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The stereochemistry of organometallic compounds

XXXVI *. Rhodium-catalysed reactions of unsaturated amines with hydrogen and carbon monoxide. A new synthesis of 2-piperidinones **

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Abstract

Rhodium-catalysed reactions of 5-aminopent-1-enes with carbon monoxide and hydrogen give 2-piperidinone derivatives in high yields under mild conditions. Reaction of allylamine under similar conditions gave exclusively 2-pyrrolidone in high yield and reactions of 4-aminobut-1-enes gave mixtures of 2-piperidinones and 2-pyrrolidinones. The role of the hydrogen in these reactions is discussed.

Introduction

In a previous paper [1] the hydroformylation of *ortho*-propenylanilines was shown to give 7-membered ring benzazepine derivatives as the major products with small but significant amounts of 3-methylquinoline derivatives also being formed. The latter compounds arose from formation of aldehydes at the internal carbon atom of the double bond and it was argued that the transition state leading to these compounds was stabilised by chelation between the aniline nitrogen atom and the rhodium catalyst. In the absence of this chelation (e.g. in reactions of analogous phenols), it was shown that the products arose exclusively from aldehyde formation at the terminal carbon atom, presumably as a result of steric effects.

In this paper we explore the effects of increasing the nucleophilicity and ligand bonding strength of the nitrogen atom by studying the reactions of unsaturated aliphatic rather than aromatic amines. Few reports of attempted hydroformylation of unsaturated amines exist but piperidine aldehydes were formed from reactions of *N*-methyl-Δ3-piperidines [2]. More relevantly, reactions of substituted diallylamines

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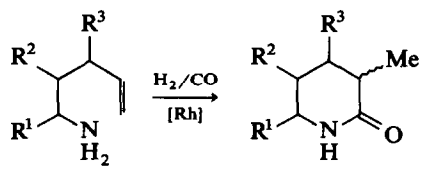
gave either the products of hydroformylation or of carbonylation depending on the nature of the substituents and of the catalyst used [3].

Hydroformylation of allylamine using a rhodium catalyst system gave mixtures of the products of hydroformylation (dihydropyrrole) or carbonylation (2-pyrrolidinone), the proportion depending on the solvent [4]. The latter products have been reported previously from the cobalt-catalysed carbonylation of allylamines [5].

Discussion

Reaction of a series of 5-aminopent-1-enes (**1**) with hydrogen and carbon monoxide was found to give 2-piperidinones (**2**) as the exclusive products in excellent yields under relatively mild conditions. The yields of products from a series of unsaturated amines are summarised in Table 1.



(**1**) (**2**)

The regioselectivity of reaction was not affected by the steric effects arising from the introduction of a substituent at C3 (entry 5) and the results strongly suggest that chelation of the basic amino-nitrogen with the rhodium catalyst dominates the regioselectivity.

The exclusive formation of the products of carbonylation under these mild conditions (40–50 °C, 400 p.s.i. of CO/H_2) is in contrast to previously reported cobalt catalysed carbonylations of unsaturated amines which require much more severe

Table 1

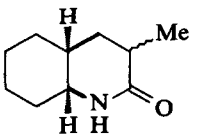
Yields of products from reactions of 5-aminopent-1-enes with hydrogen and carbon monoxide [a]

Entry	Reactant 1			Yield of piperidinone 2 (%)	Ratio of diastereoisomers
	R^1	R^2	R^3		
1	Me	H	H	95	75:25
2	Ph	H	H	91	70:30
3			H	83	50:50
4			H	89	50:50
5	H	H	Me	83	50:50

[a] Reactions were carried out in a Parr autoclave using ethyl acetate solutions of the unsaturated amine (1), $[Rh(OAc)_2]_2$, and PPh_3 in the ratio 200:1:4 and H_2/CO (1:1) at an initial pressure of 2760 kPa (400 p.s.i.) for 20 h at 50 °C.

conditions [3,6]. Ruthenium and rhodium catalysts were reported to be even less effective for these reactions [6]. The results are also in contrast to intermolecular reactions of amines, alkenes, carbon monoxide and hydrogen in the presence of rhodium catalysts which give saturated amines arising from hydroformylation, imine formation and hydrogenation [7].

The reaction gave good yields irrespective of the pattern of substitution at C4, 5 and 6 in the product piperidinones. Each product was formed as a mixture of diastereoisomers which were not readily separated by thin layer chromatography. The diastereoisomers did not appear to arise due to equilibration of stereochemistry of the substituent at C6, for reactions of *cis*- and *trans*-cyclohexylamines (entries 3 and 4) gave products in which the stereochemistry at this centre was retained. Thus the *cis*-amine gave the *cis*-fused product **3** as a mixture of stereoisomers due to the configuration of the methyl group at C3. The *trans*-amine gave a corresponding *trans*-fused product.



(3)

The effect of varying the ligand on the diastereoselectivity was briefly examined using reactions of 5-aminohex-1-ene (**1**; R^1 = Me, $R^2 = R^3$ = H). The results are summarised in Table 2. The use of 1,4-diphosphines BINAP, BPPM, and DIOP gave good yields of 2-piperidinone but with no significant improvement in diastereoselectivity. Attempted reaction using the 1,2-diphosphine, Chiraphos led to recovery of starting material in keeping with the previous observation that metal complexes containing 5-ring chelates are frequently poor catalysts in organometallic chemistry [8]. Several of these ligands were also used in the platinum(II) chloride and tin(II) chloride catalyst system [9] but all attempted reactions led to recovery of starting material.

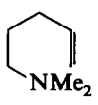
Table 2

Reactions of 5-aminohex-1-ene (1; R^1 = Me, $R^2 = R^3$ = H) with carbon monoxide and hydrogen using rhodium catalysts [a]

Entry	Rhodium precursor	Ligand	Yield (%)	Ratio [a]
6	$[Rh(OAc)_2]_2$	PPh_3	82	75:25
7	$Rh_4(CO)_{12}$	–	87	56:44
8	$[Rh(CO)_2Cl]_2$	(−)-BINAP	66	53:47
9	$[Rh(CO)_2Cl]_2$	(−)-BPPM	85	60:40
10	$[Rh(CO)_2Cl]_2$	(−)-Chiraphos	[c]	–
11	$[Rh(CO)_2Cl]_2$	(−)-DIOP	73	60:40

[a] Reactions were carried out at 60° for 20 h. [b] Values were estimated by ^1H and ^{13}C NMR and reproducible to ±5%. [c] Starting material was recovered.

Attempted reaction of the unsaturated amines **4**, **5** and **6** under the standard conditions (see Table 1) led to a recovery of starting materials and



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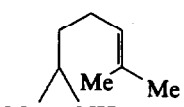

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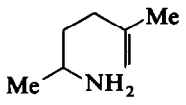
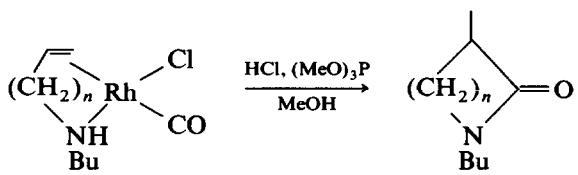


(7)

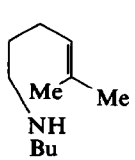
attempted reactions at higher temperatures (80 to 120 °C), either led to low product recoveries or the formation of acetamides from **6** and **7** when ethyl acetate was used as solvent. It thus appears that it is necessary to have a primary (or secondary) amine and a double bond capable of reaction at the internal carbon atom (leading to 6-membered ring formation) for reaction to occur under these relatively mild conditions. Rhodium(III) intermediates **8**, in which the rhodium atom is coordinated to an amino nitrogen have recently been isolated from reactions of unsaturated amines with stoichiometric amounts of $[Rh(CO)_2Cl]_2$ [10]. Reaction of



(8) (9)

these complexes with hydrochloric acid and trimethylphosphite in methanol [11] gave amino esters or lactams. The lactams were formed with formation of the new carbon–carbon bond at the more substituted carbon atom. Thus 4-aminobut-1-enes (**8**; $n = 2$) gave 5-ring lactams (**9**; $n = 2$) and 5-aminopent-1-enes (**8**; $n = 3$) gave 6-ring lactams (**9**; $n = 3$). The formation of 2-piperidinone from the 5-aminopent-1-enes thus appears to be a stoichiometric analogue of the catalytic reactions reported in this paper. In addition, Krafft et al. [11] reported that a hindered alkenylamine **10**, closely related to **6**, failed to form the monodentate carbonyl complex (**8**; $n = 3$), also in agreement with our work.

The good correlation between the results of stoichiometric and catalysed systems did not extend to reactions involving the shorter chain 4-aminobut-1-ene (**11**).



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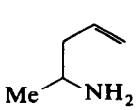

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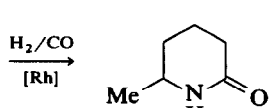

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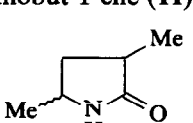
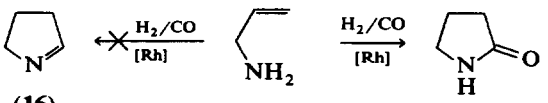


(13)

In contrast to the stoichiometric reaction which gave exclusively the pyrrolidinone (**9**; $n = 2$), reaction of **11** under our standard catalytic conditions gave a mixture of the 2-piperidinone (**12**) and the 2-pyrrolidinone (**13**) in ratio 70 : 30 and in good yield. It was shown that a sample of 2-piperidinone did not equilibrate when placed back under the reaction conditions. Thus the regiochemistry of stoichiometric and catalytic reactions appears to be controlled by different factors.

Interestingly, a recent paper has described the formation of dihydro-2-pyridones together with smaller amounts of 2-pyrrolinones from catalysed reactions of 3-butenamide with hydrogen and carbon monoxide [12].



(16) (14) (15)

Reactions of 3-aminoprop-1-ene (**14**) (allylamine or prop-2-en-1-amine) under similar conditions to those used previously only using benzene as a solvent gave 2-pyrrolidinone (**15**) as the exclusive product in excellent yield (86%). This result contrasts with the literature where a rhodium catalysed reaction of **14** in toluene gave an equimolar mixture of **15** and the pyrroline **16** and reaction in another solvent, dimethyl phthalate, gave only **16** [4].

Mechanistic comments

The mild conditions used in these rhodium catalysed reactions of unsaturated amines with hydrogen and carbon monoxide which give the products of carbonylation (and not hydroformylation), contrast with the severe conditions required to obtain the same products from carbonylation reactions in the absence of hydrogen. No conversion occurred when pure carbon monoxide was used in place of synthesis gas in attempted reactions of the 5-aminopent-1-enes (**1**). A low yield of lactam was obtained for a $[Rh(OAc)_2]_2$ catalysed reaction (**1**; $R^1 = Me$, $R^2 = R^3 = H$), using pure carbon monoxide but only at a higher temperature (70 °C). Use of the preformed metal hydride, $HRh(CO)(PPh_3)_3$, under similar reactions using carbon monoxide gave a significant yield of lactam but only at a significantly higher temperature (120 °C).

It thus appears that the transfer of the amino hydrogens during the reaction does not occur as readily as has been proposed [13] and that molecular hydrogen makes a significant direct contribution to the reaction. A reaction of (**1**; $R^1 = Me$, $R^2 = R^3 = H$) with deuterium and carbon monoxide gave a mixture of the diastereoisomeric 3,6-dimethyl-2-piperidinones in which the 3-methyl group was ca. 50% CH_2D and 50% CH_3 in support of this proposal.

Experimental

General

General conditions are as described previously [1,14].

Preparation of unsaturated amines

The following unsaturated amines were prepared by literature methods: hex-5-en-2-amine (**1**; $R^1 = Me$, $R^2 = R^3 = H$) [15]; 3-methylpent-4-en-1-amine (**1**; $R^1 = H$, $R^2 = Me$, $R^3 = H$) [16]; 5-methylhex-5-en-2-amine (**7**) [17]; and 6-methylhept-5-en-2-amine (**6**) [17,18]. 1-Phenylpent-4-en-1-one and 2-(prop-2-enyl)cyclohexanone were prepared by the method of Lorette and Howard [19]. These ketones were converted into their oximes [20] and reduced to 1-phenylpent-4-en-1-amine (**1**; $R^1 = Ph$, $R^2 = R^3 = H$) and *trans*-2-(prop-2-enyl)cyclohexylamine using sodium in ethanol [21]. *cis*-2-(Prop-2-enyl)cyclohexylamine [22], *N*,*N*-dimethylpent-4-en-1-amine (**5**)

[23] (using the method of Singh et al. [24]), pent-4-en-2-amine (**11**) [25], and but-3-en-1-amine [26] were prepared by literature methods.

Reactions of unsaturated amines with hydrogen and carbon monoxide *

*Hex-5-en-2-amine (**1**; $R^1 = Me$, $R^2 = R^3 = H$).* Rhodium(II) acetate dimer (0.0045 g, 0.0010 mmol), triphenylphosphine (0.010 g, 0.04 mmol) and (**1**; R^1 = Me, $R^2 = R^3$ = H) (0.20 g, 2.0 mmol) were reacted with carbon monoxide and hydrogen at 40 °C for 20 h according to the general procedure. The ^{1}H and ^{13}C NMR spectra of the crude product indicated that a 75 : 25 mixture of diastereoisomers was present. The crude product was obtained as a yellow frothy viscous liquid which was dissolved in ether (40 ml) and cooled (−30 °C) to precipitate the spent catalyst. The suspension was filtered through a Celite pad and the filtrate evaporated under reduced pressure to yield the product (0.23, 91%), free from most of the catalyst. 3,6-Dimethyl-2-piperidinone (**2**; R^1 = Me, $R^2 = R^3$ = H) was obtained analytically pure after sublimation of a portion of the ether washed product. Sublimed 40–50 °C/0.1 mmHg m.p. 60.7-61.0 °C (Found: C, 65.9; H, 10.4; N, 11.3. $C_7H_{13}NO$ calcd.: C, 66.1; H, 10.3; N, 11.0%). (Found: *M* 127.100 ± 0.001. $C_7H_{13}NO$ requires 127.099). ν_{max} 3289bs, 1660s, 1625s cm^{-1}. GLC (Conditions A): R_t 8.8 min (75%), 8.9 (25). ^{1}H NMR δ (300 MHz): 1.16, d, *J* 6.2 Hz, Me-C3(a); 1.19, d, *J* 6.2 Hz, Me-C3(b); 1.22, d, *J* 7.0 Hz, Me-C6(a); 1.25, d, *J* 7.0 Hz, Me-C6(b); 1.29–1.69, m, H4; 1.75–2.05, m, H5; 2.27, m, H3(a); 2.42, m, H3(b); 3.50, m, H6; 5.80, bs, NH. ^{13}C NMR δ (50 MHz): the major diastereoisomer **a** is quoted first; 17.10 Me(C6); 23.05 Me(C3); 29.29 (C5); 30.91 (C4); 35.83 (C6); 49.54 (C3); 175.28 (C2). **b**: 18.02 Me(C6); 22.94 Me(C3); 26.66 (C5); 27.30 (C4); 34.96 (C6); 48.52 (C3); 175.85 (C2). Mass spectrum: *m/z* 127(*M*, 41%), 112(100), 99(5), 84(10), 69(82), 56(54). Both the ^{1}H and ^{13}C NMR spectra indicated that a 75 : 25 mixture of diastereoisomers was present.

Similar reactions carried out at 50, 60 and 70 °C for 20 h gave similar yields (82–95%) of 3,6-dimethyl-2-piperidinone with an identical 75 : 25 diastereoisomeric ratio.

*3-Methylpent-4-en-1-amine (**1**; $R^1 = R^2 = H$, $R^3 = Me$).* Rhodium(II) acetate dimer (0.015 g, 0.034 mmol), triphenylphosphine (0.036 g, 0.14 mmol) and the amine (**1**, $R^1 = R^2$ = H, R^3 = Me) (0.67 g, 6.77 mmol) in ethyl acetate (10 ml) were reacted with carbon monoxide and hydrogen at 50 °C for 20 h according to the general reaction conditions. The solvent was evaporated and the crude product was dissolved in ether, cooled (−30 °C) and the spent catalyst which precipitated was filtered through a Celite pad. The lactam (**2**; $R^1 = R^2$ = H, R^3 = Me) was obtained analytically pure after slow sublimation (heating rate ca. 0.5 °/min) of a small amount of the washed product. (0.71 g, 83%) sublimed 45–50 °/0.1 mmHg m.p. the melt solidifies at 59 °C and remelts at 69.5–70.4 °C (Found: C, 65.8; H, 10.6; N, 11.3. $C_7H_{13}NO$ calcd.: C, 66.1; H, 10.3; N, 11.0%). ν_{max} 3283bs, 1660s cm^{-1}. GLC (Conditions B): R_t 9.2 min (54%), 9.6(46). ^{1}H NMR δ (300 MHz): the ^{1}H NMR spectrum is of the purified diastereoisomeric (ca. 50 : 50) mixture and thus the assignments are uncertain; 0.97, d, *J* 7.0 Hz and 1.06, d, *J* 6.3 Hz, Me-C4; 1.15, d, *J* 7.4 Hz and 1.26, d, *J* 7.3 Hz, Me-C3; 1.46–1.89, m, 1.95, pentet, *J* 7.1 Hz, 2.09,

* All reactions gave mixture of diastereoisomers. ^{1}H and ^{13}C NMR spectra of the diastereoisomers are identified as **a** and **b** where the spectra are distinguishable and where **a** refers to the major isomer.

m, *J* 5.0 Hz and 2.47, m, *J* 5.0 Hz, H5 and H6; 3.22–3.37, m, H3 and H4; 3.30, bs and 3.35, bs, NH. ^{13}C NMR δ (50 MHz): consistent with the ^{1}H NMR spectrum, the peak heights of the methyl signals also indicated a 1 : 1 diastereoisomeric ratio; 12.71, 15.28, 15.35, 20.24, (Me); 26.85, 30.03, 30.63, 34.54, (C5 and C6); 40.28, 40.51, 41.02, 43.49, (C3 and C4); 175.18, 175.94, (C2). Mass spectrum *m/z*: 127 (*M*, 60%), 112(44), 98(17), 86(7), 85(30), 84(26), 83(12), 82(8), 71(7), 70(8), 69(21), 57(14), 56(100), 55(40).

1-Phenylpent-4-en-1-amine (1; R^1 = Ph, $R^2 = R^3$ = H). Ethyl acetate (10 ml), rhodium(II) acetate dimer, (0.0195 g, 0.044 mmol), triphenylphosphine (0.046 g, 0.18 mmol) and 1-phenylpent-4-en-1-amine (**1**, R^1 = Ph, $R^2 = R^3$ = H) (1.42 g, 8.80 mmol) were reacted at 50 °C for 20 h. The crude product was dissolved in ether and cooled (−30 °C) to precipitate the spent catalyst which was filtered on a Celite pad. The ethereal solution was evaporated under reduced pressure to yield 3-methyl-6-phenyl-2-piperidinone (**2**; R^1 = Ph, $R^2 = R^3$ = H) as a 70 : 30 mixture of diastereoisomers as indicated by ^{1}H NMR spectroscopy on the crude product. A sample of the lactam was obtained analytically pure after sublimation at 95–100 °C/0.3 mmHg. (1.51 g, 91%) m.p. 107–121 °C lit. [27] [*cis*-isomer 131–132 °C] (Found: C, 76.5; H, 7.9; N, 7.4. $C_{12}H_{15}NO$ calcd.: C, 76.2; H, 8.0; N, 7.4%). ν_{max} 3289bs, 1651s cm^{-1}. ^{1}H NMR δ (300 MHz): the ^{1}H NMR spectrum is of the purified (70 : 30) diastereomeric mixture and most of the signals were not distinguishable; 1.20, d, *J* 7.1 Hz, Me; 1.46–1.80, m, H4; 1.96–2.19, m, H5; 2.37–2.61, m, H3; 4.51, m, H6(**a**); 4.60, m, H6(**b**); 5.80, bs, NH(**a**); 5.89, bs, NH(**b**); 7.27–7.42, m, Ph. ^{13}C NMR δ (50 MHz): major diastereoisomer, **a**; 17.15 (Me); 20.34, 32.60 (CH_2); 36.12 (C3); 58.71 (C6); *16.04* *, 128.04, *128.88* (Arom. CH); 142.63 (Arom. C); 175.46 (C2). Minor diastereoisomer, **b**: 17.97 (Me); 26.12, 29.34 (CH_2); 35.49 (C3); 57.26 (C6); *127.78*, 128.64, *128.78* (Arom. CH); 142.73 (Arom. C); 176.02 (C2). The ratio of the diastereoisomers as determined from the peak heights of the methyl signals in the ^{13}C NMR spectrum was also found to be 70 : 30. Mass spectrum *m/z*: 189 (*M*, 100%), 174(2), 161(36), 133(38), 119(14), 112(23), 106(94), 91(20), 83(23), 77(29), 69(35), 56(32), 51(18).

cis-2-(Prop-2-enyl)cyclohexylamine (1; $R^1 = R^2$ = cis-$(CH_2)_4$–, R^3 = H). Rhodium(II) acetate dimer (0.0024 g, 0.0054 mmol), triphenylphosphine (0.0057 g, 0.0022 mmol) and *cis*-2-(prop-2-enyl)cyclohexylamine (0.15 g, 1.10 mmol) in ethyl acetate (10 ml) were reacted with carbon monoxide and hydrogen at 50 °C for 20 h according to the general reaction conditions. The ^{1}H and ^{13}C NMR spectra of the crude product indicated the presence of a 50 : 50 diastereoisomeric mixture of 3-methyl-*cis*-octahydro-2-quinolinone (**2**; $R^1 = R^2$ = *cis*-$(CH_2)_4$–, R^3 = H). The crude product was dissolved in ether, and cooled (−30 °C) to precipitate the spent catalyst which was filtered through a Celite pad to yield the lactams (0.16 g, 89%). The lactams were obtained analytically pure after slow sublimation using a heating rate ca. 1 °C/min (110–125 °C/0.1 mmHg) on a small scale (ca. 10 mg). m.p. 88–95 °C (Found: C, 71.5; H, 10.5; N, 8.2. $C_{10}H_{17}NO$ calcd.: C, 71.8; H, 10.3; N, 8.4%). (Found: *M*, 167.130 ± 0.002. $C_{10}H_{17}NO$ calcd.: 167.131). ν_{max} 3190m, 1652s cm^{-1}. ^{1}H NMR δ (200 MHz): 1.22, d, 3H, *J* 7.0 Hz, 1.24, d, 3H, *J* 7.2 Hz, Me;

* The value in italics indicates a signal due to two equivalent carbon atoms.

1.39–1.82, m, 18H, CH_2(ring); 1.86–1.99, m, 2H and 2.11–2.52, m, 4H, CH_2(ring), CH(ring) and H4a; 3.35, m, 1H, $W_{h/2}$ 20.4 Hz and 3.58, q, 1H, *J* 3.7 Hz, H8a; 5.44, bs, 1H and 5.79, bs, 1H, NH. ^{13}C NMR δ (50 MHz): assignment of the signals for each of the diastereoisomers was not attempted; 17.13, 17.97 (Me); 20.31, 20.97, 24.02, 24.36, 25.63, 30.13, 30.93, 31.31, 31.56 (CH_2); 32.19, 32.59, 33.18 (CH); 34.42 (CH_2); 35.99 (CH); 52.27, 53.01 (C8a); 175.21, 175.85 (C2). Mass spectrum; *m/z* 167 (*M*, 24%), 166(3), 152(1), 139(2), 125(1), 124(100), 110(4), 97(4), 96(14), 83(4), 82(7), 81(7), 69(13), 68(11), 67(12), 57(6), 56(12), 55(11), 54(6).

A similar reaction conducted at 40 °C resulted in the recovery of the starting material (32% by GLC analysis) and the formation of the lactams in a 40% yield.

trans-*2-(Prop-2-enyl)cyclohexylamine (1; $R^1 = R^2$* = trans-*$(CH_2)_4$–, $R^3 = H$).* Rhodium(II) acetate dimer (0.0032 g, 0.0072 mmol), triphenylphosphine (0.0075 g, 0.29 mmol) and *trans*-2-(prop-2-enyl)cyclohexylamine (0.20 g, 1.43 mmol) in ethyl acetate (10 ml) were reacted at 50 °C for 20 h according to the general reaction conditions. The ^{1}H and ^{13}C NMR spectra of the crude reaction product indicated a ca. 50 : 50 diastereoisomeric mixture of the 3-methyl-*trans*-octahydro-2-quinolinone (**2**; $R^1 = R^2$ = *cis*-$(CH_2)_4$–, R^3 = H) was present. The crude product was washed with ether to precipitate the spent catalyst and the lactams were obtained analytically pure after sublimation at 120–130 °C/0.1 mmHg (0.19 g, 83%) m.p. 109 °C solid remelts 116–119 °C (Found: C, 71.8; H, 10.6; N, 8.1. $C_{10}H_{17}NO$ calcd.: C, 71.8; H, 10.3; N, 8.4%). ν_{max} 3187m, 1656s cm^{-1}. ^{1}H NMR δ (300 MHz): most of the signals were not distinguishable; 1.22, d, 3H, *J* 7.1 Hz and 1.28, d, 3H, *J* 7.5 Hz, Me; 1.23–1.89, m, 7H, CH_2(ring); 2.30–2.49, m, 1H and 2.49–2.63, m, 1H, H4a; 2.76–2.97, m, 2H, H8a; 5.71, bs, 1H and 5.78, bs, 1H, NH. There was also ca. 4% of the 3-methyl-*cis*-octahydro-2-quinolinone present (refer above). ^{13}C NMR δ (50 MHz): from the peak heights of the methyl signals, the ratio of the diastereoisomer was determined as 55 : 45 (a); 17.36 (Me); 22.26, *25.65* *, 30.79, 33.28 (CH_2); 35.38 (C3); 37.35 (CH_2); 40.46 (C4a); 58.31 (C8a); 175.24 (C2). (b): 19.68 (Me); 24.26, *25.76*, 30.93, 33.14 (CH_2); *35.38* (C3); 36.24 (CH_2); 36.77 (C4a); 57.87 (C8a); 176.03 (C2). Mass spectrum: *m/z* 167 (M, 4%), 166(2), 152(2), 147(2), 146(2), 136(3), 125(14), 24(10), 110(2), 96(3), 86(14), 85(10), 84(22), 83(14), 75(5), 74(60), 73(18), 61(14), 59(100).

A similar reaction conducted at 40 °C resulted in the recovery of the starting material (40% by GLC analysis), and the formation of the octahydroquinolinone (40% by GLC analysis; 33% isolated yield).

Attempted reactions of the 'hindered' aminoalkenes (5), (6) and (7)

N,N-*Dimethylpent-4-en-1-amine (5).* Attempted reactions of this amine using standard conditions but at higher temperatures gave starting material **5** as the major product at 60 °C (70%) and 70 °C (50%) and a complex mixture with a low mass recovery at 80 °C.

6-Methylhept-5-en-2-amine (6). (a) In benzene: Attempted reaction under the standard conditions in benzene at 120 ° gave recovered starting material (90%). (b) In ethyl acetate: Attempted reaction of the amine (0.3 g) using the standard reagents in ethyl acetate for 75 h at 120 °C gave starting amine **6** (14%) and *N*-(1,5-dimethyl-

* The value in italics is a tentative assignment.

hex-4-enyl)acetamide (0.21 g, 54%) after Kugelrohr distillation. b.p. (oven) 80–90 °C/0.35 mm (Found: C, 70.6; H, 10.9; N, 8.6. $C_{10}H_{19}NO$ calcd.: C, 71.0; H, 11.3, N, 8.3%). ν_{max} 3284s, 1652s cm^{-1}. GLC (Conditions A): R_t 11.3 min (97%). ^1H NMR δ (200 MHz): 1.09, d, 3H, J 6.7 Hz, Me-Cl; 1.35–1.53, m, 2H, J 7.4, 2.1 Hz, H3; 1.59 and 1.68, s, each 3H, Me-C5; 1.96, s, 3H, NHCO*Me*; 1.97–2.16, m, 2H, H2; 3.97, sextet, 1H, J 6.7 Hz, H1; 5.09, m, 1H, H4; 6.15, bs, 1H, NH. ^{13}C NMR δ (50 MHz): 20.86 Me(C5); 23.38 Me(C1); 24.69 (C3); 25.70 (NHCO*Me*); 36.81 (C2); 45.10 (C1); 123.77 (C4); 131.91 (C5); 169.61 (C=O). Mass spectrum: m/z 169 (M, 73%), 145(3), 131(13), 121(100), 118(23), 105(22), 91(13), 65(3), 51(8).

5-Methylhex-5-en-2-amine (7). (a) In benzene: Attempted reactions in benzene under the standard conditions at temperatures up to 120 °C gave recovered starting material as the major product. (b) In ethyl acetate: Reaction of the amine **7** (0.3 g) in ethyl acetate for 75 h at 120 °C gave *N*-(1,4-dimethylpent-4-enyl)acetamide (0.18 g, 44%) after distillation b.p. (oven) 80 °C/0.3 mmHg (Found: C, 69.8; H, 10.8; N, 8.6, $C_9H_{17}NO$ calcd.: C, 69.6; H, 11.0; N, 9.0%). ν_{max} 3281bs, 1651s cm^{-1}. ^1H NMR δ (200 MHz): 1.14, d, 3H, J 6.4 Hz, Me-C1; 1.46–1.66, m, 2H, H3; 1.71, s, 3H, Me-C4; 1.94, s, 3H, NHCO*Me*; 1.98–2.22, m, 2H, H2; 3.97, sextet, 1H, J 6.7 Hz, H1; 4.68, s, 1H, H5; 4.71, s, 1H, H5′; 5.80, bs, 1H, NH. ^{13}C NMR δ (50 MHz): 20.85, 22.52, 23.46 (Me); 34.19, 34.79 (CH_2); 45.17 (C1); 110.05 (C5); 145.28 (C4); 164.48 (C=O). Mass spectrum: m/z 155 (M, 1%), 154(5), 140(4), 126(5), 112(17), 99(12), 96(60), 87(24), 86(100), 81(68), 72(21), 60(24), 58(18), 57(36), 55(14).

Similar reactions conducted at either lower temperatures and/or shorter reaction times resulted in similar mixtures with starting material **7** also present.

*Reactions of hex-5-en-2-amine (**1**; $R^1 = Me$, $R^2 = R^3 = H$) using different catalysts and reaction gases*

Use of diphosphine ligands

(1) Rhodium catalysts. Bis[chlorodicarbonylrhodium(I)], phosphine ligand [(−)-BINAP, (−)-BPPM, (−)-Chiraphos or (−)-DIOP] and hex-5-en-2-amine in the ratio 1 : 2 : 300 in benzene were reacted with carbon monoxide and hydrogen (400 p.s.i.) at 60 °C for 20 h. After cooling, a sample of the contents of the autoclave was analysed by GLC (Conditions A) to determine the proportion of unreacted amine. Isomeric ratios were estimated from the ^1H NMR spectrum and the ratio of the peak heights of methyl signals in the ^{13}C NMR spectrum and are quoted in Table 2.

(2) Platinum catalysts. The platinum catalyst ([(−)-BPPM]$PtCl_2$, [(−)-Chiraphos]$PtCl_2$ or [(−)-DIOP]$PtCl_2$), tin(II) chloride dihydrate and hex-5-en-2-amine in the ratio 1 : 2 : 300 in benzene (7 ml) were reacted with carbon monoxide and hydrogen (400 p.s.i.) for 20 h at temperatures ranging from 60 to 80 °C. All reactions showed recovered amine.

Use of different reaction gases

Using rhodium(II) acetate dimer. All reactions used rhodium(II) acetate dimer, triphenylphosphine and hex-5-en-2-amine in the ratio 1 : 4 : 200 in ethyl acetate (7 ml). A reaction with carbon monoxide only (400 p.s.i.) at 70 °C for 20 h showed starting amine as the major component (70%). After the usual work-up procedure, 3,6-dimethyl-2-piperidinone (**2**; $R' = Me$, $R^2 = R^3 = H$) isolated as a 75 : 25 mixture of diastereoisomers (0.12 g, 26%).

Reaction with carbon monoxide (200 p.s.i.) and deuterium (200 p.s.i.) for 20 h at 70 °C gave the lactam (**2**; R^1 = Me, R^2 = R^3 = H) as a white solid (68%). The ^{1}H NMR spectrum was identical to that reported for 3,6-dimethyl-2-piperidinone, except for the methyl region, < 1.3 ppm. The ^{13}C NMR spectrum suggested that a 50 : 50 mixture of deuterated and non-deuterated lactams was present, each as a 75 : 25 diastereoisomeric mixture. The signals relevant only to deuterated compound have been reported. ^{13}C NMR δ (50 MHz): **a**; 16.44, 16.83, 17.22, t, *J* 19.6 Hz, (CH_2-D); 23.01 Me(C3); 29.25 (C5); 30.88 (C4); 35.74 (C6); 49.52 (C3); 175.34 (C2). **b**: 17.35, 17.74, 18.12, t, *J* 18.5 Hz, (CH_2-D); 22.81 Me(C6); 26.64 (C5); 27.27 (C4); 34.87 (C6); 48.50 (C3); 175.93 (C2). ^{2}H NMR δ (46 MHz): 1.23 (CH_2-D). Mass spectrum: *m/z* 129[*M*(^{2}H + 1), 5%], 128[*M*(^{2}H) or *M*(^{1}H + 1), 33], 127[*M*(^{1}H), 45], 126(7), 114(10), 113(78), 112(100), 100(3), 99(5), 85(7), 84(10), 72(8), 71(11), 70(56), 69(79), 57(33), 56(52), 55(33).

A similar reaction conducted at 50 °C for 20 h resulted in the isolation of a similar mixture, but starting amine (6% by GLC analysis), was also recovered.

Using hydridocarbonyltris(triphenylphosphine)rhodium(I). Hydridocarbonyltris-(triphenylphosphine)rhodium(I) (0.0046 g, 0.0051 mmol), triphenylphosphine (0.0026, 0.010 mmol) and hex-5-en-2-amine (0.15 g, 1.52 mmol) in benzene (7 ml) were reacted with carbon monoxide (400 p.s.i.) at 120 °C for 20 h. GLC analysis of the crude reaction mixture indicated the presence of 30% of starting amine. After the usual work-up procedure, both diastereoisomers of 3,6-dimethyl-2-piperidinone were obtained in the ratio 75 : 25, (0.10 g, 52%).

Using dodecacarbonyltetrarhodium(I). A mixture of dodecacarbonyltetrarhodium(I) (0.0045 g, 0.0061 mmol) and hex-5-en-2-amine (0.12 g, 1.21 mmol) in benzene (10 ml) was reacted with carbon monoxide and hydrogen with no added ligand at 60 °C for 20 h and gave products as in Table 2.

Reaction of prop-2-en-1-amine (allylamine) (14)

Rhodium(II) acetate dimer (0.0058 g, 0.013 mmol), triphenylphosphine (0.0138g, 0.053 mmol) and prop-2-en-1-amine (**14**) (0.15 g, 2.63 mmol) in benzene (10 ml) were reacted with carbon monoxide and hydrogen at 70 °C for 20 h. The ^{1}H and ^{13}C NMR spectra of the crude reaction mixture indicated 2-pyrrolidinone (**15**) was the only product present with minor signals probably due to polymerised starting material. Kugelrohr distillation afforded 2-pyrrolidinone (**15**) as a colourless liquid. (0.19 g, 86%) b.p. (oven) 50 °C/0.2 mmHg ν_{max} 3250bs, 1650s cm^{-1}. ^{1}H NMR δ (200 MHz): 2.10, m, 2H, *J* 7.0 Hz, H4; 2.28, t, 2H, *J* 7.2 Hz, H3; 3.38, t, 2H, *J* 7.0 Hz, H5; 6.50, bs, NH. ^{13}C NMR δ (50 MHz): 20.74 (C4); 30.28 (C3); 42.40 (C5); 179.49 (C2). Mass spectrum: *m/z* 86 (*M* + 1, 16%), 85 (*M*, 100), 84(22), 70(8), 69(4), 68(4), 57(20), 56(7). The spectroscopic data are in good agreement with reported literature data [28,29].

Similar reactions conducted at 50 ° and 60 ° resulted in a low mass recovery of **15** (ca. 0.0035 g), suggesting that unreacted prop-2-en-1-amine (**14**) was lost in the work-up procedure.

Reaction of pent-4-en-2-amine (4-aminobut-1-ene) (11)

Rhodium(II) acetate dimer (0.0088 g, 0.020 mmol), triphenylphosphine (0.021 g, 0.080 mmol) and pent-4-en-2-amine (**11**) (0.34 g, 4.0 mmol) in ethyl acetate (10 ml) were reacted with carbon monoxide and hydrogen at 50 °C for 20 h in accordance

with the general reaction procedure. Both the ^{1}H and ^{13}C NMR spectra of the crude product indicated that 6-methyl-2-piperidinone (**12**) and 3,5-dimethyl-2-pyrrolidinone (**13**) were present in the ratio 75 : 25, the latter present as a 50 : 50 mixture of diastereoisomers. The products were separated from the catalyst using preparative TLC (Silica; ether/light petroleum, 1 : 1). An attempt to separate the compounds using preparative TLC (Silica) and a solvent gradient starting with ether, graded to ether/ethanol (1 : 1) was partly successful. The spectral data quoted are those of the purified mixture. (0.36 g, 80%) m.p. 67.7–78.0 °C (Found: C, 63.6; H, 10.1; N, 12.1. $C_6H_{11}NO$ calcd.: C, 63.7; H, 9.8; N, 12.4%). ν_{max} 3189s, 3074s, 1634m cm^{-1}.

6-Methyl-2-piperidinone (12) m.p. 77.7–80 °C (lit. [30] 79–80.5 °C) ^{1}H NMR δ (200 MHz): 1.19, d, 3H, J 6.4 Hz and 1.37, dd, 1H, J 11.6, 2.0 Hz, H3: 1.56–1.81, m, 1H and 1.81–2.01, m, 2H, H4 and H5; 2.39–2.63, m, 1H, H6; 6.39, bs, 1H, NH. ^{13}C NMR δ (50 MHz): 19.79 (Me); 22.77, 30.39, 30.95 (CH_2); 48.74 (C6); 172.39 (C2).

3,5-Dimethyl-2-pyrrolidinone (13). Only a small amount of **13** was separated, thus the poor signal to noise ratio prevented an accurate determination of splitting patterns. ^{1}H NMR δ (200 MHz): 1.14–1.28, dd (overlapping), 6H, J 7.7, 1.7 Hz, Me; 1.62–1.87, dd, 2H, J 8.0, 5.8 Hz, H4; 2.39–2.61, m, 1H, H3; 3.60–3.81, m, 1H, H5; 5.80, bs, 1H, NH. ^{13}C NMR δ (50 MHz): all signals were doubled up due to the presence of the two diastereoisomers; 15.97, 16.14 Me(C5); 22.08, 22.15 Me(C3); 35.28, 37.24, 37.28, 38.83 (CH_2); 47.66, 48.02 (C5); 180.53, 180.81 (C2).

Mass spectrum: m/z [(**12**) and (**13**)] 113(M, 15%), 112(2), 99(5), 98(100), 85(4), 70(10), 57(13), 56(5), 55(88).

Reaction of but-3-en-1-amine

Reaction of but-3-en-1-amine (0.15 g) under the standard conditions gave a mixture of 2-pyrrolidinone and 3-methyl-2-piperidinone as a 70 : 30 mixture. Spectral data were obtained on the purified mixture after preparative TLC (Alumina; ether). (0.13 g, 63%) ν_{max} 3450bs, 1700m, 1634bs cm^{-1}.

2-Piperidinone ^{1}H NMR δ (200 MHz): 1.23–1.56, m, 4H, H4 and H5; 1.82–2.04, m, 2H, H3; 2.76–3.01, m, 2H, H6; 7.80, bs, 1H, NH. ^{13}C NMR δ (50 MHz): 20.86 (C4); 22.24 (C5); 31.46 (C3); 42.05 (C6); 172.85 (C2).

3-Methyl-2-pyrrolidinone ^{1}H NMR δ (200 MHz): 1.18, d, 3H, J 6.8 Hz, Me; 1.50–1.79, m, 4H, H4 and H5; 2.32–2.40, m, 1H, H3; 7.50, bs, 1H, NH. ^{13}C NMR δ (50 MHz): 15.86 (Me); 29.77 (C4); 36.01 (C3); 40.33 (C5); 181.79 (C2). Mass spectrum: m/z 100(7%), 99(M + 1, 100), 98(M, 16), 84(3), 71(8), 70(11), 56(50). The spectroscopic data was in good agreement with the literature data [31].

Attempted equilibration of 2-piperidinone

Rhodium(II) acetate dimer (0.0033 g, 0.0076 mmol), triphenylphosphine (0.0079 g, 0.030 mmol) and a commercial sample of 2-piperidinone (0.15 g, 1.51 mmol) in ethyl acetate (7 ml) were reacted at 50 °C for 20 h with carbon monoxide and hydrogen as described in the general procedure. Analysis by GLC, ^{1}H and ^{13}C NMR spectroscopy indicated that the starting material was recovered unchanged.

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