probable unsymmetric nature of the π-complex[25] may render the converse true.[26]

We continue to investigate the mechanism, generality and synthetic utility of this new regioselective rearrangement.

Acknowledgment. R.S.B. thanks Professor Charles P. Casey for helpful discussions and suggestions and the NSF for partial support under its EPSCOR program.

Registry No. 1, 92471-94-8; 2, 92471-96-0; 3, 92471-97-1; 3 deuterated isomer, 92471-98-2; 4, 92472-00-9; 4 deuterated isomer, 92472-02-1; 5, 823-02-9.

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Novel Catalytic and Stoichiometric Approaches to Azetidine-2,4-diones from α-Lactams Using Rhodium and Cobalt Complexes, Respectively

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Summary: Although α-lactams are regiospecifically converted to azetidine-2,4-diones in fine yields with use of rhodium(I) [e.g., $[Rh(CO)_2Cl]_2$] and cobalt(0) [e.g., $Co_2(CO)_8$] complexes, the two processes are significantly different: the rhodium reaction occurs under carbon monoxide and is catalytic; the cobalt reaction is inhibited by carbon monoxide and is not catalytic.

Transition-metal organometallics are useful reagents and catalysts for the synthesis and manipulation of heterocyclic nitrogen compounds.[1-3] Recently, one of us reported the first example of ring expansion and carbonylation of an aziridine to a β-lactam, using chlorodicarbonylrhodium(I) dimer as the catalyst.[4] What would be the consequence of a significant structural change in the aziridine moiety? α-Lactams (aziridinones) (1) are fascinating strained ring systems[5] that are easy to synthesize[6] and undergo some interesting organic transformations.[5,7] If one were to attempt to carbonylate such a reactant, then ring expansion or ring cleavage may take place. In the event that the four-membered ring compound is formed, then the question arises as to whether the azetidine-2,4-dione(2) or azetidine-2,3-dione (3) or both will be produced in the metal(I)-catalyzed reactions. While some elegant work has been published on carbonylation reactions involving amides as reactants (i.e., amidocarbonylation),[8,9] there have been no publications on the carbonylation of α-lactams. This communication describes the regiospecific, catalytic rhodium(I) and the stoichiometric cobalt(0), ring expansion of α-lactams. Although the products are the same in both cases, there are fundamental differences using the two types of metal complexes.

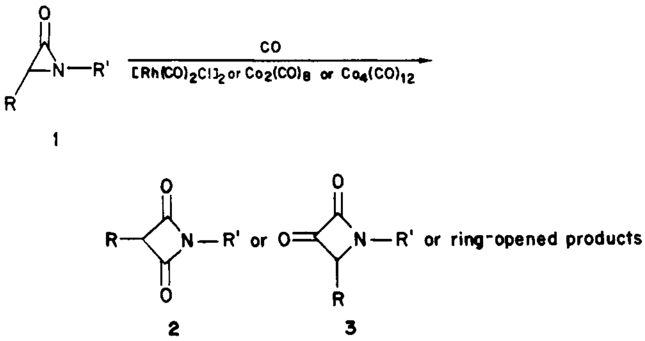
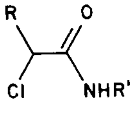


Table I. Yields of Azetidine-2,4-diones Obtained from the Rhodium(I)-Catalyzed or the Cobalt(0)-Induced Carbonylation of 1[a]

2, R =, R′ =	ML_n	yield,[b] %	mp, °C
$(CH_3)_3C$, $(CH_3)_3C$	$[Rh(CO)_2Cl]_2$	100	38-40
	$[1,5\text{-HDRhCl}]_2$	70	
	$[1,5\text{-CODRhCl}]_2$	75	
	$Co_2(CO)_8$	90	
	$Co_4(CO)_{12}$	84	
$(CH_3)_3C$, 1-adamantyl	$[Rh(CO)_2Cl]_2$	51	75-85
	$Co_2(CO)_8$	51	
1-adamantyl, $(CH_3)_3C$	$[Rh(CO)_2Cl]_2$	90	68-70
1-adamantyl, 1-adamantyl	$[Rh(CO)_2Cl]_2$	80	200-204
	$Co_2(CO)_8$	95	
	$Co_4(CO)_{12}$	100	

[a] Satisfactory C, H, N analyses were obtained in all cases. [b] Yields are of pure materials.

When 1,3-di-*tert*-butylaziridinone [1, R = R′ = $(CH_3)_3C$][6] was reacted with carbon monoxide and a catalytic amount of chlorodicarbonylrhodium(I) dimer [10:1 ratio of 1/Rh(I)] in dry benzene at 40 °C and 30 atm (overnight), the azetidine-2,4-dione [2, R = R′ = $(CH_3)_3C$] was obtained in quantitative yield. This transformation can also be achieved at atmospheric pressure, but it is a slower reaction. Other rhodium(I) catalysts can be used including the dimers of chloro(1,5-hexadiene)rhodium(I) and chloro(1,5-cyclooctadiene)rhodium(I); however, the rhodium(0) complex $Rh_6(CO)_{16}$ and tetrakis(triphenylphosphine)palladium(0) were inert. The use of dry benzene must be stressed, since the presence of any water results in conversion of some of the α-lactam to the chloro amide 4.[10]



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Fine yields of azetidine-2,4-diones (2) were obtained by using a number of other α-lactams as substrates. The

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[10] A very acidic solution (pH 2) is formed on treatment of $[Rh(CO)_2Cl]_2$ with water (or wet benzene). It is known that α-chloro amides are obtained on reaction of α-lactams with hydrochloric acid.[2,4] If one assumes that HCl is the acidic species formed when the rhodium catalyst reacts with water, the acid would convert 1 to 4 [the use of stoichiometric quantities of the rhodium(I) complex results in complete conversion of 1 to 4]. The presence of water in effect poisons the rhodium(I) catalyst.

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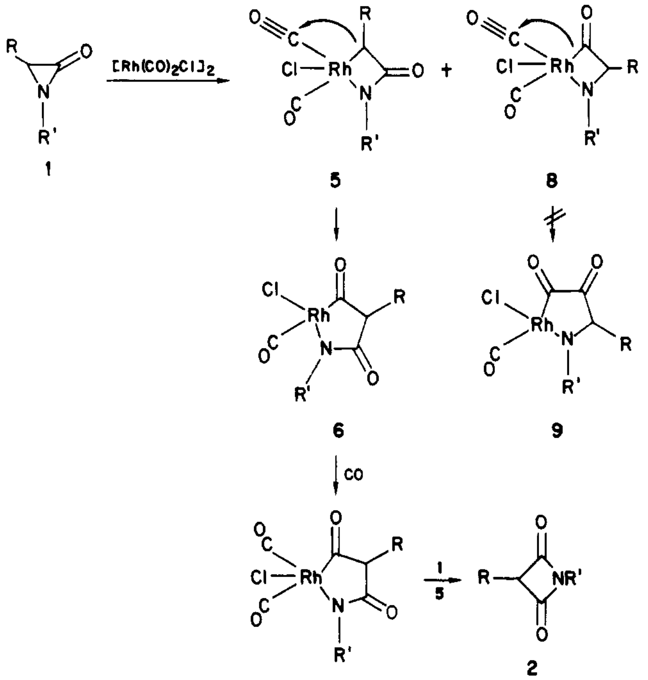
Table II. Pertinent Spectral Properties for 2

2, R =, R' =	IR ν_{CO}, cm^{-1}	NMR, δ ^{1}H	NMR, δ ^{13}C	MS, *m/e* [M$^+$]	MS, *m/e* ketene fragment
$(CH_3)_3C$, $(CH_3)_3C$	1725	1.08 (s, 9 H, $(CH_3)_3C$), 1.47 (s, 9 H, $(CH_3)_3CN$), 3.23 (s, 1 H, CH)	26.98 (methyls of $(CH_3)_3C$ attached to ring carbon), 27.77 (methyls of $(CH_3)_3CN$), 31.64 $[(CH_3)_3\mathit{C}]$, 56.36 $[(CH_3)_3\mathit{C}N]$, 69.51 (CH), 170.72 (CO)	197	98
$(CH_3)_3C$, 1-adamantyl	1725	1.10 (s, 9 H, $(CH_3)_3C$), 1.67–2.17 (m, 15 H, adamantyl protons), 3.23 (s, 1 H, CH)		275	98
1-adamantyl, $(CH_3)_3C$	1725	1.45 (s, 9 H, $(CH_3)_3C$), 1.65–2.17 (m, 15 H, adamantyl protons), 3.06 (s, 1 H, CH)		275	176
1-adamantyl, 1-adamantyl	1725	1.67–2.17 (m, 30 H, adamantyl protons), 3.08 (s, 1 H, CH)	27.03 (methyls of $(CH_3)_3C$), 28.94 (methine carbons of adamantyl group), 35.91 (three methylene carbons of adamantyl group), 40.07 (three methylene carbons attached to carbon bearing nitrogen), 57.80 (CN), 69.40 (CH), 170.70 (CO)	353	176

yields for the products are listed in Table I, and pertinent spectral data is presented in Table II. The azetidine-2,4-diones were identified on the basis of analytical and spectral data including a carbonyl stretching absorption in the infrared region at 1725 cm^{-1},[11] a methine proton signal at δ 3.06–3.23 in the proton magnetic resonance spectrum and one carbonyl carbon resonance at δ 170.70–170.72, and a molecular ion peak in the mass spectrum and an abundant ketene fragment.[12]

A possible mechanism for the ring expansion reaction is outlined in Scheme I. Insertion of rhodium(I) into the saturated carbon–nitrogen bond of **1** would give **5** which on ligand migration to **6**, followed by addition of carbon monoxide (**7**) and reductive elimination, would afford the azetidine-2,4-dione **2**. This mechanism is analogous to that proposed for the conversion of aziridines to β-lactams.[4]

Scheme I



Why is no azetidine-2,3-dione **3** formed in these reactions? Let us assume that rhodium(I) could insert into the carbonyl carbon–nitrogen bond of the α-lactam, giving the rhodium(III) complex **8**. The next step, ligand migration to **9**, would result in the formation of an α-dicarbonyl compound. In 1977, we[13] described the first example of a metal (cobalt carbonyl) and phase-transfer-catalyzed double-carbonylation reaction, whereby *o*-methylbenzyl bromide is carbonylated to an alkylated α-keto acid. It was proposed[14] that the insertion (ligand migration) of the second carbon monoxide occurs into a vinyl carbon–cobalt bond [i.e., of an enol] and not into a carbonyl carbon–metal bond. Subsequent studies by others[15,16] support this mechanism. Similarly, two groups have reported on the organopalladium complex catalyzed carbonylation of halides to α-keto amides in the presence of secondary amines.[17,18] Mechanistic studies by Sen[19] and Yamamoto[20,21] and their co-workers indicate that the palladium-catalyzed reaction does not proceed via direct double carbonylation; rather, reductive elimination occurs from a palladium intermediate bearing acyl and amide ligands. These results suggest that the conversion of **8** to

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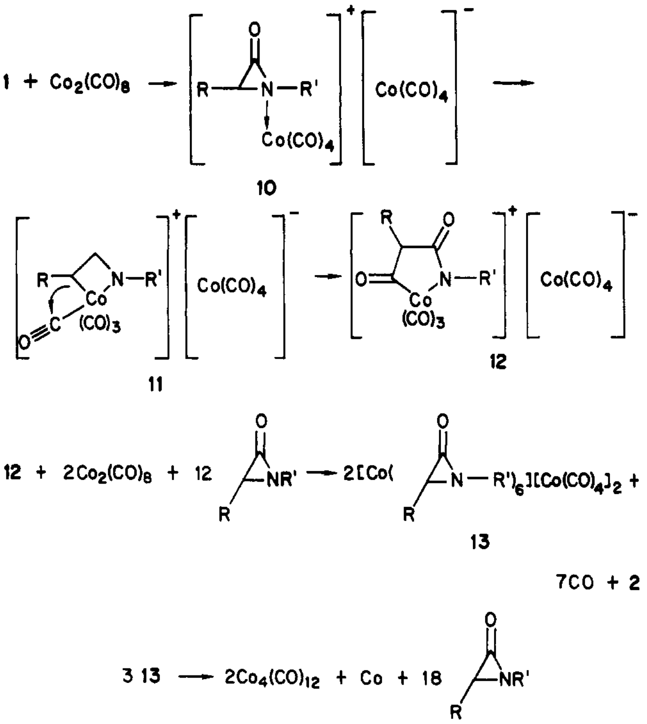
Scheme II



9 would be an unfavorable process.

Cobalt complexes are capable of inducing some interesting heterocycle forming reactions including the cyclopentadienylcobalt dicarbonyl catalyzed photolytic cocyclization of alkynes with α,ω-cyanoalkynes or isocyanatoalkynes to give annulated pyridines[22] or 5-indolizinones,[23] respectively, the cyclocarbonylation of Schiff bases catalyzed by cobalt carbonyl,[24] and the synthesis of indoles from azirines and cobalt carbonyl.[25] We anticipated that cobalt carbonyls would, like rhodium(I) complexes, catalyze the carbonylation of α-lactams to azetidine-2,4-diones. While carbonylation does indeed occur there are, as noted above, significant differences in the behavior of the cobalt and rhodium complexes toward α-lactams.

Exposure of 1,3-di-*tert*-butylaziridinone [1, R = R' = $(CH_3)_3C$] to an equimolar amount of dicobalt octacarbonyl in benzene, overnight at 65 °C and under a nitrogen atmosphere, affords 2, R = R' = $(CH_3)_3C$, in 90% yield. A byproduct was tetracobalt dodecacarbonyl [intense carbonyl stretching bands at 2060 and 1860 cm^{-1}–identical spectrum with that of authentic $Co_4(CO)_{12}$].[26] It is known that dicobalt octacarbonyl, on heating at 60 °C in hydrocarbon solvents, is converted to tetracobalt dodecacarbonyl, thus raising the possibility that the metal cluster may be the active reagent for the carbonyl insertion process.[27]

Either $Co_2(CO)_8$ or $Co_4(CO)_{12}$ are effective reagents for the production of azetidine-2,4-diones from several other α-lactams (Table I). Note that, as in the case of rhodium, the ring expansion process is a completely regiospecific one (i.e., 3 was not formed).

The stoichiometric cobalt carbonyl reaction affording azetidine-2,4-diones can be accounted for by the pathway outlined in Scheme II (illustrated for $Co_2(CO)_8$). The α-lactam may function as a Lewis base, inducing disproportionation of cobalt carbonyl to complex **10**. Such reactions have been observed previously for a variety of Lewis bases including the amide dimethylformamide.[28] The cationic portion of **10** can rearrange to the metallacycle **11** and undergo ligand migration affording **12**. Reaction of the latter with additional cobalt carbonyl and α-lactam would give the product, a new complex **13**, and carbon monoxide. Collapse of **13** would generate $Co_4(CO)_{12}$, the reaction byproduct. The conversion of related complexes (e.g., of aniline[29] and *tert*-butyl alcohol[30]) to $Co_4(CO)_{12}$ has been described before. An analogous scheme can be written utilizing $Co_4(CO)_{12}$ as the reactant.

It is important to note that use of a carbon monoxide instead of a nitrogen atmosphere retards the cobalt reactions, while the rhodium(I) reactions occur in a facile manner under CO. This may be due to the fact that the presence of carbon monoxide would inhibit the azetidine-2,4-dione forming step in the reaction scheme. Consequently, the process is not catalytic with respect to cobalt, in direct contrast to the rhodium(I) reaction. Therefore, irrespective of other mechanistic details, the pathways for the cobalt and rhodium reactions are different.

The following general procedure was used. Rhodium—a mixture of the α-lactam (0.9–4.0 mmol) and the rhodium(I) catalyst [10:1 ratio of 1/Rh(I)] in benzene (10–25 mL) was reacted overnight with carbon monoxide at 40 °C and 30 atm (alternatively, carbon monoxide was bubbled through the solution at 40 °C and 1 atm for 2–4 days). The solution was filtered, and concentration of the filtrate gave crude 2. Pure azetidine-2,4-dione was obtained by column or thin-layer chromatography (silica gel) with hexane–ethyl acetate (4–9.5/1.0) as the eluant or developing agent, respectively. Cobalt—the α-lactam (0.4–3.6 mmol) and either $Co_2(CO)_8$ [equimolar] or $Co_4(CO)_{12}$ in dry benzene (5–15 mL) was stirred overnight at 65 °C (nitrogen atmosphere). Workup was affected in the same manner as described for the rhodium reactions.

In summary, novel catalytic and stoichiometric ring expansion reactions of α-lactams to azetidine-2,4-diones have now been observed. While photochemical routes to these compounds by ring contraction are known,[11] the present reaction is the first approach to such heterocycles by ring expansion using carbon monoxide. Azetidine-2,4-diones are of considerable pharmacological interest. For example, several such compounds are useful hypnotic-inducing drugs.[31]

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Registry No. 1 (R = R' = *t*-Bu), 14387-89-4; 1 (R = *t*-Bu; R' = 1-Ad), 62993-79-7; 1 (R = 1-Ad; R' = *t*-Bu), 16664-32-7; 1 (R = R' = 1-Ad), 17385-51-2; 2 (R = R' = *t*-Bu), 92014-33-0; 2 (R = *t*-Bu; R' = 1-Ad), 92014-34-1; 2 (R = 1-Ad; R' = *t*-Bu), 92055-19-1; 2 (R = R' = 1-Ad), 92014-35-2; $[Rh(CO)_2Cl]_2$, 14523-22-9; $[1,5\text{-HDRhCl}]_2$, 32965-49-4; $[1,5\text{-CODRhCl}]_2$, 12092-47-6; $Co_2(CO)_8$, 10210-68-1; $Co_4(CO)_{12}$, 17786-31-1.

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