Synthesis of β-Lactams from π-Allyltricarbonyliron (Lactone) Complexes

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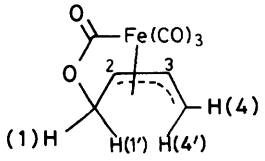
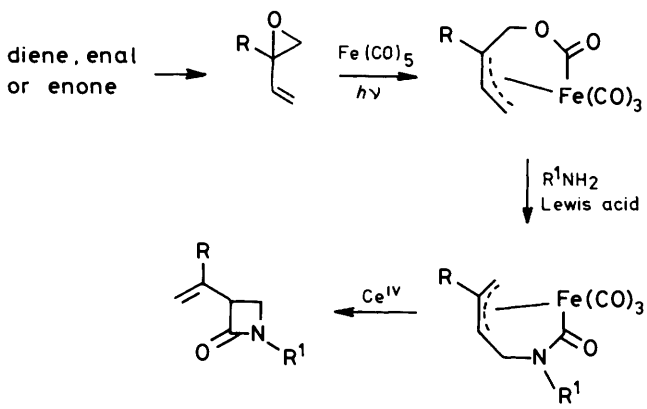
Several π-allyltricarbonyliron (lactone) complexes have been treated with an excess of benzylamine in the presence of Lewis acids to afford the corresponding lactam complexes by an S_N2'-like process. These lactam complexes were oxidised in good yield with ceric ammonium nitrate to provide a novel route to a variety of β-lactam compounds. Simple chemical transformations of the resulting β-lactams have been investigated; these include the conversion of the vinyl and isopropenyl side chains into hydroxyethyl substituents and the reductive removal of benzyl groups to afford the parent NH β-lactams.

Owing to the recent extensive interest in structurally novel β-lactam antibiotics such as thienamycin,[1] the olivanic acids,[2] nocardicin,[3] and the monobactams,[4] new methods for constructing the inherent azetidinone ring system have become increasingly important. Here we report in full the use of π-allyltricarbonyliron (lactone) complexes as novel precursors for β-lactams.[5] The process involves the conversion of dienes, enals or enones into regiospecific vinyl epoxides, which upon treatment with pentacarbonyliron afford π-allyltricarbonyliron (lactone) complexes.[6] These complexes react with amines in the presence of Lewis acids to give π-allyltricarbonyliron (lactam) complexes corresponding to nucleophilic attack by the amine at the 4-position of the allyl system [see numbering in (A)] in an overall S_N2'-type process. The complexes, on



(A)

oxidation with ceric ammonium nitrate, give good yields of the corresponding β-lactams (Scheme 1). The preparation of the π-allyltricarbonyliron complexes (1)—(6) used in this work has been reported previously.[6,8a] The preparation of the complex (7) was achieved by reaction of cinnamaldehyde with dimethylsulphonium methylide under phase-transfer conditions to give the vinyl epoxide (8) in 95% yield [7] followed by reaction with $Fe(CO)_5$ under the usual reaction conditions to give (7) (68%). The structure of (7) was deduced to have a *syn-anti* configuration from a detailed analysis of the high-field (250 MHz) ^1H n.m.r. spectrum and was confirmed by a single-crystal *X*-ray structure determination.† The coupling constants for compound (7) of $J_{2,3}$ 7.5 Hz and $J_{3,4'}$ 12.5 Hz agree well with our other π-allyltricarbonyl iron lactone complexes suggesting a similar *syn-anti* configuration in these cases. Each of the above π-allyltricarbonyliron (lactone) complexes was converted into the corresponding lactam complexes (9)—(14) by treatment with an excess of benzylamine in the presence of a Lewis acid (Table 1). Generally, the yields in these reactions were good. The use of diethylaluminium chloride as a catalyst often gave higher yields of lactam complex. More



Scheme 1.

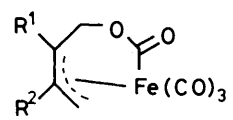
Table 1. Preparation of π-allyltricarbonyl (lactam) complexes

Complex	Catalyst (equiv.)	Reaction time (h)	Lactam complex	Yield (%)
(1)	$ZnCl_2$	0.5	(9)	82
(2)	$ZnCl_2$	1.5	(10)	95
	$ZnCl_2$·TMEDA	0.2		100
	Et_2AlCl	0.5		98
(3)	$ZnCl_2$	1.5	(11)	75
(4)	$ZnCl_2$	2.5	(12)	36
	Et_2AlCl	0.75		68
(5)	$ZnCl_2$	3.0	(12) + (13)	12 + 23
(6)	$ZnCl_2$	3.0	(14)	82
(7)	Et_2AlCl	0.5	(15)	80

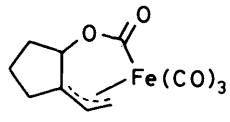
recent work ‡ indicates that the use of zinc chloride–tetramethylenediamine gives even better yields, requiring less amine and shorter reaction times. Both aluminium trichloride and aluminium oxide have been reported by others [8] to be effective catalysts in similar types of reaction but generally the above methods are superior. In all cases, except during the reaction of (5) with benzylamine, which gave mixtures of (13) and (12), the product of the reaction was that derived by an S_N2' like process. In the exceptional case, however, after extended periods of time (27 h), more of the desired lactam isomer (13) was produced to give a ratio of

† We thank Dr. D. J. Williams, Imperial College, for this determination.

‡ D. M. Hollinshead, unpublished observations.



(1) $R^1 = R^2 = H$
(2) $R^1 = Me, R^2 = H$
(3) $R^1 = R^2 = Me$



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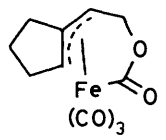

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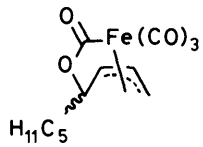

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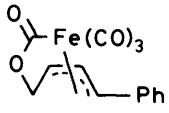

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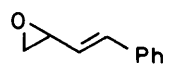

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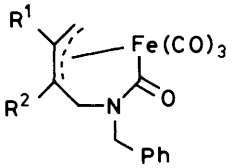
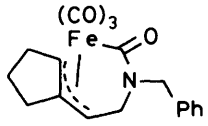


(9) $R^1 = R^2 = H$
(10) $R^1 = Me, R^2 = H$
(11) $R^1 = R^2 = Me$



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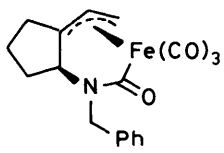

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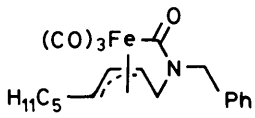

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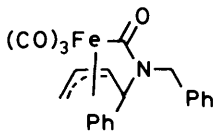
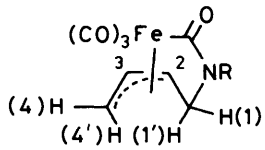


(15)

6 : 1 for (13) to (12). Lewis acid-mediated insertion of benzylamine into the π-allyltricarbonyliron (lactone) complex (7) gives (15), the configuration of which is assigned on the basis of the known '*exo*' attack by external nucleophiles at the 4-position with allyl migration leading to inversion at C-1 and C-4 [8a] [see (B)].



(B)

Table 2. Oxidation of π-allyltricarbonyliron (lactam) complexes with ceric ammonium nitrate

Complex	Reaction conditions *	Product(s)	Yield (%)
(9)	−30 °C → R.T.	(16)	75
(10)	−30 °C → R.T.	(17)	88
(11)	0 °C → R.T.	(18)	34
		(19)	54
(12)	R.T.	(20)	84
(13)	−30 °C → R.T.	(21)	75
(14)	−5 °C	(22)	64
(15)	−30 °C → R.T.	(23)	78

* R.T. = room temp.

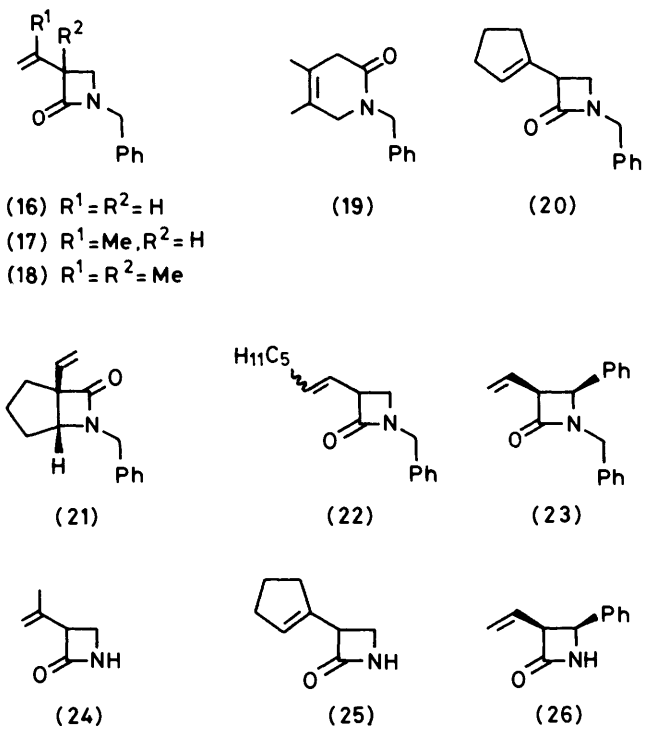
In accord with our earlier observations that π-allyltricarbonyliron (lactone) complexes afford β-lactones upon oxidation with ceric ammonium nitrate, it was found that the lactam complexes similarly gave the β-lactam product (Table 2). This new method of β-lactam formation compares favourably with other procedures in terms of yield. Further, it has a feature of particular interest, and potential advantage, namely the β-lactam products are regioisomers of those normally resulting from addition of chlorosulphonyl isocyanate (CSI) to dienes.[9]

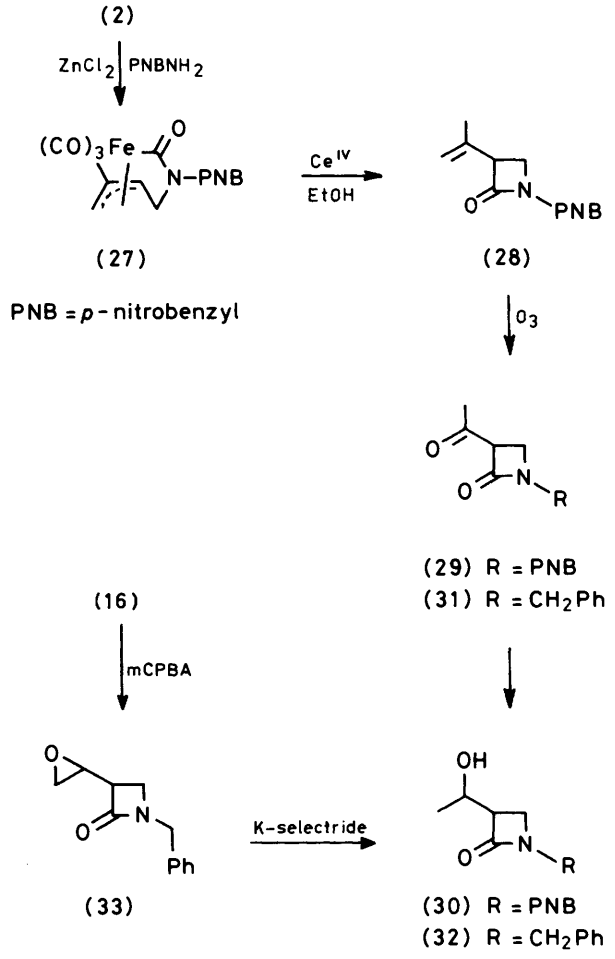
From Table 2 it is clear that only in special circumstances, as in the oxidation of compound (11), do δ-lactam products arise. The formation of (19) as the major product from (11) is best explained in terms of the increased steric requirements needed to form the β-lactam (18) containing the angular methyl substituent at C-3. Entries (13) and (15) in Table 2 indicate that the initial stereochemical features of the lactam complexes are maintained in the formation of the products. This observation obviously has relevance for the construction of more elaborate β-lactam systems. The characterisation of the products in Table 2 follows from full analysis of their spectral properties. That the β-lactam (23) contains a *cis*-arrangement of functional groups was shown by the *cis* coupling constant of 5.5 Hz for the C(3),C(4) protons which is typical of other such β-lactams.[10] This *cis*-arrangement lends further evidence to the structure assigned to (15) assuming that the oxidative extrusion of iron affords a product derived from coupling on the same face of the allyl system.[6] The alkenyl substituted β-lactam products in Table 2 are unusual in that only a very few other such species are presently known. It was also shown that, at least in one case, the β-lactam (23) could be prepared from the lactone complex (7) in 62% yield without isolation of the intermediate lactam species (15).

With these derivatives to hand we briefly studied some of their chemistry. For example, it was important to investigate how easily these could be converted into the parent N–H β-lactams by reductive removal of the benzyl group. All catalytic hydrogenolysis methods were unsuccessful and led only to hydrogenation of the alkenyl side chains. However, the use of sodium in liquid ammonia [11] proved satisfactory. Thus compounds (17) and (20) were converted into the parent N–H β-lactams (24) and (25) in 88 and 68% yields respectively. Attempted removal of the benzyl protecting group in (23) to give (26) was, not surprisingly, unsuccessful due to the second benzylic position present which also appeared to be cleaved, leading to destruction of the azetidinone nucleus.

Other chemical conversions of these alkenyl-substituted β-lactams involved the modification of the side chain to the hydroxyethyl group, a unit which is common to many of the biologically active β-lactam antibiotics.

Thus reaction of the complex (2) with *p*-nitrobenzylamine





Scheme 2.

in the presence of zinc chloride gave the lactam complex (27) in 85% yield which, on oxidation with Ce^{IV}, gave the β-lactam (28) in 70% yield. Ozonolysis of the isopropenyl side chain in (28) followed by work-up with triphenylphosphine afforded an 80% yield of the corresponding 3-acetyl derivative (29). Reduction of (29) with sodium borohydride gave a 1 : 1 mixture of diastereoisomeric alcohols (30) (Scheme 2). Similar ozonolysis of (17) at −25 °C gave the ketone (31) (87%) which upon reduction with K-selectride afforded a mixture of alcohols (32) (50%). Epoxidation of (16) with *m*-chloroperbenzoic acid gave (33) in 51% yield which was reduced to the alcohols (32) in 40% yield by K-selectride (Scheme 2).

The above studies demonstrate the use of π-allyltricarbonyliron (lactone) complexes for the preparation of simple β-lactam compounds. Clearly, by using more structurally complex starting materials, routes to pharmaceutically interesting β-lactams should ensue.

Experimental

M.p.s were determine on a Kofler hot-stage apparatus. I.r. spectra were recorded on Perkin-Elmer 197 and 298 spectrometers as thin films for liquids and Nujol mulls for solids unless otherwise stated. ^1H N.m.r. spectra were determined on Varian XL 100, EM 360-A and Brucker WM 250 instruments using $SiMe_4$ as internal standard. Mass spectra were recorded on a V.G. Micromass 7070 spectrometer at 70 eV. Column chromatography was performed under low pressure on silica gel (Merck 9385). All solvents were purified and dried by standard methods. Ether refers to diethyl ether.

Preparation of the Complexes (1)—(6).—The preparation of these compounds has been described in full previously.[6,8a]

Preparation of the Complex (7).—A solution of pentacarbonyliron (3 ml, 23 mmol) and *trans*-3,4-epoxyphenylbutadiene (8)[7] (605 mg, 4.1 mmol) in dry degassed benzene (350 ml) was irradiated (with a 450 W Applied Photophysics lamp in an internal well system using a circulating sodium bromide solution filter) for 12 min under a constant stream of argon. The green reaction mixture was filtered, frozen, then freeze dried on a rotary evaporator whereby the volatile components were trapped on a cold (−78 °C) condenser. The brown crystalline residue was stirred with ether and filtered through a Celite pad. Removal of solvent under reduced pressure gave 2—4-η^3-(1-*formyloxy*-4-*phenylbut*-3-*enylato*)*tricarbonyliron* (7) (878 mg, 68%) as yellow crystals, m.p. >120 °C (with decomp.); $\nu_{max.}$ ($CHCl_3$) 2 080, 2 030, 1 665, and 984 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.42—7.28 (5 H, m), 5.62 (1 H, dd, *J* 12.5 and 7.5 Hz, 3-H), 4.82 (1 H, d, *J* 12.5 Hz, 4-H), 4.78 (1 H, ddd, *J* 7.5, 5.5 and 1.5 Hz, 2-H), 4.17 (1 H, dd, *J* 12.5 and 1.5 Hz, 1-H) and 4.05 (1 H, dd, *J* 12.5 and 5.5 Hz) (Found: C, 53.75; H, 3.2. $C_{14}H_{10}FeO_5$ requires C, 53.54; H, 3.21%).

General Procedure for the Preparation of the π-Allyltricarbonyliron (Lactam) Complexes.—To a solution of the appropriate π-allyltricarbonyliron (lactone) complex (*ca.* 100 mg) in ether or ether–THF (5 ml) was added an excess of benzylamine (up to 10 equiv.) and zinc chloride (2 equiv.) (or other catalyst). The mixture was stirred at room temperature until no further starting material was indicated by t.l.c. The suspension was filtered, solvent removed under reduced pressure, and the product(s) isolated by column chromatography on silica gel.

Preparation of the Lactam Complex (9).—Treatment of the lactone complex (1) (100 mg, 0.42 mmol) with zinc chloride (110 mg, 0.84 mmol) and benzylamine (540 mg, 5 mmol) in

THF–ether (1 : 3, 5 ml) gave, after chromatography (ether/light petroleum, 2 : 1) 2—4-η³-[1-(α-*formylanilino*)*but*-3-*en*-2-*ylato*]*tricarbonyliron* (9) (117 mg, 82%) as white crystals, m.p. 76—78 °C; $\nu_{max.}$ 3 080, 2 980, 2 850, 2 070, 2 010, 1 585, 1 570, 1 405, and 1 165 cm^{-1}; δ($CDCl_3$; 100 MHz) 7.35—7.04 (5 H, m), 4.84 (1 H, ddd, *J* 13, 8, and 8 Hz, 3-H), 4.40 (1 H, m, 2-H), 4.26 (1 H, d, *J* 15 Hz), 4.14 (1 H, d, *J* 15 Hz), 3.73 (1 H, ddd, *J* 8, 2, and 2 Hz, 4-H) 3.29 (1 H, dd, *J* 13 and 6 Hz, 1-H), 3.16 (1 H, dd, *J* 13 and 2 Hz, 1-H′), and 2.88 (1 H, dd, *J* 13 and 2 Hz, 4′-H) (Found: C, 54.8; H, 3.95; N, 4.25. $C_{15}H_{13}FeNO_4$ requires C, 55.08; H, 4.01; N, 4.28%).

Preparation of the Lactam Complex (10).—Treatment of the lactone complex (2) (100 mg, 0.4 mmol) with zinc chloride (107 mg, 0.8 mmol) and benzylamine (510 mg, 4.7 mmol) in THF–ether (1 : 3, 5 ml, gave after chromatography (ether–light petroleum, 2 : 1), 2—4-η³-[1-(α-*formylanilino*)-3-*methylbut*-2-*en*-2-*ylato*]*tricarbonyliron* (10) (128 mg, 95%) as white crystals, m.p. 70—72 °C; $\nu_{max.}$ 3 025, 2 920, 2 850, 2 060, 2 000, 1 980, 1 590, 1 175, 700, and 665 cm^{-1}; δ($CDCl_3$); 100 MHz) 7.34—7.06 (5 H, m), 4.24 (3 H, m, $PhCH_2$ and 2-H), 3.56 (1 H, dd, *J* 2 and 2 Hz, 4-H), 3.33 (1 H, dd, *J* 13 and 6 Hz, 1-H), 3.14 (1 H, dd, *J* 13 and 2 Hz, 1′-H), 2.70 (1 H, d, *J* 2 Hz, 4′-H), and 1.94 (3 H, s, CH_3) (Found: C, 56.35; H, 4.45; N, 4.1. $C_{16}H_{15}FeNO_4$ requires C, 56.04; H, 4.4; N, 4.07%). For preparation of (10) using other catalysts see Table 1.

Preparation of the Lactam Complex (11).—Treatment of the lactone complex (3) (1 g, 3.7 mmol), with zinc chloride (1 g, 7.5 mmol), and benzylamine (4 g, 3.7 mmol) in ether (60 ml) gave after chromatography (ether), 2—4-η³-[1-(α-*formylanilino*)-2,3-*dimethylbut*-3-*en*-2-*ylato*]*tricarbonyliron* (11) (1 g, 75%) as yellow crystals, m.p. 98—100 °C; $\nu_{max.}$ ($CHCl_3$) 2 900, 2 025, 1 990, 1 570, 1 440, 1 185, and 705 cm^{-1}; δ 7.33—7.08 (5 H, m), 4.28 (2 H, s), 3.42 (1 H, d, *J* 2 Hz, 4-H) 3.14 (2 H, s, 1-H and 1′-H), 2.44 (1 H, d, *J* 2 Hz, 4′-H), 2.08 (3 H, s), and 1.89 (3 H, s) (Found: C, 57.55; H, 4.8; N, 3.9. $C_{17}H_{17}FeNO_4$ requires C, 57.50; H, 4.80; N, 3.95%).

Preparation of the Lactam Complex (12).—Treatment of a mixture of the *syn*- and *anti*-lactone complexes (4) (100 mg, 0.4 mmol) with zinc chloride (98 mg, 0.8 mmol) and benzylamine (462 mg, 4.3 mmol) in THF–ether (1 : 4; 10 ml) gave, after chromatography (ether–light petroleum, 1 : 1), 2,1,1′-η³-{2-[*benzyl*(*formyl*)*amino*]*ethylcyclopent*-1-*enylato*}*tricarbonyliron* (12) (48 mg, 36%) as white crystals, m.p. 95—98 °C; $\nu_{max.}$ 3 080, 3 060, 2 960, 2 860, 2 070, 2 000, 1 590, 1 490, 1 171, and 660 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.34—7.18 (3 H, m), 7.16—7.07 (2 H, m), 4.35 (1 H, d, *J* 15 Hz), 4.27 (1 H, d, *J* 6 Hz, 2-H), 4.22 (1 H, br s, 4-H) 4.13 (1 H, d, *J* 15 Hz), 3.37 (1 H, dd, *J* 13 and 6 Hz, 1-H), 3.21 (1 H, d, *J* 13 Hz, 1′-H), 2.92—2.75 (1 H, m), 2.48—2.37 (2 H, m), 2.02 (1 H, dd, *J* 15 and 8 Hz), 1.96—1.82 (1 H, m), and 1.58—1.37 (1 H, m) (Found: C, 58.9; H, 4.65; N, 3.8. $C_{18}H_{17}FeNO_4$ requires C, 58.88; H, 4.67; N, 3.81%). Use of diethylaluminium chloride in place of zinc chloride afforded (12) in 68% yield (Table 1).

Preparation of the Lactam Complexes (12) *and* (13).—Treatment of the lactone complex (5) (200 mg, 0.7 mmol) with zinc chloride (196 mg, 1.4 mmol) and benzylamine (770 mg, 7.2 mmol) in THF–ether (1 : 4, 10 ml) gave after chromatography (ether–light petroleum, 1 : 1), 1,1′,2′-η³-{2-[*benzyl*(*formyl*)*amino*]*ethyl*-1-*vinylcyclopentylato*}*tricarbonyliron* (13) (61 mg, 23%) as white crystals, m.p. 95—98 °C; $\nu_{max.}$ 3 080, 3 060, 3 020, 2 960, 2 860, 2 070, 2 000, 1 590, 1 490, 1 400, 1 390, 1 170, and 660 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.34—7.17 (3 H, m), 7.17—7.04 (2 H, m), 5.07 (1 H, dd, *J* 13.4 and 8 Hz, 3-H), 4.88 (1 H, d, *J* 14 Hz), 3.68 (1 H, d, *J* 14 Hz), 3.68 (1 H, d, *J* 14 Hz), 3.39 (1 H, dd, *J* 8.0 and 1.8 Hz, 4-H), 3.31 (1 H, dd, *J* 8 and 6.7 Hz, 1-H), and 2.65—1.52 (7 H, m) (Found: C, 58.9; H, 4.65; N, 3.80. $C_{18}H_{17}FeNO_4$ requires C, 55.88; H, 4.67; N, 3.81%) and complex (12) (32 mg, 12%) as white crystals identical with the previous sample.

Preparation of the Lactam Complex (14).—Treatment of the isomeric lactone complexes (6) (0.46 g, 1.48 mmol) with zinc chloride (200 mg, 1.47 mmol) and benzylamine (0.75 g, 0.7 mmol) in ether (10 ml) gave, after chromatography (ether–light petroleum, 2 : 1) 2—4-η³-{1-[*benzyl*(*formyl*)-*amino*]*non*-3-*en*-2-*ylato*}*tricarbonyliron* (14) as an oil (0.5 g, 82%) which solidified with time to give crystals, m.p. 80—86 °C; $\nu_{max.}$ 2 900, 2 850, 1 995, 1 980, and 1 590 cm^{-1}; δ($CDCl_3$; 360 MHz) 7.25 (3 H, m), 7.13 (2 H, d, *J* 6 Hz), 4.64 (1 H, dd, *J* 12 and 8 Hz, 3-H), 4.31 (1 H, d, *J* 14 Hz), 4.15 (1 H, d, *J* 14 Hz), 4.17 (1 H, ddd, *J* 8, 6, and 2 Hz, 2-H), 3.78 (1 H, ddd, *J* 12, 9, and 5 Hz, 4-H), 3.26 (1 H, dd, *J* 13 and 6 Hz, 1-H), 3.09 (1 H, dd, *J* 13 and 2 Hz, 1′-H), 2.27 (1 H, m), 1.72 (1 H, m), 1.64—1.41 (2 H, m), 1.35 (4 H, m), and 0.91 (3 H, t, *J* 6 Hz) (Found: C 60.5; H, 5.8; N, 3.5. $C_{20}H_{23}FeNO_4$ requires C, 60.6; H, 5.9; N, 3.5%).

Preparation of the Complex (15).—Treatment of the lactone complex (7) (103 mg, 0.33 mmol) with diethylaluminium chloride (387 μl of a 25% solution in hexane, 0.66 mmol) and benzylamine (144 μl, 1.32 mmol), gave after chromatography (3 : 1. ether–light petroleum), 2—4-η³-{1-[*benzyl*(*formyl*)-*amino*]-1-*phenylbut*-3-*en*-2-*ylato*}*tricarbonyliron* (15) (105 mg, 80%) as white crystals, m.p. 138—140 °C (with decomp.); $\nu_{max.}$ ($CHCl_3$) 2 970, 2 078, 2 020, 2 010, and 1 582 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.39—7.17 (6 H, m), 6.86—7.08 (4 H, m), 5.12 (1 H, d, *J* 14 Hz), 4.68 (1 H, dd, *J* 8 and 6 Hz, 2-H), 4.54 (1 H, ddd, *J* 12.5, 8 and 8 Hz 3-H), 4.38 (1 H, d, *J* 6 Hz, 1-H), 3.82 (1 H, dd, *J* 8 and 1 Hz, 4-H), 3.41 (1 H, dd, *J* 12.5 and 1 Hz, 4′-H), and 2.97 (1 H, d, *J* 14 Hz) (Found: C, 62.45; H, 4.15; N, 3.45. $C_{21}H_{17}FeNO_4$ requires C, 62.55; H, 4.25; N, 3.47%).

Preparation of the Lactam Complex (27).—Treatment of the lactone complex (2) (70 mg, 0.3 mmol) with zinc chloride (82 mg, 0.6 mmol) and *p*-nitrobenzylamine (456 mg, 3 mol) in THF–ether (1 : 2, 9 ml) gave, after chromatography (ether–light petroleum, 2 : 1), 2—4-η³-{1-[*formyl*(p-*nitrobenzyl*)-*amino*]-3-*methylbut*-3-*en*-2-*ylato*}*tricarbonyliron* (27) (89 mg, 85%) as yellow crystals, m.p. 118—123 °C; $\nu_{max.}$ ($CHCl_3$) 3 040, 3 000, 2 950, 2 870, 2 095, 2 025, 2 000, 1 580, 1 525, 1 355, 1 215, and 750 cm^{-1}; δ($CDCl_3$) 8.25—8.10 (2 H, m), 7.42—7.20 (2 H, m), 4.39 (1 H, d, *J* 15 Hz), 4.39—4.19 (1 H, m, 2-H), 4.20 (1 H, d, *J* 15 Hz), 3.68—3.51 (1 H, m, 4-H), 3.34—3.18 (2 H, m, 1-H and 1′-H), 2.66 (1 H, br s, 4′-H), and 2.03 (3 H, s) (Found: C, 50.0; H, 3.75; N, 7.25. $C_{16}H_{14}FeN_2O_6$ requires C, 49.77; H, 3.65; N, 7.26%).

General Procedure for the Oxidation of π-Allyltricarbonyliron (Lactam) Complexes by Ceric Ammonium Nitrate.—To a stirred solution of the π-allyltricarbonyliron (lactam) complex in ethanol at −30 °C was added an ethanolic solution of ceric ammonium nitrate (4 equiv.) during a period of a few minutes. The reaction mixture was allowed to warm slowly to room temperature and stirred until t.l.c. indicated complete reaction. Solvent was removed under reduced pressure, and the residue diluted with water. The products were extracted with ether and isolated by column chromatography after drying and removal of solvent.

Preparation of 1-*Benzyl*-3-*isopropenylazetidin*-2-*one* (17).—Oxidation of the lactam complex (10) (498 mg, 1.46 mmol) in

ethanol (65 ml) with ceric ammonium nitrate (3.60 g, 6.6 mmol) gave, after chromatography (ether–light petroleum, 1 : 1) 1-*benzyl*-3-*isopropenylazetidin*-2-*one* (17) (258 mg, 88%) as an oil; $\nu_{max.}$ 3 080, 3 060, 3 030, 2 970, 2 900, 1 745, 1 645, 1 605, 1 400, 900, and 730 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.4—7.22 (5 H, m), 4.95 (1 H, br s, $=CH_2$), 4.91 (1 H, br s, $=CH_2$), 4.47 (1 H, d, *J* 14.5 Hz), 4.32 (1 H, d, *J* 14.5 Hz), 3.86—3.80 (1 H, m, 3-H), 3.28 (1 H, dd, *J* 5.5 and 5.5 Hz, *cis*-4-H), 3.04 (1 H, dd, *J* 5.5 and 2.5 Hz, *trans*-4-H), and 1.78 (3 H, s) (Found: C, 77.7; H, 7.75; N, 6.9. $C_{13}H_{15}NO$ requires C, 77.58; H, 7.51; N, 6.96%).

Preparation of 1-*Benzyl*-3-*isopropenyl*-3-*methylazetidin*-2-*one* (18) *and* 1-*Benzyl*-3,6-*dihydro*-4,5-*dimethyl*-2-*pyridone* (19).—Oxidation of the lactam complex (11) (1 g, 2.8 mmol) in ethanol (65 ml) with ceric ammonium nitrate (3.36 g, 6.1 mmol) gave, after chromatography (ether) 1-benzyl-3-isopropenyl-3-methylazetidin-2-one (18) (207 mg, 34%) as an oil; $\nu_{max.}$ 2 860, 1 740, 1 640, 1 400, and 700 cm^{-1}; δ($CDCl_3$) 7.37—7.17 (5 H, m), 5.02 (1 H, br s, $=CH_2$), 4.86 (1 H, m, $=CH_2$), 4.40 (2 H, br s, $PhCH_2$), 3.16 (1 H, d, *J* 5 Hz, 4-H), 2.9 (1 H, d, *J* 5 Hz, 4-H), 1.77 (3 H, s), and 1.45 (3 H, s) (Found: M^+, 215.1310. $C_{14}H_{17}NO$ requires *M*, 215.1309), and 1-*benzyl*-3,6-*dihydro*-4,5-*dimethyl*-2-*pyridone* (19) (349 mg, 54%) as white crystals, m.p. 78—80 °C; $\nu_{max.}$ 2 900, 1 640, 1 495, 1 265, 725, and 715 cm^{-1}; δ($CDCl_3$) 7.35—7.18 (5 H, m), 4.73 (2 H, s, $PhCH_2$), 3.73 (2 H, br s, CH_2CO), 3.03 (2 H, br s, CH_2N), and 1.70 (6 H, s) (Found: C, 78.0; H, 8.15; N, 6.35. $C_{14}H_{17}NO$ requires C, 78.15; H, 7.90; N, 6.50%).

Preparation of 1-*Benzyl*-3-(*cyclopent*-1-*enyl*)*azetidin*-2-*one* (20).—Oxidation of the lactam complex (12) (190 mg, 0.52 mmol) in ethanol (15 ml) with ceric ammonium nitrate (1.35 g, 2.4 mmol) gave 1-*benzyl*-3-(*cyclopent*-1-*enyl*)*azetidin*-2-*one* (20) (99 mg, 84%) as an oil; $\nu_{max.}$ 2 860 and 1 740 cm^{-1}; δ($CDCl_3$) 7.25 (5 H, m), 5.67 (1 H, br s, =CHR), 4.45 (2 H, br s, $PhCH_2$), 4.00 (1 H, m, 3-H), 3.34 (1 H, dd, *J* 6 and 6 Hz, *cis*-4-H), 3.09 (1 H, dd, *J* 6 and 3 Hz, *trans*-4-H), and 2.63—1.47 (6 H, m) (Found: C, 79.0; H, 7.7; N, 6.2. $C_{15}H_{17}NO$ requires C, 79.25; H, 7.55; N, 6.15%).

Preparation of 6-*Benzyl*-1-*vinyl*-6-*azabicyclo*[3.2.0]*heptan*-7-*one* (21).—Oxidation of the lactam complex (13) (80 mg, 0.2 mmol) in ethanol with ceric ammonium nitrate (500 mg, 0.9 mmol) gave 6-benzyl-1-vinyl-6-azabicyclo[3.2.0]heptan-7-one (21) (31 mg, 75%) as an oil; $\nu_{max.}$ 2 950, 2 900, 1 745, 1 300, 1 100, 900, and 650 cm^{-1}; δ($CDCl_3$; 100 MHz) 7.44—7.18 (5 H, m), 6.18—5.88 (1 H, m, RCH=), 5.48—5.10 (2 H, m, $=CH_2$), 4.66 (1 H, d, *J* 15 Hz), 4.14 (1 H, d, *J* 15 Hz), 3.73 (1 H, d, *J* 4 Hz, 5-H), and 2.38—1.42 (6 H, m) (Found: M^+, 227.1312. $C_{15}H_{17}NO$ requires *M*, 227.1310).

Preparation of 1-*Benzyl*-3-*hept*-1-*enylazetidin*-2-*one* (22).—Oxidation of the lactam complex (14) (0.63 g, 1.58 mmol) with ceric ammonium nitrate (4.1 g, 7.5 mmol) in ethanol (10 ml) gave, after chromatography (ether–light petroleum, 3 : 1) the *cis*- and *trans*-1-benzyl-3-hept-1-enylazetidin-2-ones (22) as an oil (0.26 g, 64%); $\nu_{max.}$ 2 900, 1 745, and 1 390 cm^{-1}; δ($CDCl_3$) 7.3 (5 H, m), 6.0—5.0 (2 H, m, CH=CH), 4.37 (2 H, m), 3.9—3.4 (1 H, m, 3-H), 3.32 (1 H, dd, *J* 5 and 5 Hz, *cis*-4-H), 2.9 (1 H, dd, *J* 5 and 3 Hz, *trans*-4-H), and 2.25—0.6 (17 H, m) (Found: M^+, 257.1772. $C_{17}H_{25}NO$ requires 257.1779).

Preparation of cis-1-*Benzyl*-4-*phenyl*-3-*vinylazetidin*-2-*one* (23).—Oxidation of the lactam complex (15) (53 mg, 0.13 mmol) with ceric ammonium nitrate (0.4 g, 0.7 mmol) in ethanol (11 ml) gave, after chromatography (1 : 4 ether–light petroleum) cis-1-*benzyl*-4-*phenyl*-3-*vinylazetidin*-2-*one* (23) (27 mg, 78%) as a colourless oil, $\nu_{max.}$ ($CHCl_3$) 3 460, 3 045, 3 080, 2 920, 1 736, 1 640, 1 604, 1 394, 1 356, 988, and 930 cm^{-1}; δ($CDCl_3$; 250 MHz), 7.40—7.12 (10 H, m), 5.29 (2 H, m, $=CH_2$), 5.04 (1 H, m, RCH=), 4.91 (1 H, d, *J* 14.5 Hz), 4.65 (1 H, d, *J* 5.5 Hz, 4-H), 4.11 (1 H, m, 3-H), and 3.91 (1 H, d, *J* 14.5 Hz) (Found: C, 81.9; H, 6.75; N, 5.25. $C_{18}H_{17}NO$ requires C, 82.10; H, 6.51; N, 5.32%). A small amount of 1-benzyl-3,6-dihydro-6-phenylpyridone (1.5 mg, <1%), $\nu_{max.}$ 1 675 cm^{-1}, M^+ 263 was also isolated from this reaction but not fully characterised.

Preparation of 3-*Isopropenyl*-1-p-*nitrobenzylazetidin*-2-*one* (28).—Oxidation of the lactam complex (27) (150 mg, 0.4 mmol) with ceric ammonium nitrate (853 mg, 1.6 mmol) in ethanol (25 ml) gave, after chromatography (ether–light petroleum, 2 : 1), 3-isopropenyl-1-*p*-nitrobenzylazetidin-2-one (36) (69 mg, 72%) as an oil; $\nu_{max.}$ ($CHCl_3$) 3 080, 2 950, 2915, 2 850, 1 740, 1 600, 1 520, 1 340, and 1 100 cm^{-1}; δ($CDCl_3$; 90 MHz) 8.30—8.13 (2 H, m), 7.54—7.34 (2 H, m), 4.96 (2 H, m, $=CH_2$), 4.59 (1 H, d, *J* 16 Hz), 4.41 (1 H, d, *J* 16 Hz), 3.89 (1 H, m, 3-H), 3.36 (1 H, dd, *J* 5.6 and 5.5 Hz, *cis*-4-H), 3.10 (1 H, dd, *J* 5.6 and 2.8 Hz, *trans*-4-H), and 1.78 (3 H, s) (Found: M^+, 246.1007. $C_{13}H_{14}N_2O_3$ requires *M*, 246.1004).

Preparation of 3-*Isopropenylazetidin*-2-*one* (24).—Sodium (0.6 g, 26 mg-atom) was added in small pieces to a stirred solution of 1-benzyl-3-isopropenylazetidinone (17) (0.85 g, 4.23 mmol) in liquid ammonia (200 ml), ethanol (10 ml), and ether (25 ml) cooled to −78 °C. Ammonia was evaporated by passage of a stream of nitrogen and the residue treated with water. The product was extracted with ether, dried ($MgSO_4$), and evaporated under reduced pressure to give 3-*isopropenylazetidin*-2-*one* (24) (0.4 g, 88%) as white crystals, m.p. 61—63 °C, $\nu_{max.}$ 3 420, 3 200, 2 930, 2 920, 1 770, 1 753, 1 650, 1 450, and 1 270 cm^{-1}; δ($CDCl_3$; 250 MHz) 5.67 (1 H, br s, NH), 4.96 (2 H, m, $=CH_2$), 3.89 (1 H, m, 3-H), 3.48 (1 H, dd, *J* 5.9 and 5.9 Hz, *cis*-4-H), 3.24 (1 H, dd, *J* 5.9 and 2.8 Hz, *trans*-4-H), and 1.81 (3 H, m) (Found: C, 64.9; H, 8.25; N, 12.55. C_6H_9NO requires C, 64.84; H, 8.16; N, 12.6%).

Preparation of 3-*Cyclopent*-1-*enylazetidinone* (25).—In a similar manner to the previous experiment, compound (20) (0.157 g, 0.69 mmol) in liquid ammonia (100 ml) gave after chromatography (ether) 3-cyclopent-1-enylazetidin-2-one (25) (64 mg, 68%) as a white crystalline solid, m.p. 86—91 °C, $\nu_{max.}$ ($CHCl_3$) 3 490, 2 960, 2 940, 2 860, 2 820, 1 740, and 1 340 cm^{-1}; δ($CDCl_3$; 250 MHz) 5.87 (1 H, br s, NH), 5.66 (1 H, m, RCH=), 4.03 (1 H, m, 3-H), 3.48 (1 H, dd, *J* 5.5 and 5.5 Hz, *cis*-4-H), 3.23 (1 H, dd, *J* 5.5 and 3 Hz, *trans*-4-H), 2.34 (4 H, m), and 1.92 (2 H, m) (Found: M^+, 138.0918. $C_8H_{12}NO$ requires *M*, 138.0919).

Ozonolysis of 3-*Isopropenyl*-1-p-*nitrobenzylazetidin*-2-*one* (28).—Compound (28) (40 mg, 0.16 mmol) in methylene chloride (10 ml) was cooled to −78 °C and treated with ozone until a blue colour persisted. The mixture was purged with argon to remove excess of ozone after which time triphenylphosphine (43 mg, 0.16 mmol) was added and the solution was warmed to room temperature with stirring for 1 h. Solvent was removed under reduced pressure and the resulting oil chromatographed (ethyl acetate) to give 3-acetyl-1-*p*-nitrobenzylazetidin-2-one (29) (32 mg, 82%) as an oil; $\nu_{max.}$ ($CHCl_3$) 1 760, 1 720, 1 615, 1 525, and 1 355 cm^{-1}; δ($CDCl_3$) 8.3—8.16 (2 H, m), 7.53—7.35 (2 H, m), 4.56 (2 H, s, $PhCH_2$), 4.29 (1 H, dd, *J* 5 and 3 Hz, 3-H), 3.64 (1 H, dd, *J* 5 and 3 Hz, *trans*-4-H), 3.19 (1 H, dd, *J* 5 and 3 Hz, *cis*-4-H), and 2.33 (3 H, s,

CH_3CO) (Found: M^+, 248.0792. $C_{12}H_{12}N_2O_4$ requires M, 248.0797).

Preparation of 3-(1-*Hydroxyethyl*)-1-p-*nitrobenzylazetidin*-2-*one* (30).—To the methyl ketone (29) (70 mg, 0.3 mmol) prepared above in ethanol (7 ml) at 0 °C was added sodium borohydride (5 mg, 0.15 mmol) in ethanol (8 ml). The solution was stirred for 1 h, the solvent removed under reduced pressure, and the resulting oil chromatographed (ethyl acetate) to give 3-(1-hydroxyethyl)-1-*p*-nitrobenzylazetidinone (30) (50 mg, 71%) as a diastereoisomeric mixture; $\nu_{max.}$ ($CHCl_3$) 3 450, 3 060, 2 940, 2 910, 1 740, 1 610, 1 525, 1 350, 1 050, and 640 cm^{-1}; δ($CDCl_3$; 90 MHz) 8.27—8.04 (2 H, m), 7.59—7.38 (2 H, m), 4.57 (1 H, d, *J* 16 Hz), 4.36 (1 H, d, *J* 16 Hz), 4.30—3.90 (1 H, m, CHOH), 3.40—3.08 (3 H, m, 3-H, *trans*-4-H and *cis*-4-H), 3.00—2.80 (1 H, br s, OH), 1.36 (3 H, d, *J* 7 Hz), and 1.24 (3 H, d, *J* 7 Hz, CH_3) (Found: M^+, 250.0950. $C_{12}H_{14}N_2O_4$ requires M, 250.0954).

Ozonolysis of 1-*Benzyl*-3-*isopropenylazetidin*-2-*one* (17).—A solution of compound (17) (0.1 g, 0.5 mmol) in CH_2Cl_2 (5 ml) was treated with ozone at −25 °C for 40 min. After purging of the solution with nitrogen, dimethyl sulphide (excess) was added and the mixture allowed to warm to room temperature. The mixture was evaporated under reduced pressure and the residue chromatographed (ether) to give 3-*acetyl*-1-*benzylazetidin*-2-*one* (31) (88 mg, 87%) as a colourless oil; $\nu_{max.}$ 3 020, 3 000, 2 960, 2 900, 1 750, 1 710, 1 400, 1 235, 1 165, 1 030, 730, and 700 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.39—7.22 (5 H, m), 4.42 (1 H, d, *J* 15.1 Hz), 4.33 (1 H, d, *J* 15.1 Hz), 4.22 (1 H, dd, *J* 4.9 and 2.5 Hz, 3-H), 3.59 (1 H, dd, *J* 5.7 and 2.5 Hz, *trans*-4-H), 3.13 (1 H, dd, *J* 5.7 and 4.9 Hz, *cis*-4-H), and 2.23 (3 H, s, CH_3) (Found: C, 70.85; H, 6.75; N, 7.25. $C_{12}H_{13}NO_2$ requires C, 70.92; H, 6.45; N, 6.89%).

Preparation of 1-*Benzyl*-3-(1-*hydroxyethyl*)*azetidin*-2-*ones* (32).—A solution of K-selectride (1.4 ml, 0.7 mmol; 0.5M in THF) was added to a stirred solution of compound (31) (62 mg, 0.3 mmol) in THF (2 ml), cooled to −78 °C under argon. After 0.5 h the mixture was treated with water and extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was subjected to chromatography (ether) to give 1-*benzyl*-3-(1-*hydroxyethyl*)*azetidin*-2-*one* (32) (31 mg, 50%) as a crystalline mixture of diastereoisomers, m.p. 34—36 °C; $\nu_{max.}$ ($CHCl_3$) 3 400, 2 960, 2 940, 2 900, 1 735, 1 590, 1 380, 1 110, and 880 cm^{-1}; δ($CDCl_3$; 250 MHz) 7.38—7.23 (5 H, m), 4.38 (2 H, m, $PhCH_2$), 4.18 and 4.05 (1 H, m, C*H*OH), 3.2 (2½ H, m, 3-H, *trans*-4-H and *cis*-4-H), 3.02 (½ H, dd, *J* 5.2 and 2.1 Hz, *trans*-4-H), 2.76 (1 H, br s, OH), and 1.28 and 1.25 (3 H, d, *J* 5.9 Hz, CH_3) (Found: C, 69.95; H, 7.45; N, 6.6. $C_{12}H_{15}NO_2$ requires C, 70.22; H, 7.37; N, 6.82%).

Preparation of 1-*Benzyl*-3-*oxiranylazetidin*-2-*one* (33).—A solution of compound (16) (205 mg, 1.1 mmol) with 80% *m*-chloroperbenzoic acid (473 mg, 2.2 mmol) and sodium carbonate (320 mg, 3 mmol) in methylene chloride (10 ml) was stirred for 48 h. The suspension was filtered off, washed with saturated aqueous sodium hydrogen carbonate (5 ml), dried, and solvent removed under reduced pressure. Chromatography of the resulting oil [ethyl acetate–light petroleum (b.p. 60—80 °C), 1 : 1] gave 1-benzyl-3-oxiranylazetidin-2-one (33) (112 mg, 51%) as a diastereoisomeric mixture; $\nu_{max.}$ 3 060, 2 980, 1 750, 1 600, 1 395, and 700 cm^{-1}; δ($CDCl_3$) 7.52—7.15 (5 H, m), 4.36 (2 H, s, $PhCH_2$), 3.71—3.5 (1 H, m, 3-H), and 3.33—2.46 (5 H, m); *m/z* 187 (M^+ − 70, C_4H_6O fragment) and 91 (M^+ − 112).

Reduction of Compound (33).—A solution of K-selectride (1 ml, 0.5 mmol; 0.5M in THF) was added to a stirred solution of compound (33) (100 mg, 0.53 mmol) in THF (5 ml) cooled to −78 °C under argon. The mixture was worked up in the usual manner to give 1-benzyl-3-(1-hydroxyethylazetidin-2-one (32) (40 mg, 40%) identical with the previously prepared sample.

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