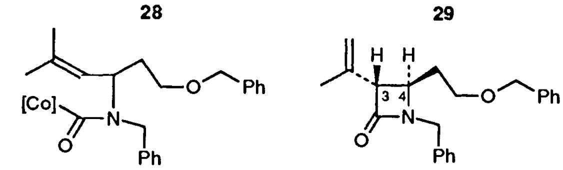


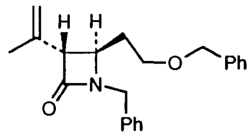
[Co] = Co(salophen)

30 31

hydrogen carbonate. Acylation of **28** using triphosgene,[9] followed by treatment of the resulting carbamoyl chloride **29** with sodium cobalt(I) salophen finally provided the carbamoylcobalt salophen **30** as red crystals in 35% yield over two steps.

When a solution of the carbamoylcobalt **30** in dry toluene was heated under reflux in an inert atmosphere for 24 h, similar to the model compound **20** it underwent sequential homolytic cleavage, 4-*exo-trig* cyclisation, and dehydrocobaltation producing exclusively the 3,4-*trans*-disubstituted β-lactam **31** in an overall yield of 40%. Like the model system **20**–**21**, the *trans* geometry in **31** followed conclusively from the magnitude of the vicinal coupling ($J_{3,4}$ 2.2 Hz) between 3-CH and 4-CH in the ^{1}H NMR spectrum.

We now needed to convert the 3-propenyl group in **31** into the corresponding hydroxyethyl unit in order to complete our synthesis of thienamycin. To achieve this, we used a protocol developed by Ley *et al.*[5] Thus, oxidative cleavage of the propenyl side chain in **31** in the presence of ozone at −78 °C followed by reductive work-up with triphenylphosphine first gave the corresponding ketone **32** in 83% yield. Treatment of the ketone **32** with the bulky reducing agent potassium selectride–KI was found to be highly stereoselective and gave the desired 3-(1*R*′-hydroxyethyl) β-lactam **34** contaminated with *ca.* 15% of the corresponding 1*S*′-alcohol in 83% yield. The stereoselectivity observed in this reduction is most likely a consequence of the high ionic nature of K-selectride™ which is further exaggerated by the addition of potassium iodide.[10] The free potassium cation is thought to chelate to the oxygen atoms of both of the carbonyl groups in **32** which allows the bulky boron reagent to deliver its hydride ion from the resulting less hindered face of the complex intermediate **33** thereby leading to the desired 1*R*′-alcohol **34**. The β-lactam **34** has been converted in three steps into the bicyclic molecule **35**[11] which is the key intermediate in the synthesis of thienamycin **1** described by Merck and Co.[2] Our new strategy for the synthesis of the azetidin-4-one **34** based on the novel and unusual disconnection



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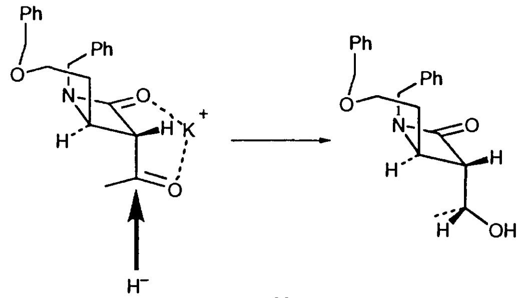

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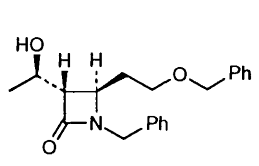

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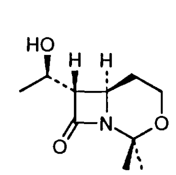

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2→3, therefore constitutes a new formal synthesis of (±)-thienamycin.

Experimental

For general experimental details see immediately preceding paper, ref. 6.

N-*Benzyl*-N-*but*-2-*enylideneamine* **8**.—Benzylamine (2.19 cm^3, 20 mmol) was added dropwise over 1 min to a stirred solution of but-2-enal (1.66 cm^3, 20 mmol) in dry dichloromethane (50 cm^3) over activated 3 Å molecular sieves under an atmosphere of nitrogen. The mixture was stirred under an atmosphere of nitrogen for 24 h and then filtered through magnesium sulfate. The filtrate was evaporated to dryness under reduced pressure to leave the *title compound* (3.2 g, 100%) as a yellow liquid; ν_{max}(film)/cm^{-3} 3090, 3070, 3030, 2970, 2915, 2840, 1655 (C=N), 1625 (C=C), 1495, 1450, 1375, 1170, 1030, 995, 970, 735 and 700; δ_H(80.13 MHz; $CDCl_3$) 7.95 (1 H, m, 1-CH), 7.25 (5 H, m, ArH), 6.35–6.15 (2 H, m, 2-CH and 3-CH), 4.65 (2 H, br s, NCH_2) and 1.9 (3 H, d, *J* 4.9, 4-CH_3).

N-*Benzyl*-N-*but*-2-*enylamine* **9**.—Sodium borohydride (284 mg, 7.5 mmol) was added portionwise over 1 min to a stirred and cooled (0 °C) solution of the imine **8** (3.2 g, 20 mmol) in dry methanol (50 cm^3) under an atmosphere of nitrogen. The solution was allowed to warm to ambient temperature and then stirred for 18 h under an atmosphere of nitrogen, during which time the yellow colour of the solution faded. The solution was cooled (0 °C) and then concentrated hydrochloric acid was added dropwise to it until the mixture attained pH 1. The resulting suspension was evaporated under reduced pressure to leave a white solid residue. The residue was dissolved in water (50 cm^3) and the resulting aqueous solution was then washed with diethyl ether (2 × 50 cm^3). The remaining aqueous solution was cooled (0 °C) and brought to pH 10 by careful addition of potassium hydroxide pellets. The liberated amine was extracted into diethyl ether (3 × 50 cm^3). The combined organic phases were dried ($MgSO_4$) and then evaporated to dryness under reduced pressure to leave a pale yellow liquid. This was further purified by Kugelröhr distillation to yield the *amine* (1.77 g, 55%)[12] as a colourless liquid, b.p. 180 °C/25 Torr; λ_{max}(EtOH)/nm 194.3 (ε/dm^3 mol^{-1} cm^{-1} 24 750); ν_{max}(film)/cm^{-1} 3100, 3075, 3040, 2915, 2860, 2820, 1600, 1495, 1455, 1380, 1365, 1115, 1035, 975, 740 and 705; δ_H(80.13 MHz; $CDCl_3$) 7.3 (5 H, br s, ArH), 5.6 (2 H, m, 2-CH and 3-CH), 3.75 (2 H, s, NCH_2Ph), 3.2 (2 H, m, 1-CH_2), 1.7 (3 H, dd *J* 4.7 and 1.2 Hz, 4-CH_3) and 1.35 (1 H, br s, NH); *m*/*z* (EI) 160 (M^+ − 1, 4%) 105 (M^+ − C_4H_8, 100) and 91 (CH_2Ph, 67).

N-*Benzyl*-N-(*but*-2-*enyl*)*carbamoyl Chloride* **10**.—A solution of the amine **9** (918 mg, 5.7 mmol) in dry benzene (2 cm^3) was added dropwise over 0.5 min to a stirred suspension of triphosgene (563 mg, 1.9 mmol)[9] and pyridine (450 mg, 5.7 mmol) in dry benzene (30 cm^3) under an atmosphere of nitrogen. The resulting suspension was stirred under an atmosphere of nitrogen for 96 h and then filtered under nitrogen. The filtrate was evaporated to dryness under reduced pressure to leave the *carbamoyl chloride* (1.27 g, 99.5%) as a yellow liquid; ν_{max}(film)/cm^{-1} 3100, 3070, 3040, 2970, 2940, 2880, 1740 (CO), 1675, 1610, 1500, 1460, 1405, 1370, 1270, 1190, 1160, 1115, 980, 740 and 700; δ_H(80.13 MHz; $CDCl_3$) 7.3 (5 H, s, ArH), 5.8–5.4 (2 H, br m, 2-CH and 3-CH), 4.7 (1 H, br s, NC*H*HPh), 455 (1 H, br s, NCH*H*Ph), 3.9 (2 H, br s, 1-CH_2) and 1.75 (3 H, br d *J* 4.9, 4-CH_3).

N-*Benzyl*-N-(*but*-2-*enyl*)*carbamoyl*(*salophen*)*cobalt*(III)* **11**.—A deoxygenated solution of the carbamoyl chloride **10** (1.23 g, 5.5 mmol) in dry THF (10 cm^3) was injected dropwise over 1 min into a stirred and deoxygenated green solution of sodium salophencobalt(I) (6.9 mmol)[6] in dry THF (180 cm^3) in the dark under an atmosphere of nitrogen. The resulting brown solution was stirred for a further 1 h and then filtered *in vacuo* in the dark. The filtrate was evaporated to dryness under reduced pressure in the dark at ambient temperature to leave a red-brown solid residue. The residue was pre-adsorbed onto Woelm alumina and purified by column chromatography on Woelm alumina, using diethyl ether and then methanol–dichloromethane (1:100) as eluent to yield the carbamoyl(salophen)cobalt (969 mg, 32%) as a deep red crystalline solid, m.p. > 100 °C (decomp.); λ_{max}(EtOH)/nm 201.5 (ε/dm^3 mol^{-1} cm^{-1} 33 250), 229.7 (18 100), 256.2 (18 100), 299.2 (10 950) and 363.7 (7300); ν_{max}($CHCl_3$)/cm^{-1} 2910, 2850, 1640 (CO), 1610, 1580, 1510, 1490, 1460, 1430, 1275, 1230, 1150, 1130, 1110, 980 and 960; δ_H(250 MHz; $CDCl_3$) 8.7 (2 H, s, HC=N), 8.1 (2 H, m, ArH), 7.5–6.4 (15 H, m, ArH), 5.35 (1 H, m, =CH), 5.2 (1 H, m, =CH), 4.7–4.4 and 3.7 (4 H, m, 1-CH_2 and NCH_2) and 1.5 (3 H, d, *J* 5.2 Hz, 4-CH_3); *m*/*z* (FAB) 561 (M^+, 23%), 373 (CO(salophen), 100), 188 (M^+-Co(salophen), 5) and 91 (CH_2Ph, 58).

1-*Benzyl*-3-(E)-*ethylideneazetidin*-2-*one* **12**, 1-*Benzyl*-3-(Z)-*ethylideneazetidin*-2-*one* **13**, *and* 1-*Benzyl*-3-*vinylazetidin*-2-*one* **14**.—A deoxygenated solution of the carbamoylsalophencobalt **11** (440 mg, 0.78 mmol) in dry toluene (40 cm^3) was stirred and heated under reflux in an atmosphere of nitrogen for 48 h. The resulting mixture was cooled and then evaporated to dryness under reduced pressure to leave a brown solid residue. The residue was pre-adsorbed onto silica and purified by column chromatography on silica using diethyl ether–light petroleum (b.p. 40–60 °C) (1:5) as eluent to yield: (i) the (Z)-*azetidin*-2-*one* **13** (16 mg, 11%) (eluted first) as a colourless oil; λ_{max}(EtOH)/nm 206 (ε/dm^3 mol^{-1} cm^{-1} 24 800) and 233 (7900); ν_{max}($CHCl_3$)/cm^{-1} 3000, 2960, 2890, 1730 (CO), 1720 (C=C), 1390, 1115, 1030 and 855; δ_H(250 MHz; $CDCl_3$) 7.35 (5 H, m,

* For convenience, hereafter, salophen is used to refer to the coordinated ligand *N*,*N'*-*o*-phenylenediaminebis(salicylideneaminato).

ArH), 5.65 (1 H, q *J* 7.1, 1'-CH), 4.5 (2 H, s, NCH_2Ph), 3.55 (2 H, s, 4-CH_2) and 2.05 (3 H, d *J* 7.1, CH_3); δ_C(100.6 MHz; $CDCl_3$) 164.3 (s, 2-C), 136.8 (s, 3-C), 135.9 (s), 128.8 (d), 128.1 (d), 127.7 (d), 125.1 (d, 1'-C), 47.2 (t), 45.9 (t) and 14.6 (q); *m/z* (EI) 187 (M^+, 10%), 133 ($M^+ - C_4H_6$, 7) and 91 (CH_2Ph, 78): (ii) the 3-*vinylazetidin-2-one* **14** (29 mg, 19%) (eluted second) as a colourless oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 1745 (CO), 1665, 1605, 1400, 1360, 1130, 995 and 930; δ_H(250 MHz; $CDCl_3$) 7.3 (5 H, m, ArH), 5.9 (1 H, ddd *J* 17.2, 10.3 and 7.6, 1'-CH), 5.3 [1 H, ddd (*ca.* dt) *J* 17.3, 1.3 and 1.3 Hz, 2'-C*H*H], 5.2 [1 H, ddd (*ca.* dt) *J* 10.3, 1.2 and 1.2, 2'-CH*H*], 4.45 (1 H, d J_{AB} 15.1, NC*H*HPh), 4.35 (1 H, d J_{AB} 15.1, NCH*H*Ph), 3.85 (1 H, m, 3-CH), 3.4 [1 H, *J* dd (*ca.* t) 5.4 and 5.4 Hz, 4-C*H*H] and 3.05 (1 H, dd *J* 5.5 and 2.5, 4-CH*H*); *m/z* 187.0959 (M^+, $C_{12}H_{13}NO$ requires 187.0997, 8%), 133 ($M^+ - C_4H_6$, 35), 96 ($M^+ - CH_2Ph$, 5) and 91 (CH_2Ph, 100) and; (iii) the (E)-azetidin-2-one **12** (15 mg, 10%) (eluted third) as a colourless oil; λ_{max}(EtOH)/nm 198.6 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 29 500), 205 (30 100) and 232 (8200); $\nu_{max}(CHCl_3)/cm^{-1}$ 2940, 1740 (CO), 1710, 1385 and 1030; δ_H(80.13 MHz; $CDCl_3$) 7.25 (5 H, s, ArH), 6.1 (1 H, qt *J* 7.1 and 1.2, 1'-CH), 4.45 (2 H, s, NCH_2Ph), 3.55 (2 H, d *J* 1.0, 4-CH_2) and 1.6 (3 H, d *J* 7.0, CH_3); δ_C(100.6 MHz; $CDCl_3$) 164.0 (s, 2-C), 138.2 (s, 3-C), 135.7 (s), 128.8 (d), 128.0 (d), 127.7 (d), 121.5 (d, 1'-C), 46.5 (t), 46.0 (t) and 14.2 (q); *m/z* (EI) 187.0993 (M^+, $C_{12}H_{13}NO$ requires 187.0997, 29%), 172 ($M^+ - CH_3$, 14), 133 ($M^+ - C_4H_6$, 25) and 91 (CH_2Ph, 100). [The azetidin-2-one was contaminated with traces (< 5%) of N-(*but-2-enyl*)-N-*benzylformamide* which had: $\nu_{max}(CHCl_3)/cm^{-1}$ 1665 (CO); *m/z* 189.1136 (M^+, $C_{12}H_{15}NO$ requires 189.1154, 5%).]

3-[1'-(2,2,6,6-*Tetramethylpiperidin*-1-*yloxy*)*ethyl*]-1-*benzylazetidin-2-one* **16** *and* 2,2,6,6-*Tetramethylpiperidinyl*-1-*yl* N-*Benzyl*-N-(*but-2-enyl*)*carbamate* **17**.—A deoxygenated solution of the carbamoyl(salophen)cobalt **11** (120 mg, 0.21 mmol) and TEMPO (34 mg, 0.21 mmol) in dry toluene (25 cm^3) was stirred and heated under reflux under an atmosphere of nitrogen for 2 h. The resulting mixture was evaporated to dryness under reduced pressure to leave a brown solid residue. This was pre-adsorbed onto silica and purified by column chromatography on silica using diethyl ether–light petroleum (b.p. 40–60 °C) (1:3) as eluent to yield: (i) the carbamate (63 mg, 86%) (eluted first) as a colourless oil; $\nu_{max}(film)/cm^{-1}$ 3060, 3030, 3010, 2980, 2940, 2880, 1730 (CO), 1500, 1460, 1410, 1380, 1365, 1270, 1250, 1220, 1050, 930 and 740; δ_H(250 MHz; $CDCl_3$) 7.3 (5 H, m, ArH), 5.6 (1 H, dtq *J* 15.2, 6.2 and 1.0, 3-CH), 5.45 (1 H, br m, 2-CH), 4.5 (2 H, s, NCH_2Ph), 3.9 (1 H, br, 1-C*H*H), 3.75 (1 H, br, 1-CH*H*), 1.7 (3 H, dd *J* 6.2 and 1.0, 4-CH_3), 1.8–1.3 [6 H, br m, $(CH_2)_3$], 1.15 (9 H, br s, CH_3) and 1.0 (3 H, br s, CH_3); *m/z* (FAB) 345 ($M^+ + 1$, 75%), 329 ($M^+ - CH_3$, 11), 188 (M^+ −TEMPO, 42) and 156 (TEMPO, 61) and, (ii) the *azetidin-2-one* (4 mg, 6%) (eluted second) as a yellow oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 2940, 2860, 1740 (CO), 1665, 1450, 1380, 1365, 1130, 1080, 1030 and 930; *m/z* (FAB) 345 ($M^+ + 1$, 42%), 329 ($M^+ - CH_3$, 3), 188 (M^+ − TEMPO, 44) and 156 (TEMPO, 46).

N-*Benzyl*-N-(1,3-*dimethylbut-2-enyl*)*amine* **19**.—Benzylamine (2.18 cm^3, 20 mmol) was added dropwise over 1 min to a stirred solution of 1,3-dimethylbuten-2-one (2.29 g, 20 mmol) in dry dichloromethane (20 cm^3) over activated 3 Å molecular sieves in an atmosphere of nitrogen. The mixture was stirred for 6 days under an atmosphere of nitrogen and then filtered through magnesium sulfate. The filtrate was evaporated to dryness under reduced pressure to leave the crude *N*-(1,3-dimethylbutylidene)-*N*-benzylamine **18** as a yellow liquid; $\nu_{max}(film)/cm^{-1}$ 3090, 3070, 3030, 2980, 2920, 1665 (C=N), 1620 (C=C), 1495, 1450, 1360, 1225, 1170, 970, 735 and 700; δ_H(80.13 MHz; $CDCl_3$) 7.3 (5 H, s, ArH), 6.05 (1 H, br s, 2-CH), 4.45 (2 H, br s, NCH_2), 2.1 (3 H, s, CH_3), 2.05 (3 H, s, CH_3) and 1.85 (3 H, s, CH_3). Sodium borohydride (1.51 g, 40 mmol) was added portionwise to a stirred solution of the crude imine in dry methanol (50 cm^3) under an atmosphere of nitrogen and the resulting solution was then stirred under an atmosphere of nitrogen for 4 h. The solution was cooled (0 °C) and concentrated hydrochloric acid was then added dropwise to it until pH 1 was attained. The resulting suspension was evaporated to dryness under reduced pressure to leave a white solid. The solid was dissolved in water (100 cm^3) and then washed with diethyl ether (2 × 100 cm^3). The remaining aqueous phase was cooled (0 °C) and then brought to pH 10 by careful addition of potassium hydroxide pellets. The liberated amine was extracted into diethyl ether (3 × 100 cm^3) and the combined organic phases were dried ($MgSO_4$) and then evaporated to dryness under reduced pressure to leave a yellow oil. This was purified by Kugelröhr distillation to yield the *amine* **19** (228 mg, 6% from the ketone) as a colourless oil, b.p. 175 °C/Torr; $\nu_{max}(film)/cm^{-1}$ 3090, 3070, 3040, 2975, 2930, 2870, 1600, 1500, 1460, 1380, 1120, 740 and 705; δ_H(80.13 MHz; $CDCl_3$) 7.3 (5 H, s, ArH), 5.05 (1 H, *ca.* d quint. *J* 8.9 and 1.2, 2-CH), 3.8 (1 H, d J_{AB} 4.2, NC*H*H), 3.7 (1 H, d J_{AB} 4.2 Hz, NCH*H*), 3.45 (1 H, dq 8.8 and 6.5, 1-CH), 1.75 (3 H, d *J* 1.0 Hz, CH_3), 1.6 (3 H, d *J* 1.1 Hz, CH_3), 1.25 (1 H, br, NH) and 1.1 (3 H, d *J* 6.4, CH_3).

N-*Benzyl*-N-(1,3-*dimethylbut-2-enyl*)*carbamoyl*(*salophen*)-*cobalt*(III) **20**.—A solution of the amine **19** (228 mg, 1.2 mmol) in dry benzene (1 cm^3) was added to a stirred suspension of triphosgene (119 mg, 0.4 mmol)[9] and dry pyridine (95 mg, 1.2 mmol) in dry benzene (15 cm^3) under an atmosphere of nitrogen. The resulting suspension was stirred under an atmosphere of nitrogen for 72 h and then filtered under nitrogen. The filtrate was evaporated to dryness under reduced pressure to leave the *N*-benzyl-*N*-(1,3-dimethylbut-2-enyl)carbamoyl chloride (293 mg, 97%) as a yellow oil; $\nu_{max}(film)/cm^{-1}$ 3080, 3050, 2990, 2950, 1735 (CO), 1680, 1500, 1460, 1400, 1200, 1160, 1140, 1085 and 970; δ_H(80.13 MHz; $CDCl_3$) 7.3 (5 H, s, ArH), 5.1 (1 H, br, 2-CH), 4.6 (3 H, br, NCH_2 and 1-CH), 1.6 (6 H, s, CH_3) and 1.15 (3 H, d *J* 6.2, CH_3). A deoxygenated solution of the carbamoyl chloride (293 mg, 1.16 mmol) in dry THF (5 cm^3) was injected dropwise over 1 min to a stirred and deoxygenated green solution of sodium salophencobalt(I) (1.2 mmol)[6] in dry THF (150 cm^3) in the dark under an atmosphere of nitrogen. The resulting brown solution was stirred in the dark under an atmosphere of nitrogen for 1 h and then filtered *in vacuo*. The filtrate was then evaporated to dryness under reduced pressure in the dark at ambient temperature to leave a red–brown solid residue. The residue was pre-adsorbed onto Woelm alumina and then purified by column chromatography on Woelm alumina using diethyl ether and then methanol–dichloromethane (1:100) as eluent to yield the title compound **20** (148 mg, 22%) as a Woelm alumina-unstable, deep red crystalline solid which was used immediately.

trans-3-*Allyl*-1-*benzyl*-4-*methylazetidin-2-one* **21**.—A deoxygenated solution of the complex **20** (148 mg, 0.25 mmol) in dry toluene (20 cm^3) was stirred and heated under reflux under an atmosphere of nitrogen for 48 h. The resulting suspension was cooled to ambient temperature and then evaporated to dryness under reduced pressure to leave a brown solid residue. This was pre-adsorbed onto silica and then purified by column chromatography on silica using diethyl ether–light petroleum (b.p. 40–60 °C) (1:5) as eluent to yield the *azetidin-2-one* (15.5 mg, 29%) as a colourless oil; λ_{max}(EtOH)/nm 196 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 31 150); $\nu_{max}(CHCl_3)/cm^{-1}$ 3080, 3040, 2975, 2925, 2860, 1745 (CO), 1645, 1500, 1460, 1405, 1380, 1355, 900 and 710; δ_H(400

MHz; $CDCl_3$) 7.3 (5 H, m, ArH), 4.95 (1 H, d *J* 1.0 Hz, =C*H*H), 4.9 [1 H, dq (*ca.* quint.) *J* 1.3 and 1.0 Hz, =CH*H*], 4.7 (1 H, d J_{AB} 15.2, NC*H*HPh), 4.05 (1 H, d J_{AB} 15.2, NCH*H*Ph), 3.4 (1 H, dq *J* 6.1 and 2.3, 4-CH), 3.35 (1 H, br s, 3-CH), 1.75 (3 H, d *J* 1.0, CH_3) and 1.25 (3 H, d *J* 6.3, CH_3CH=CH_2); δ_C(100.6 MHz; $CDCl_3$) 167.3 (s, 2-C), 138.8 (s, 5-C), 135.9 (s), 128.7 (d), 128.2 (d), 127.6 (d), 113.5 (t), 64.2 (d, 3-C), 52.7 (d, 4-C), 44.0 (t), 20.35 (q) and 17.9 (q, 1'-C); *m/z* (EI) 215.1311 (M^+, $C_{14}H_{17}NO$ requires 215.1310, 1%) and 91 (CH_2Ph, 32).

2-(tert-*Butoxycarbonylamino*)-γ-*butyrolactone* **22**.—Dry triethylamine (13.4 g, 18.5 cm^3, 0.133 mol) was added dropwise over 1 min to a stirred and cooled (0 °C) suspension of commercially available (±)-α-amino-γ-butyrolactone hydrobromide (24.2 g, 0.132 mol) in dry dichloromethane (250 cm^3) under an atmosphere of nitrogen. A solution of di-*tert*-butyl dicarbonate (32.0 g, 0.145 mol) in dry dichloromethane (50 cm^3) was then added to it with care over 10 min. The resulting suspension was allowed to warm to ambient temperature and then stirred under an atmosphere of nitrogen for 96 h. The resulting solution was washed with aqueous citric acid (100 cm^3) and water (100 cm^3), dried ($MgSO_4$) and evaporated to dryness under reduced pressure to leave a white solid. This was recrystallised from diisopropyl ether to yield the *title compound* **22** (25.2 g, 95%) as a white crystalline solid, m.p. 116.5–117 °C (Found: C, 53.3; H, 7.4; N, 6.8. $C_9H_{15}NO_4$ requires C, 53.7; H, 7.5; N, 7.0%); ν_{max}(KBr)/cm^{-1} 3340 (NH), 2990, 2935, 1780 (CO), 1695 (NCO), 1675 (NCO), 1530, 1485, 1370, 1295, 1155 and 1020; δ_H(250 MHz; $CDCl_3$) 5.2 (1 H, br, NH), 4.4 [1 H, ddd (*ca.* dt) *J* 9.1, 9.1 and 1.0, 4-C*H*H], 4.35 (1 H, br, 2-CH), 4.2 (1 H, ddd *J* 11.1, 9.2 and 5.8, 4-CH*H*), 2.7 (1 H, m, 3-C*H*H), 2.2 (1 H, m, 3-CH*H*) and 1.45 (9 H, s, CH_3); δ_C(100.6 MHz; $CDCl_3$) 175.7 (s, 1-C), 155.7 (s, NCO), 80.5 (s), 65.8 (t, 4-C), 50.2 (d, 2-C), 30.3 (t, 3-C) and 28.3 (q); *m/z* (FAB) 202 (M^+ + 1, 47%), 146 (M^+ + 1 − C_4H_8, 100) and 128 (M^+ − C_4H_9O, 4).

2-(tert-*Butoxycarbonylamino*)-γ-*butyrolactol* **23** *and* 2-(tert-*Butoxycarbonylamino*)*butane*-1,4-*diol* **24**.—A solution of diisobutylaluminium hydride (DIBAH)[13] (1.0 mol dm^{-3} in hexanes; 372 cm^3, 0.372 mol) was added over 5 min to a stirred and cooled (−48 °C) solution of the lactone **22** (25.2 g, 0.124 mol) in dry dichloromethane (350 cm^3) under an atmosphere of nitrogen. The resulting solution was maintained at −48 °C for 30 min and then water (100 cm^3) was added to it over 5 min to form an emulsion. Aqueous hydrochloric acid (2 mol dm^{-3}; 100 cm^3) was added over 5 min to the emulsion to disperse it and then the organic phase was separated. The aqueous phase was further extracted with dichloromethane (2 × 400 cm^3) and then the combined organic phases were dried ($MgSO_4$) and evaporated to dryness under reduced pressure to leave a thick yellow oil. This was pre-adsorbed onto Woelm alumina and purified by column chromatography on Woelm alumina using diethyl ether as eluent to yield: (i) the *lactol* **23** (20.9 g, 83%) (eluted first) as a slow crystallising white solid, m.p. 99–101 °C (Found: C, 53.2; H, 8.6; N, 6.8. $C_9H_{17}NO_4$ requires C, 53.2; H, 8.4; N, 6.9%); ν_{max}(film)/cm^{-1} 3355 (OH), 2980, 1685 (NCO), 1530, 1370, 1160 and 1020; δ_H(250 MHz; $CDCl_3$) 5.25 (1 H, dd *J* 7 and 3, 1-CH), 5.2 (1 H, br, NH), 4.5 (1 H, d *J* 3, OH), 4.25–3.7 (3 H, m, 2-CH and 4-CH_2), 2.5–2.2 (1 H, m, 3-C*H*H), 1.9–1.7 (1 H, m, 3-CH*H*) and 1.4 (9 H, s, CH_3); δ_C(100.6 MHz; $CDCl_3$) 155.8 and 155.7 (s, NCO), 101.7 and 94.9 (d, 1-C), 79.8 and 79.7 (s), 66.1 and 65.8 (t, 4-C), 57.0 and 53.4 (d, 2-C), 29.2 (t, 3-C) and 28.4 (q); *m/z* (FAB) 204 (M^+ + 1, 19%), 186 (M^+ + 1 − H_2O, 21), 146 (M^+ −C_4H_9, 9), 130 (M^+ − C_4H_9O, 100) and 102 (M^+ − C_4H_9OCO, 11) and: (ii) the *diol* **24** (4.1 g, 16%) (eluted second) as a viscous colourless oil; ν_{max}(film)/cm^{-1} 3345 (OH), 2975, 2930, 1690 (NCO), 1510, 1390, 1365, 1250, 1170 and 1055; δ_H(400 MHz; $CDCl_3$) 5.15 (1 H, br d *J* 8, NH), 3.85–3.55 (5 H, m, 2 × CH_2OH and 2-CH), 3.2 (1 H, br, OH), 2.1 (1 H, br, OH), 1.8 (1 H, ddd *J* 18.9, 8.0 and 4, 3-C*H*H), 1.6 (1 H, m, 3-CH*H*) and 1.45 (9 H, s, CH_3); δ_C(100.6 MHz; $CDCl_3$) 157.2 (s, NCO), 80.0 (s), 65.1 (t, 1-C), 58.8 (t, 4-C), 49.5 (d, 2-C), 34.8 (t, 3-C) and 28.4 (q); *m/z* (FAB) 206 (M^+ + 1, 37%), 150 (M^+ + 1 −C_4H_8, 100) and 106 (M^+ + 1 − C_4H_8OCO, 73).

3-(tert-*Butoxycarbonylamino*)-5-*methylhex*-4-*enol* **25**.—A solution of the lactol **23** (4.15 g, 20.4 mmol) in dry dichloromethane (130 cm^3) was added over 1 min to a stirred solution of sodium amide and isopropyltriphenylphosphonium bromide mixture (42 g, 96.6 mmol) in dry dichloromethane (210 cm^3) under an atmosphere of nitrogen. Dry toluene (500 cm^3) was added to the mixture and the resulting suspension was then heated and stirred under reflux (72 °C) under an atmosphere of nitrogen for 75 min. The mixture was cooled and the dichloromethane was then evaporated under reduced pressure. The resulting suspension was filtered *in vacuo* and the filtrate was then evaporated to dryness under reduced pressure to leave a solid residue. The residue was pre-adsorbed onto Woelm alumina and purified by column chromatography on Woelm alumina using diethyl ether–light petroleum (b.p. 40–60 °C)–methanol (50:50:1) as eluent to yield the *olefinic alcohol* (2.54 g, 54%) as a colourless oil; ν_{max}(film)/cm^{-1} 3340 (OH), 2975, 2930, 2850, 1690 (NCO), 1520, 1365, 1300, 1320, 1170 and 1050; δ_H(400 MHz; $CDCl_3$; assignments made from ^1H homonuclear two-dimensional shift correlation experiments) 5.0 (1 H, app. dquint. *J* 8.4 and 1.3, 4-CH), 4.6 (1 H, br d *J* 7.0, NH), 4.5 (1 H, m, 3-CH), 3.6 (2 H, br, 1-CH_2), 3.5 (1 H, br s, OH), 1.75 (1 H, m, 2-CHH), 1.70 (3 H, d *J* 1.3, CH_3), 1.68 (3 H, d *J* 1.3, CH_3), 1.45 (1 H, m, 2-CH*H*) and 1.4 (9 H, s, CH_3); δ_C(100.6 MHz; $CDCl_3$) 156.6 (s), 135.6 (s, 5-C), 125.0 (d, 4-C), 79.7 (s), 58.8 (t, 1-C), 45.7 (d, 3-C), 39.6 (t, 2-C), 28.4 (q), 25.5 (q) and 16.3 (q); *m/z* (FAB) 230 (M^+ + 1, 38%), 212 (M^+ + 1 − H_2O, 5), 174 (M^+ + 1 − C_4H_8, 55) and 128 (M^+ − C_4H_9OCO, 43).

N-*Benzyl*-N-[1-(2'-*benzyloxyethyl*)-3-*methylbut*-2-*enyl*]-N-(tert-*butoxycarbonyl*)*amine* **26**.—Sodium hydride (60% dispersion; 0.85 g, 21.2 mmol) was added with care to a stirred and cooled (0 °C) solution of the alcohol **25** (2.43 g, 10.6 mmol) in dry THF (25 cm^3) under an atmosphere of nitrogen. Tetrabutylammonium iodide (78 mg, 0.21 mmol) was then added in one portion to the mixture followed by benzyl bromide (3.63 g, 21.2 mmol) added over 2 min. The resulting suspension was stirred at 0 °C for 1 h and then at ambient temperature for 18 h under an atmosphere of nitrogen. Water (20 cm^3) was added dropwise to the suspension and the resulting mixture was then extracted into diethyl ether (3 × 50 cm^3). The combined organic phases were dried ($MgSO_4$) and then evaporated to dryness under reduced pressure to leave a yellow liquid. This was purified by column chromatography on silica using diethyl ether–light petroleum (b.p. 40–60 °C) (1:10) as eluent to yield the *dibenzylated product* **26** (2.16 g, 50%) as a colourless oil; λ_{max}(EtOH)/nm 198.9 (ε/dm^3 mol^{-1} cm^{-1} 22 050); ν_{max}($CHCl_3$)/cm^{-1} 2910, 2860, 1670 (NCO), 1600, 1400, 1365 and 1165; δ_H(80.13 MHz; $CDCl_3$) 7.2 (5 H, s, ArH), 7.15 (5 H, s, ArH), 5.1 (1 H, *ca.* dquint. *J* 9.0 and 1.0, 2-CH), 4.7 (1 H, br m, 1-CH), 4.35 (2 H, s, OCH_2Ph), 4.3 (2 H, s, NCH_2Ph), 3.3 (2 H, t *J* 6.6, 2'-CH_2), 2.15–1.5 (2 H, m, 1'-CH_2), 1.55 (3 H, d *J* 1.0, CH_3), 1.5 (3 H, s, CH_3) and 1.3 (9 H, s, CH_3); δ_C(20.15 MHz; $CDCl_3$) 156.2 (s, NCO), 140.8 (s, 3-C), 139.0 (s), 135.9 (s), 128.1 (d), 128.0 (d), 127.4 (d), 127.2 (d), 126.5 (d), 124.0 (d, 2-C), 79.35 (s), 72.8 (t, 3'-C), 67.4 (t, 2'-C), 51.8 (d, 1-C), 48.2 (t, 1''-C), 34.5 (t, 1'-C), 28.4 (q), 25.45 (q) and 18.2 (q); *m/z* (FAB) 410 (M^+ + 1, 18%), 352 (M^+ − C_4H_9, 23), 336 (M^+ − C_4H_9O, 7) and 308 (M^+ − C_4H_9OCO, 92). The reaction proceeded *via* the corresponding *O*-benzylated product, a colourless oil; λ_{max}-

(EtOH)/nm 195.5 (ε/dm^3 mol^{-1} cm^{-1} 21 100); ν_{max}(CHCl$_3$)/cm^{-1} 3440 (NH), 2980, 2930, 1705 (NCO), 1600, 1495, 1365 and 1170; δ_H(400 MHz; CDCl$_3$) 7.35 (5 H, m, ArH), 5.0 (1 H, br d *J* 8.0, 2-CH), 4.8 (1 H, br s, NH), 4.5 (2 H, s, OC*H*$_2$Ph), 4.4 (1 H, br m, 1-CH), 3.5 (2 H, m, 2′-CH$_2$), 1.85 (1 H, m, 1′-C*H*H), 1.75 (1 H, m, 1′-CH*H*), 1.69 (3 H, d *J* 1.5, CH$_3$), 1.68 (3 H, d *J* 1.2, CH$_3$) and 1.4 (9 H, s, CH$_3$); *m*/*z* (CI) 320 (M$^+$ + 1, 100%), 264 (M$^+$ + 1 − C$_4$H$_8$, 10) and 246 (M$^+$ − C$_4$H$_9$O, 12).

N-*Benzyl*-N-[1-(2′-*benzyloxyethyl*)-3-*methylbut*-2-*enyl*]-*ammonium Toluene*-p-*sulfonate Monohydrate* **27**.—A solution of the protected amine **26** (2.16 g, 5.27 mmol) and toluene-*p*-sulfonic acid monohydrate (1.1 g, 5.8 mmol) in ethanol (20 cm^3) was evaporated to dryness under reduced pressure. The residue was dissolved in ethanol (20 cm^3) and the solution was then evaporated to dryness under reduced pressure to leave a homogenous liquid. This was stored *in vacuo* (0.5 mmHg) for 48 h over which time crystallisation occurred. Diethyl ether was added to the crystalline material and the resulting suspension was then filtered to yield the *amine salt* (2.08 g, 79%) as a white hydroscopic crystalline solid, m.p. 97–98.5 °C (Found: C, 67.0; H, 7.1; N, 3.0. C$_{28}$H$_{37}$NO$_5$S requires C, 67.3; H, 7.4; N, 2.8%); λ_{max}(EtOH)/nm 198.6 (ε/dm^3 mol^{-1} cm^{-1} 47 300) and 205.2 (29 150); ν_{max}(CHCl$_3$)/cm^{-1} 3300, 2920, 2850, 2700, 1600, 1450, 1160, 1125 and 1010; δ_H(250 MHz; CDCl$_3$) 8.9 (1 H, br, NH), 8.7 (1 H, br, NH), 8.0 (2 H, br, OH$_2$), 7.7 (2 H, d *J* 8.1, TolH), 7.4–7.1 (10 H, m, ArH), 7.1 (2 H, d *J* 8.2, TolH), 5.2 (1 H, d *J* 10.2, 2-CH), 4.4 (1 H, d J_{AB} 11.7, OC*H*HPh), 4.3 (1 H, d J_{AB} 11.7, OCH*H*Ph), 4.2 (1 H, br d *J* 11, 1-CH), 3.85 (2 H, m, NCH$_2$Ph), 3.4 [1 H, ddd (*ca.* td) *J* 9.6, 9.6 and 4.7, 2′-C*H*H], 3.25 [1 H, ddd (*ca.* td) 9.5, 9.5 and 3.9 Hz, 2′-CH*H*], 2.3 (3 H, s, ArC*H*$_3$), 2.3 (1 H, m, 1′-CHH), 1.8 (1 H, m, 1′-CH*H*), 1.7 (3 H, s, CH$_3$) and 1.4 (3 H, s, CH$_3$); *m*/*z* (FAB) 791 (2M$^+$ + 2 + 1 toluene-*p*-sulfonate, 7%) and 310 (M$^+$ + 1, 100).

N-*Benzyl*-N-[1-(2′-*benzyloxyethyl*)-3-*methylbut*-2-*enyl*]-*amine* **28**.—Aqueous sodium hydrogen carbonate (2 mol dm^{-3}; 50 cm^3) was added over 5 min to a solution of the amine salt **27** (2.08 g, 4.16 mmol) in water (25 cm^3). The free amine was liberated as an oil and the resulting two-phase mixture was extracted into dichloromethane (3 × 75 cm^3). The combined organic phases were dried (MgSO$_4$) and then evaporated to dryness under reduced pressure to yield the *amine* (1.26 g, 98%) as a colourless oil; λ_{max}(EtOH)/nm 197.1 (ε/dm^3 mol^{-1} cm^{-1} 16 700); ν_{max}(film)/cm^{-1} 3060, 3030, 2920, 2860, 1600, 1580, 1480, 1450, 1360, 1100, 740 and 700; δ_H(250 MHz; CDCl$_3$) 7.2 (10 H, m, ArH), 4.9 (1 H, *ca.* dquint. *J* 9.4 and 1.2, 2-CH), 4.4 (2 H, s, OC*H*$_2$Ph), 3.7 (1 H, d, J_{AB} 13.1, NC*H*HPh), 3.55 (1 H, d J_{AB} 13.1, NCH*H*Ph), 3.4 (3 H, m, 2′-CH$_2$ and 1-CH), 1.8 (1 H, m, 1′-C*H*H), 1.7 (3 H, d *J* 1.2, CH$_3$), 1.7 (1 H, s, NH), 1.6 (1 H, m, 1′-CH*H*) and 1.5 (3 H, d *J* 1.2, CH$_3$); δ_C(100.6 MHz; CDCl$_3$, not all quaternary centres were visible) 138.8 (s, 3-C), 128.4 (d), 127.7 (d), 127.6 (d), 127.0 (d, 2-C), 73.4 (t, 3′-C), 67.9 (t, 2′-C), 53.3 (d, 1-C), 51.0 (t, 1″-C), 35.7 (t, 1′-C), 25.9 (q) and 18.4 (q); *m*/*z* (FAB) 310 (M$^+$ + 1, 81%), 218 (M$^+$ − CH$_2$Ph, 7) and 203 (M$^+$ − OCH$_2$Ph, 41).

N-*Benzyl*-N-[1-(2′-*benzyloxyethyl*)-3-*methylbut*-2-*enyl*]*carbamoyl Chloride* **29**.—A solution of the amine **28** (618 mg, 2.0 mmol) in dry benzene (3 cm^3) was added dropwise over 0.5 min to a stirred suspension of dry pyridine (158 mg, 2.0 mmol) and triphosgene (198 mg, 0.66 mmol)[9] in dry benzene (30 cm^3) under an atmosphere of nitrogen. The resulting suspension was stirred under an atmosphere of nitrogen for 96 h and then filtered under nitrogen. The filtrate was evaporated to dryness under reduced pressure to leave the *carbamoyl chloride* (740 mg, 99.5%) as a yellow liquid; ν_{max}(KBr)/cm^{-1} 3065, 3030, 2925, 2855, 1735 (CO), 1675, 1495, 1455, 1210, 1195, 1105 and 700; δ_H(80.13 MHz; CDCl$_3$) 7.25 (5 H, m, ArH), 7.2 (5 H, m, ArH), 5.15 (1 H, br, 2-CH), 4.8 (1 H, br, 1-CH), 4.55 (2 H, br, NC*H*$_2$Ph), 4.3 (2 H, s, OC*H*$_2$Ph), 3.3 (2 H, t *J* 6.7, 2′-CH$_2$), 2.1–1.6 (2 H, m, 1′-CH$_2$), 1.55 (3 H, br s, CH$_3$) and 1.45 (3 H, br s, CH$_3$).

N-*Benzyl*-N-[1-(2′-*benzyloxyethyl*)-3-*methylbut*-2-*enyl*]-*carbamoyl(salophen)cobalt*(III) **30**.—A deoxygenated solution of the carbamoyl chloride **29** (740 mg, 2.0 mmol) in dry THF (15 cm^3) was injected over 1 min into a stirred green solution of sodium salophencobalt(I) (40 mmol)[6] in dry, deoxygenated THF (200 cm^3) in the dark under an atmosphere of argon. The resulting brown solution was stirred for 10 min and then filtered *in vacuo*. The filtrate was evaporated to dryness under reduced pressure in the dark at ambient temperature to leave a red-brown crystalline residue. Since the residue was not stable to chromatographic purification most was used in crude form for the next step. The remaining portion (10%, maximum 0.2 mmol), however, was pre-adsorbed onto Woelm alumina and then purified by column chromatography on Woelm alumina in the dark using pyridine–dichloromethane (1:200) as eluent to yield the carbamoyl(salophen)cobalt (34 mg, represents 24%) as a deep red crystalline solid, m.p. 142–152 °C (decomp.); λ_{max}(EtOH)/nm 199.3 (ε/dm^3 mol^{-1} cm^{-1} 38 000), 255.8 (21 350), 300.0 (11 200) and 367.8 (9300); ν_{max}(CHCl$_3$)/cm^{-1} 3040, 2920, 2860, 1625, 1610, 1580, 1430, 1370, 1330, 1150, 9050 and 9010; δ_H(250 MHz; CDCl$_3$) 8.7 (2 H, s, HC=N), 7.9 (2 H, m, ArH), 7.4–6.6 (20 H, m, ArH), 5.8 (1 H, d J_{AB} 15.6, NC*H*HPh), 4.9 (1 H, d *J* 9.0, 2-CH), 4.7 (1 H, d J_{AB} 15.9, NCH*H*Ph), 4.3 (1 H, m, 1-CH), 4.0 (1 H, d J_{AB} 11.8, OC*H*HPh), 3.95 (1 H, d J_{AB} 11.8, OCH*H*Ph), 2.75 (2 H, m, 2′-CH$_2$), 1.55 (2 H, m, 1′-CH$_2$), 1.2 (3 H, s, CH$_3$) and 0.7 (3 H, br s, CH$_3$); *m*/*z* (FAB) 1082 [M$^+$ + Co(salophen), 3%], 746 [2 × Co(salophen), 13], 710 (M$^+$ + 1, 11), 373 [Co(salophen), 100] and 336 [M$^+$ − Co(salophen), 80].

trans-3-*Allyl*-1-*benzyl*-4-(2′-*benzyloxyethyl*)*azetidin*-2-*one* **31**.—A deoxygenated solution of the crude carbamoyl(salophen)cobalt **30** (maximum 1.28 g, 1.8 mmol) in freshly distilled, dry toluene (300 cm^3) was stirred and heated under reflux under an atmosphere of argon for 18 h. The resulting mixture was cooled and then evaporated to dryness under reduced pressure to leave a brown solid. This was pre-adsorbed onto silica and purified by column chromatography on silica using diethyl ether–light petroleum (b.p. 40–60 °C) (1:3) as eluent to yield the trans-*azetidin*-2-*one* (145 mg, 22% from the amine **28** as a colourless oil; λ_{max}(EtOH)/nm 196.3 (ε/dm^3 mol^{-1} cm^{-1} 39 550); ν_{max}(CHCl$_3$)/cm^{-1} 3020, 2930, 2860, 1735 (CO), 1650, 1600, 1400 and 1105; δ_H(250 MHz; CDCl$_3$) 7.3 (10 H, m, ArH), 4.92 (1 H, br s, =C*H*H), 4.88 (1 H, m, =CH*H*), 4.65 (1 H, d J_{AB} 15.3, NC*H*HPh), 4.4 (2 H, s, OC*H*$_2$Ph), 4.1 (1 H, d J_{AB} 15.2, NCH*H*Ph), 3.5 [1 H, ddd (*ca.* dt) *J* 6.6, 6.6 and 2.2, 4-CH], 3.5 (1 H, d *J* 2.2, 3-CH), 3.45 [2 H, dd (*ca.* t) *J* 6.1 and 6.1, 2′-CH$_2$], 2.05 (1 H, m, 1′-C*H*H), 1.75 (1 H, m, 1′-CH*H*) and 1.75 (3 H, br s, CH$_3$); δ_C(100.6 MHz; CDCl$_3$) 167.8 (s, 2-C), 139.0 (s, 5-C), 137.9 (s), 136.1 (s), 128.7 (d), 128.4 (d), 128.1 (d), 127.7 (d), 127.6 (d), 113.8 (t), 73.2 (t, 3′-C), 66.8 (t, 2′-C), 62.7 (d, 3-C), 55.0 (d, 4-C), 44.4 (t, 1″-C), 32.9 (t, 1′-C) and 20.5 (q); *m*/*z* (EI) 335.1816 (M$^+$, C$_{22}$H$_{25}$NO$_2$ requires 335.1885, 0.03%) and 244 (M$^+$ − CH$_2$Ph, 1). [When the purified carbamoyl(salophen)cobalt **30** (33 mg, 0.046 mmol) was subjected to the above reaction conditions the *azetidin*-2-*one* **31** (6.2 mg, 40%) was obtained as a colourless oil whose spectroscopic data were identical with those obtained previously.]

trans-3-*Acetyl*-1-*benzyl*-4-(2′-*benzyloxyethyl*)*azetidin*-2-*one* **32**.—A stream of dry ozone was passed through a stirred and cooled (−78 °C) solution of the azetidin-2-one **31** (144 mg, 0.43

mmol) in dry dichloromethane (10 cm^3) for 10–15 min until a faint blue colour persisted.[5] The solution was first purged with oxygen for 5 min and then with argon for 5 min after which triphenylphosphine (225 mg, 0.86 mmol) was added to it in one portion. The resulting mixture was stirred and allowed to warm to room temperature over 1 h and then evaporated to dryness under reduced pressure. The residue was dissolved in diethyl ether (10 cm^3) and the solution was dried ($MgSO_4$) and evaporated to dryness under reduced pressure to leave a white solid. This was pre-adsorbed onto silica and purified by column chromatography on silica using diethyl ether as eluent to yield the *ketone* (120 mg, 83%) as an unstable colourless oil; ν_{max}(film)/cm^{-1} 3065, 3030, 2920, 2860, 1755 (NCO), 1710 (CO), 1605, 1495, 1455, 1410, 1360, 1260, 1190, 1105, 740 and 700; δ_H(250 MHz; $CDCl_3$) 7.25 (10 H, m, ArH), 4.55 (1 H, d J_{AB} 15.4, NC*H*HPh), 4.4 (1 H, d J_{AB} 11.6, OC*H*HPh), 4.35 (1 H, d J_{AB} 11.7, OCH*H*Ph), 4.2 (1 H, d J_{AB} 15.4, NCH*H*Ph), 4.05 (1 H, d *J* 2.2, 3-CH), 4.0 (1 H, ddd *J* 8.8, 4.0 and 2.2, 4-CH), 3.4 (1 H, ddd *J* 20.2, 9.5 and 5.1, 2'-C*H*H), 3.35 (1 H, ddd *J* 20.7, 9.5 and 4.7, 2'-CH*H*), 2.2 (3 H, s, CH_3), 1.9 (1 H, m, 1'-C*H*H) and 1.7 (1 H, m, 1'-CH*H*); δ_C(22.5 MHz; $CDCl_3$) 200.5 (s, 5-C), 163.1 (s, 2-C), 137.8 (s), 135.5 (s), 128.7 (d), 128.2 (d), 127.8 (d), 127.6 (d), 73.2 (t, 3'-C), 68.4 (d, 3-C), 66.8 (t, 2'-C), 52.2 (d, 4-C), 44.8 (t, 1''-C), 31.9 (t, 1'-C) and 29.6 (q); *m/z* (FAB) 338 (M^+ + 1, 54%), 230 (M^+ − OCH_2Ph, 14) and 202 (M^+ − $CH_2CH_2OCH_2Ph$, 17).

trans-1-*Benzyl*-4-(2'-*benzyloxyethyl*)-3-(1'R-*hydroxyethyl*)-*azetidin*-2-*one* **34**.—Finely powdered potassium iodide (65 mg, 0.39 mmol) was added in one portion to a stirred solution of the ketone **32** (120 mg, 0.36 mmol) in dry diethyl ether under an atmosphere of argon. The mixture was stirred for 0.5 h and then cooled to 0 °C. A solution of K-Selectride™ (1.0 mol dm^{-3}) in THF (890 μm^3, 0.89 mmol) was injected dropwise into the stirred and cooled mixture over 1 min and the resulting mixture was stirred at 0 °C under an atmosphere of argon for 1.5 h. The mixture was allowed to warm to ambient temperature when water (5 cm^3) was added to it over 1 min. The mixture was extracted with ethyl acetate (3 × 5 cm^3) and the combined organic phases were dried ($MgSO_4$) and evaporated to dryness under reduced pressure. The oily residue was purified by column chromatography on silica using ethyl acetate as eluent to give the desired *azetidin-2-one* (99 mg, 83%) as a colourless oil; ν_{max}(film)/cm^{-1} 3420 (OH), 3090, 3065, 3030, 2925, 2860, 1735 (CO), 1605, 1495, 1455, 1415, 1375, 1100, 735 and 701; δ_H(250 MHz; $CDCl_3$) 7.25 (10 H, m, ArH), 4.5 (1 H, d J_{AB} 15.4, NC*H*HPh), 4.35 (2 H, s, OCH_2Ph), 4.05 (1 H, d J_{AB} 15.4, NCH*H*Ph), 4.0 (1 H, dq *J* 7.3 and 6.3, 5'-CH), 3.5 (1 H, ddd *J* 9.3, 4.0 and 2.0, 4-CH), 3.4 [2 H, dd (*ca.* t) *J* 6.2 and 6.2, 2'-CH_2], 2.9 (1 H, dd *J* 7.4 and 1.9, 3-CH), 2.6–2.3 (1 H, br s, OH), 1.9 (1 H, m, 1'-C*H*H), 1.6 (1 H, m, 1'-CH*H*) and 1.2 (3 H, d *J* 6.3, CH_3); δ_C(20.15 MHz; $CDCl_3$) 167.6 (s, 2-C), 137.6 (s), 135.9 (s), 128.5 (d), 128.2 (d), 127.9 (d), 127.4 (d), 72.9 (t, 3'-C), 66.8 (t, 2'-C), 65.8 (d, 5-C), 62.1 (d, 3-C), 53.3 (d, 4-C), 44.3 (t, 1''-C), 31.2 (t, 1'-C) and 21.2 (q); *m/z* (FAB) 340 (M^+ + 1, 83%), 322 (M^+ + 1 − H_2O, 10) and 232 (M^+ − OCH_2Ph, 4). [The desired *R*-alcohol was contaminated with the corresponding (~15%) *S*-alcohol whose ^1H NMR spectroscopic data were identical with those of the *R*-isomer except: 4.34 (2 H, s, OCH_2Ph) and 2.93 (1 H, dd *J* 6.3 and 1.9, 3-CH).]

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