

Carbonylative Ring Expansion of Aziridines to β -Lactams with Rhodium-Complexed Dendrimers on a Resin

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Abstract: Rhodium-complexed dendrimers, supported on a resin, were evaluated as catalysts for the carbonylative ring expansion reactions of a variety of aziridines with carbon monoxide to give β -lactams. The effects of reaction temperature, solvent, time, and pressure of carbon monoxide on this transformation were also investigated. The dendritic catalysts showed comparable activity to the homogeneous analogue. More importantly, this catalytic system can be easily recovered by simple filtration and recycled without significant loss of activity.

As a convenient, versatile, and powerful method, carbonylation chemistry is widely applied in organic synthesis.¹ One example is the use of carbon monoxide for carbonylative ring expansion reactions of heterocycles in the presence of transition-metal catalysts.² This process involves the insertion of carbon monoxide into a carbon–heteroatom bond, thus affording the carbonyl-containing ring-expanded product. Reactions of this type provide a facile and direct one-step procedure for the synthesis of lactams,³ lactones,⁴ and thiolactones.⁵ Of particular note is the rhodium(I)-catalyzed carbonylation reaction of 1-alkyl-2-arylaziridines with carbon monoxide, which affords β -lactams in nearly quantitative yields.^{3b} However, like other homogeneous catalytic reactions, this transformation suffers from difficulties associated with the catalyst–product separation and loss of an expensive metal.

The development of recoverable and recyclable catalysts has become increasingly important from both

environmental and economical points of view, and various strategies have been used to recover and recycle the catalysts. One method involves the immobilization of homogeneous catalysts on a solid support which usually enables facile separation from the reaction mixture and the possible recycling of the catalysts.⁶ Unfortunately, heterogeneous catalysts prepared in this way are often much less active than their homogeneous counterparts. The search for superior catalysts that can combine the advantages of both homogeneous and heterogeneous catalysis remains a challenge to chemists.

Dendrimers have received considerable attention due to their unique architectures and properties.⁷ One of the most promising applications of dendrimers is their use in catalysis.⁸ Because of the highly branched and well-defined structure with multiple active sites, dendritic catalysts offer potential in building a bridge between homogeneous and heterogeneous catalysis.^{8b,d,e,9} Examples of the use of dendritic catalysts in organic reactions include Kharash addition,^{8b,10} hydrogenation,^{9a,11} oxidation,¹² Heck reaction,^{8g,13} Stille coupling, Knoevenagel condensation, Michael addition,¹⁴ and the asymmetric addition of diethylzinc to aldehydes.¹⁵ Recently, we investigated the immobilization of dendritic ligands on

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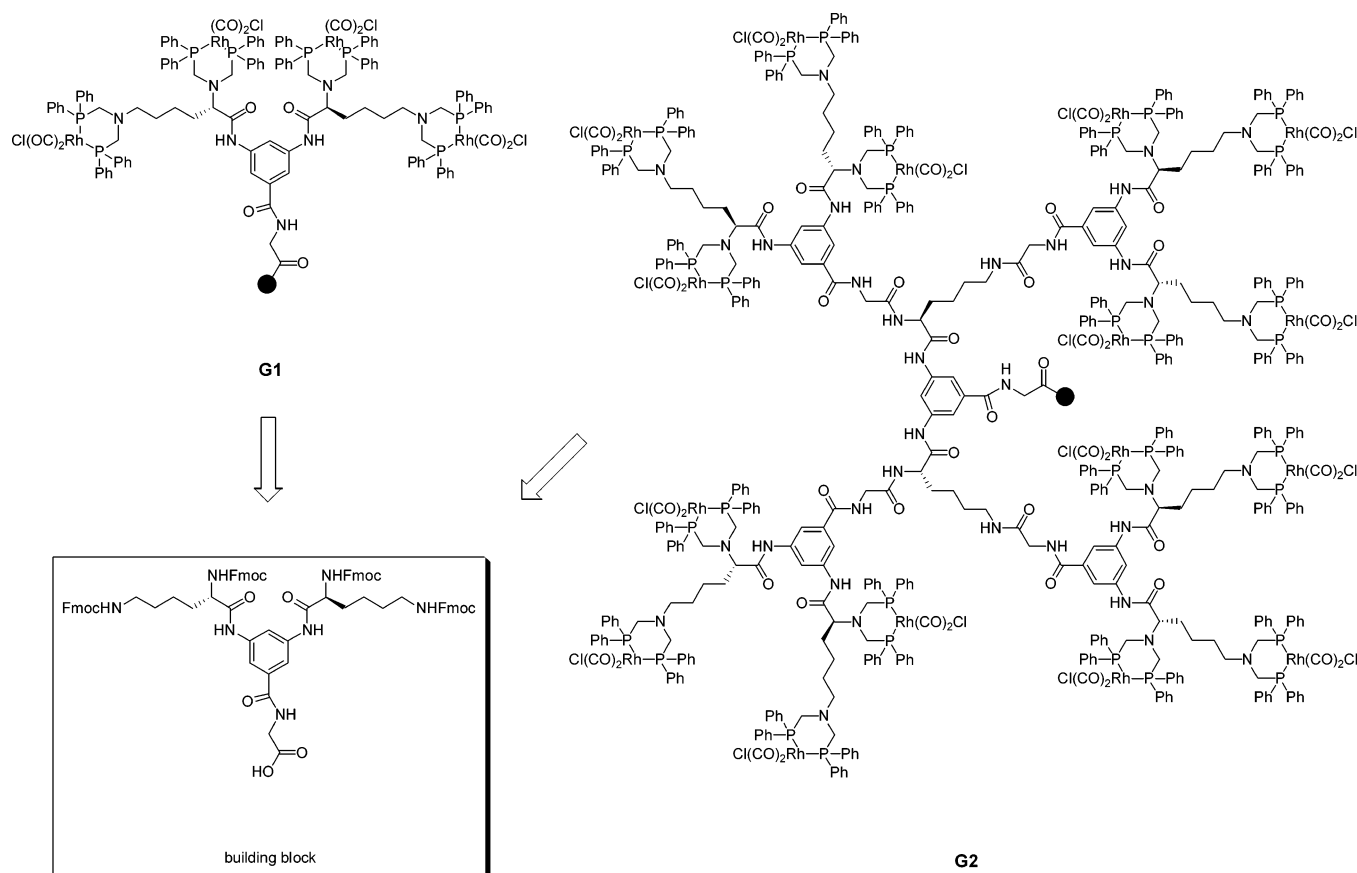


FIGURE 1. Solid-phase synthesis of rhodium-complexed dendrimers on a resin.


silica and on a resin for the hydroformylation reaction.¹⁶ In contrast to known heterogeneous catalysts, our system showed excellent activity and selectivity. To our knowledge, however, there are no reports on the carbonylation of heterocyclic compounds with metallodendrimers. In connection with our research on dendritic catalysts, we now describe the first application of rhodium-complexed

dendrimers for carbonylative ring expansion reactions of aziridines with carbon monoxide to give β -lactams.

Rhodium-complexed dendrimers on a resin were prepared according to a recently reported method.^{16a} The building-block techniques of solid-phase chemistry were used to synthesize dendrimers, followed by phosphonation of the dendrimers with diphenylphosphinomethanol. The resulting phosphonated dendrimers were then reacted with chloro(dicarbonyl)rhodium(I) dimer to give dendritic catalysts **G1** and **G2** (³¹P NMR, δ = 25 ppm; loading of rhodium: **G1**, 0.74 mmol/g; **G2**, 0.83 mmol/g).

We chose 1-*tert*-butyl-2-phenylaziridine as a model substrate and **G1** as the catalyst for the optimization of the carbonylation reaction. The influence of the reaction temperature, solvent, time, and pressure of carbon monoxide was examined, and the results are presented in Table 1. Initial studies focused on the effect of the reaction temperature on this process. Attempts to carry out the reaction of 2 mmol of 1-*tert*-butyl-2-phenylaziridine with 400 psi of carbon monoxide in the presence of catalyst **G1**, in 6 mL of anhydrous benzene at room temperature for 48 h, failed to give any β -lactam, and the starting material was recovered unchanged (Table 1, entry 1). When the reaction temperature was increased to 45 and 65 °C after 60 h, there was 36% and 51% conversion of the aziridine to the β -lactam, respectively (Table 1, entries 2 and 3). Performing the reaction at 75 °C for 48 h gave 70% conversion (Table 1, entry 4), and complete conversion of the aziridine to the β -lactam

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TABLE 1. Carbonylative Ring Expansion of 1-*tert*-Butyl-2-phenylaziridine with Rhodium-Complexed Dendrimers under Different Reaction Conditions^a


entry	pressure (psi)	solvent	<i>T</i> (°C)	time (h)	conversion ^b (%)
1	400	C ₆ H ₆	25	48	NR ^c
2	400	C ₆ H ₆	45	60	36
3	400	C ₆ H ₆	65	60	51
4	400	C ₆ H ₆	75	48	70
5	400	C ₆ H ₆	90	48	100 ^d
6	400	CH ₂ Cl ₂	90	48	99
7	400	THF	90	48	86
8	400	ether	90	48	83
9	400	CH ₃ CN	90	48	81
10	400	DME	90	48	52
11	400	C ₆ H ₆	90	13	41
12	400	C ₆ H ₆	90	24	72
13	400	C ₆ H ₆	90	38	91
14	100	C ₆ H ₆	90	48	48
15	200	C ₆ H ₆	90	48	65
16	300	C ₆ H ₆	90	48	95
17	500	C ₆ H ₆	90	42	100
18	600	C ₆ H ₆	90	38	100

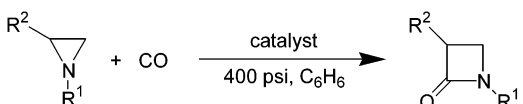
^a 2 mmol of 1-*tert*-butyl-2-phenylaziridine, 6 mL of solvent, 25 mg of **G1**. ^b Determined by ¹H NMR and GC. ^c No reaction. ^d 99% isolated yield.

was observed by raising the reaction temperature to 90 °C after 48 h (Table 1, entry 5).

As illustrated in Table 1, the solvent also plays an important role in the ring-expansion reaction. Benzene proved to be the best solvent for this transformation (Table 1, entry 5), and the reaction also proceeded smoothly in dichloromethane, affording 99% conversion (Table 1, entry 6). The use of other solvents such as tetrahydrofuran, ether, and acetonitrile gave 81–86% conversions (Table 1, entries 7–9), but when 1,2-dimethoxyethane was employed as the solvent, the conversion of the aziridine to the β -lactam decreased to 52% (Table 1, entry 10).

We further explored the effects of the reaction time and the pressure of carbon monoxide on the carbonylation of an aziridine. Treatment of 1-*tert*-butyl-2-phenylaziridine with catalyst **G1** under 400 psi of carbon monoxide in benzene at 90 °C for 13 and 24 h resulted in 41% and 72% conversion, respectively (Table 1, entries 11 and 12). The conversion was 91% when the reaction time was prolonged to 38 h under the same conditions (Table 1, entry 13). Increasing the pressure of carbon monoxide favored product formation. When the pressure of carbon monoxide was varied from 100 to 300 psi, conversions of the aziridine to the β -lactam ranged from 48 to 95% (Table 1, entries 14–16). Reaction times of 42 and 38 h are sufficient to achieve complete conversion of the substrate using 500 and 600 psi of carbon monoxide, respectively (Table 1, entries 17 and 18).

Rhodium-complexed dendrimers **G1** and **G2** were used as catalysts for the carbonylative ring expansion of 1-*tert*-butyl-2-phenylaziridine, 1-(1-adamantyl)-2-phenylaziridine, 1-*tert*-butyl-2-(biphenyl-4-yl)aziridine, 1-(1-adamantyl)-2-(biphenyl-4-yl)aziridine, and 1-*tert*-butyl-2-(4-bromophenyl)aziridine. In all cases, 2 mmol of aziridine in 6 mL of anhydrous benzene, with 25 mg of the catalyst,

TABLE 2. Carbonylative Ring Expansion of a Variety of Aziridines with Rhodium-Complexed Dendrimers^a


entry	substrate	catalyst	conversion ^b (%)
1	R ¹ = <i>t</i> -Bu, R ² = Ph	G1	100 (99) ^{c,d}
2	R ¹ = <i>t</i> -Bu, R ² = Ph	G2	100 ^d
3	R ¹ = 1-adamantyl, R ² = Ph	G1	100 (98) ^{c,d}
4	R ¹ = 1-adamantyl, R ² = Ph	G2	100 ^d
5	R ¹ = <i>t</i> -Bu, R ² = 4-PhC ₆ H ₄	G1	100
6	R ¹ = <i>t</i> -Bu, R ² = 4-PhC ₆ H ₄	G2	100
7	R ¹ = 1-adamantyl, R ² = 4-PhC ₆ H ₄	G1	100
8	R ¹ = 1-adamantyl, R ² = 4-PhC ₆ H ₄	G2	100
9	R ¹ = <i>t</i> -Bu, R ² = 4-BrC ₆ H ₄	G1	100
10	R ¹ = <i>t</i> -Bu, R ² = 4-BrC ₆ H ₄	G2	100

^a 2 mmol of aziridine, 6 mL of benzene, 25 mg of catalyst, 400 psi of CO, 90 °C, 48 h. ^b Determined by ¹H NMR and GC. ^c Isolated yield. ^d Catalyst was reused three times without significant loss of activity.

was subjected to 400 psi of carbon monoxide at 90 °C for 48 h. The results are summarized in Table 2. Catalysts **G1** and **G2** are highly reactive and regioselectively gave β -lactams. For example, the carbonylation of 1-*tert*-butyl-2-phenylaziridine using catalyst **G1** afforded the product in quantitative conversion (99% isolated yield) (Table 2, entry 1). This result indicates that the rhodium-complexed dendrimer **G1** shows comparable activity to that of the homogeneous analogue.^{3b} More importantly, the carbonylation reaction was simple in execution and workup. After the reaction was complete, the catalyst was recovered by simple filtration and washed with benzene for the subsequent cycles. Catalyst **G2** was also very efficient for the carbonylation reaction. When **G2** was employed as the catalyst, the reaction proceeded with full conversion of the aziridine to the β -lactam (Table 2, entry 2). Similar results were obtained for the carbonylative ring expansion of 1-(1-adamantyl)-2-phenylaziridine, 1-*tert*-butyl-2-(biphenyl-4-yl)aziridine, 1-(1-adamantyl)-2-(biphenyl-4-yl)aziridine, and 1-*tert*-butyl-2-(4-bromophenyl)aziridine (Table 2, entries 3–10).

In conclusion, rhodium-complexed dendrimers on a resin showed high activity for the carbonylative ring expansion reactions of aziridines with carbon monoxide to give β -lactams in good yields. This catalytic system can be easily recovered by simple filtration, reused, and recycled without significant loss of activity.

Experimental Section

Materials. Aziridines were prepared according to literature procedures.^{3b} Other chemicals were purchased from commercial sources. All solvents were dried and distilled prior to use.

General Procedure for the Carbonylation Reaction. A glass liner containing the substrate (2 mmol), catalyst (25 mg), and benzene (6 mL) was placed in a 45 mL autoclave equipped with a magnetic stirring bar. The autoclave was flushed three times with carbon monoxide and pressurized to 400 psi. The autoclave was then placed in an oil bath preset to the desired temperature on a stirring hot plate. After the appropriate reaction time (see Table 1), the autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. The resulting solution was filtered to

remove the catalyst, and the solvent was evaporated in vacuo. The products were analyzed by ^1H NMR and gas chromatography and identified by comparison with literature data.^{3b} The recovered catalyst was washed with benzene and reused for subsequent cycles.

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