

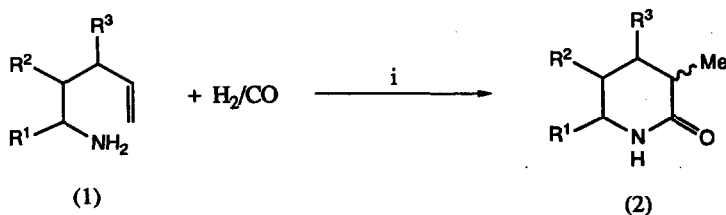
A NEW SYNTHESIS OF PIPERIDINONES FROM RHODIUM CATALYSED REACTIONS OF UNSATURATED AMINES WITH HYDROGEN AND CARBON MONOXIDE

Despina Anastasiou and W. Roy Jackson*

Department of Chemistry, Monash University, Clayton, Victoria 3168, Australia.

Reactions of 5-aminopent-1-enes with hydrogen and carbon monoxide in the presence of a rhodium catalyst give piperidinone derivatives as the only products in high yields under very mild reaction conditions.

Recent work¹ has shown reactions of *ortho*-propenylbenzenamines under hydroformylation conditions are dominated by steric effects and 7-membered ring benzazepine derivatives are the major products. There was evidence that the aniline nitrogen was exerting some chelation control which in the absence of steric effects leads to hydroformylation at the internal carbon atom of the alkene resulting in the formation of dihydroquinoline derivatives. We now report that the reactions of a series of 5-aminopent-1-enes (1) under similar conditions give piperidinones (2) as the exclusive products.

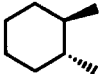
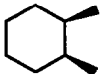


Scheme Synthesis of piperidinones (2). Reagents i, [Rh(OAc)₂]₂, PPh₃

The more nucleophilic nitrogen atom in the aliphatic amines now not only leads to exclusive formation of the six-membered ring compounds but the products now arise from carbonylation rather than hydrocarbonylation reactions. The product distribution was now insensitive to steric effects, in that reaction occurred exclusively at the internal carbon atom even when the alkene had an allylic methyl substituent. The regioselectivity thus appears to be dominated by chelation control by the amino group.

The yields of lactams formed under these mild conditions (40-50°, 400 p.s.i., CO/H₂) were excellent (80-95%) (see Table) and contrast with previously reported cobalt catalysed carbonylation reactions of unsaturated amines which required severe conditions (125-300°, 870-4400 p.s.i.).² Ruthenium and rhodium based catalysts were reported to be even less reactive.² The exclusive formation of lactams from carbonylation reactions contrasts with intermolecular rhodium-catalysed reactions of alkenes, amines, carbon monoxide and hydrogen which give mainly saturated amines derived from hydroformylation reactions.³

Table: Yields of products from reactions of 5-aminopent-1-enes with hydrogen and carbon monoxide^a

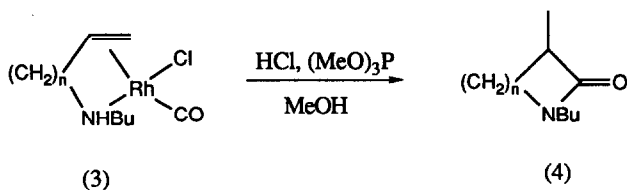
Entry	Reactant (1)			Yield of piperidinone (2) ^b
	R ¹	R ²	R ³	
1	Me	H	H	95
2	Ph	H	H	91
3			H	83
4			H	89
5	H	H	Me	83

a Reactions were carried out in a Parr autoclave using ethyl acetate solutions of the unsaturated amine(1), [Rh(OAc)₂]₂ and PPh₃ in the ratio 200:1:4 and H₂/CO (1:1) at an initial pressure of 2760 kPa (400 p.s.i.) for 20 h at 50 . All new compounds gave satisfactory analyses.

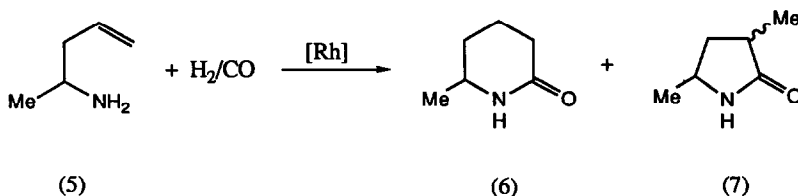
b The lactams were formed as mixtures of diastereoisomers *ca.* 1:1 (determined from their ¹³C n.m.r. spectra) which could not be separated.

Recent work has shown that rhodium(III) intermediates in which the rhodium atom is coordinated to the amino nitrogen can be isolated from reactions of unsaturated amines with stoichiometric amounts of [Rh(CO)₂Cl]₂.⁵ These compounds are readily converted into amino esters or lactams on treatment with hydrochloric acid and trimethylphosphite in methanol.⁶

The regiochemistry of these reactions was dictated by the formation of the new carbon-carbon bond at the most substituted carbon atom. Thus 4-aminobut-1-enes (3; $n=2$) gave 5-ring lactams (4; $n=2$) and 5-aminopent-1-enes (3; $n=3$) gave 6-ring lactams (4; $n=3$).



In order to see if similar regiocontrol was operative in our metal catalysed reactions, 4-amino-1-pentene (5) was reacted under the standard conditions. The piperidinone (6) and the pyrrolidinone (7) were formed in the ratio 70:30 in good yield (80%). The isomers (6) and (7) were shown not to equilibrate under the reaction conditions and thus different factors appear to control the regiochemistry of stoichiometric and catalytic reactions.



No reaction was observed under our reaction conditions when pure carbon monoxide was used instead of synthesis gas. Some lactam was formed when preformed metal hydride $\text{HRh}(\text{CO})(\text{PPh}_3)_3$ was used as a catalyst precursor in the absence of hydrogen, but only at a significantly higher temperature (120°). Only starting material was recovered from an attempted reaction at 50° . It thus appears that hydrogen gas is playing a major role in these reactions and the amino hydrogens may not be as readily available as has been proposed.⁴ A reaction of (1) ($\text{R}^1 = \text{Me}$, R^2 and $\text{R}^3 = \text{H}$) with deuterium and carbon monoxide gave a mixture of the diastereoisomeric 3,6-dimethyl-2-piperidinones (2; $\text{R}^1 = \text{Me}$; R^2 and $\text{R}^3 = \text{H}$) in which significant incorporation of a single deuterium into the 3-methyl group had occurred.

Attempts to control the diastereoselectivity of the reaction involved replacement of triphenylphosphine by several bidentate diphosphines. The use of 1,4-diphosphines, diop, binap, and bppm⁷ led to good yields of the piperidinone (2; $\text{R} = \text{Me}$; R^2 and $\text{R}^3 = \text{H}$) but with no significant improvement in the ratio of diastereoisomers. Use of the 1,2-diphosphine, chiraphos led to recovery of starting material in agreement with the observation that metal complexes containing 5-ring chelates are frequently poor catalysts in organometallic chemistry.⁸

We thank the Department of Education for the award of a postgraduate scholarship (to D.A.), the Australian Research Council for support, and Johnson Matthey Ltd. for a loan of rhodium.

References

1. D. Anastasiou and W.R. Jackson, submitted for publication.
2. J. Falbe and F. Korte, *Chem. Ber.*, 1965, 1928.
3. F. Jachimowicz and J.W. Raksis, *J. Org. Chem.*, 1982, 47, 445.
4. 'New Syntheses with Carbon Monoxide', Ed. J. Falbe Springer-Verlag, 1980, p.418.
5. M.E. Krafft, L.J. Wilson and K.D. Onan, *Organometallics.*, 1988, **7**, 2528.
6. M.E. Krafft, L.J. Wilson and K.D. Onan, *Tetrahedon Lett.*, 1988, 6421.
7. Obtained from Aldrich Chemical Company Inc.
8. P.S. Elmes and W.R. Jackson, *Aust. J. Chem.*, 1982, **35**, 2041.

(Received in UK 5 June 1990)