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Cobalt Carbonyl Mediated Carbonylative Ring Expansion Reactions of 3,6-Dihydro-2H-1,2-Oxazines

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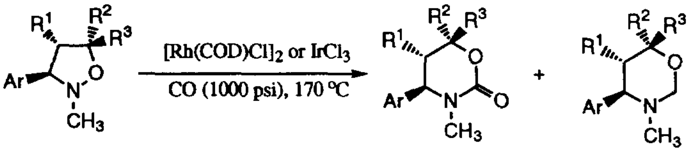
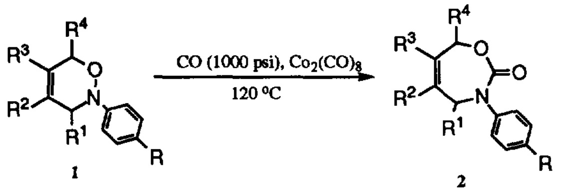
Abstract: The carbonylative ring expansion reactions of 3,6-dihydro-2H-1,2-oxazines proceeded in the presence of $Co_2(CO)_8$ to give 4,7-dihydro-1,3-oxazepin-2(3H)-ones in up to 53 % yield. Copyright © 1996 Elsevier Science Ltd

Transition metal mediated carbonylative ring expansion reactions have attracted considerable attention in the last twenty years.[1] For example, N-containing cyclic compounds such as aziridines,[2] azirines,[3] azetidines,[4] diaziridines[5] and related heterocycles[6] undergo regioselective carbonylation by an appropriate transition metal catalyst affording the corresponding lactams. The carbonylation of oxiranes[7] and oxetanes[8] to lactones has also been described. In these reactions, the high ring strain of the reactants is considered to be a driving force for the cleavage of a relatively weak carbon-heteroatom bond by transition metals, resulting in incorporation of carbon monoxide. On the other hand, larger ring heterocycles are generally less reactive toward transition metals because of the lack of ring strain, and thus relatively drastic conditions are required to achieve carbonylative ring expansion. For example, two of us have recently demonstrated that the carbonylation of isoxazolidines, which are five membered heterocycles containing a N-O bond, occured in the presence of $[Rh(COD)Cl]_2$ as the catalyst, at 170 °C under 1000 psi of carbon monoxide, to give tetrahydro-1,3-oxazin-2-ones in moderate to excellent yield (eq. 1).[9] It has been also found that iridium trichloride gives rise to carbonylation, followed by novel hydrogen transfer from another molecule of starting isoxazolidine. These findings prompted us to explore the carbonylative ring expansion reactions of 3,6-dihydro-2H-1,2-oxazines **1**, which may provide a useful route to 4,7-dihydro-1,3-oxazepin-2(3H)-ones **2** (eq. 2), since 1,2-oxazines are easily



(1)

prepared by hetero Diels-Alder reaction of nitroso compounds with conjugated dienes. Shvo and co-workers[10] investigated the reaction of several 1,2-oxazines with a *stoichiometric* quantity of $Fe_2(CO)_9$ in detail. They found that π-allyl-Fe-σ-lactone complexes were obtained as the major product and only two oxazines underwent insertion of carbon monoxide into N-O bond to form the corresponding seven membered carbamates. However, to our knowledge, there have been no studies on synthetic approaches to seven membered cyclic carbamates using metal catalyzed carbonylative ring expansion methodology. We now wish to report that cobalt carbonyl effects carbonylation of 3,6-dihydro-2H-1,2-oxazines **1** affording 4,7-dihydro-1,3-oxazepin-2(3H)-ones **2** in moderate yields (eq. 2).



(2)

No carbonylation occurred when 2-phenyl-4,5-dimethyl-3,6-dihydro-2H-1,2-oxazine (1.0 mmol) **1a**, obtained by treatment of nitrosobenzene with 2,3-dimethyl-1,3-butadiene,[11] was subjected to reaction with carbon monoxide in the presence of a catalytic amount of $[Rh(COD)Cl]_2$ (0.01 mmol) under identical conditions to those used for the carbonylation of isoxazolidines (eq. 1) [benzene (5 mL), 170 °C, 1000 psi].[9] Instead, 3,4-dimethyl-1-phenylpyrrole was isolated in 49 % yield. The rhodium catalyst promotes the reaction since the same product was formed in 29 % yield in the absence of the metal complex. While several Pd-phosphine complexes were inactive using **1a**, $Co_2(CO)_8$ was found to mediate the carbonylation. Thus, when the reaction of **1a** (1.0 mmol) was carried out using 5 mol % of $Co_2(CO)_8$ in benzene (5 mL) at 120 °C under 1000 psi of carbon monoxide, insertion of carbon monoxide took place into N-O bond to afford 4,7-dihydro-5,6-dimethyl-1,3-oxazepin-2(3H)-one **2a** in 12 % yield. The use of a stoichiometric amount of $Co_2(CO)_8$ gave **2a** in 15 % yield, along with numerous unidentified side products. The best results were obtained using a 2:1 ratio of **1a** / $Co_2(CO)_8$ and an increased volume of the solvent [0.5 mmol of substrate **1a**, 0.25 mmol of $Co_2(CO)_8$ in benzene (10 mL), 1000 psi CO at 120 °C for 24 h], which gave **2a** in 29 % yield (Table 1).[12]

A series of 3,6-dihydro-2H-1,2-oxazines **1b-k** were carbonylated under the optimum conditions described above and the results are presented in Table 1. The products were assigned on the basis of spectroscopic methods (^1H, ^{13}C-NMR, MS). It can be seen from Table 1 that the reaction is sensitive to the position and type of substituents on the oxazine ring, and at the para position of the phenyl ring of the N-aryl unit. An electron donating methoxy group at the para position of the phenyl ring enhanced the reactivity (**2a** vs. **2b**). An allyl group at the para position has no appreciable influence on the yield of **2** (compare **2a** and **2c**; **2d** and **2e**). Better results were

Table 1. Carbonylation of 3,4-Dihydro-2H-1,2-Oxazines 1[a]

Sub.	R^1	R^2	R^3	R^4	R	Yield of **2** (%)
1a	H	CH_3	CH_3	H	H	29
1b	H	CH_3	CH_3	H	OCH_3	53
1c[13]	H	CH_3	CH_3	H	$CH_2CH{=}CH_2$	28
1d	H	OCH_3	OCH_3	H	H	49
1e[13]	H	OCH_3	OCH_3	H	$CH_2CH{=}CH_2$	45
1f	H	OCH_3	OCH_3	H	$COOCH_3$	16
1g	H	CH_3	Ph	H	H	43
1h[c]	CH_3(H)	H	H	H(CH_3)	H	24[d]
1i	H	H	H	Ph	H	23
1j	H	H	H	Ph	CH_3	29
1k	H	CH_3	H	CH_3	H	37

(a) Reaction Conditions; Substrate (0.5 mmol), $Co_2(CO)_8$ (0.25 mmol), CO 1000 psi, 120 °C, 24 h.

(b) **2** was identified on the basis of analytical and spectral (^1H, ^{13}C-NMR, IR, MS) results.

(c) ($R^1{=}CH_3$):($R^4{=}CH_3$)=55:45. (d) ($R^1{=}CH_3$):($R^4{=}CH_3$)=75:25.

realized with a methoxy group at the double bond compared with methyl substituents (**2a** vs. **2d**; **2c** vs. **2e**). The carbonylation reaction also occurs when there are no substituents at the double bond (i.e. R^2, R^3=H), or a methyl group at C-4, *provided* either R^1 or $R^4 \neq H$ (**2h-2k**).

In conclusion, cobalt carbonyl effects carbonylative ring expansion reactions of 3,6-dihydro-2H-1,2-oxazines to 4,7-dihydro-1,3-oxazepin-2(3H)-ones. Although the yields are moderate, a variety of seven membered ring carbamates, which are not readily accessible by other means,[15] can be obtained by the simple method. The substrates are also easily prepared in one step by hetero Diels-Alder reactions.

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References and Notes

1. Khumtaveeporn, K.; Alper, H. *Acc. Chem. Res.* **1995**, *28*, 414 and references cited therein.
2. (a) Chamchaang, W.; Pinhas, A. R. *J. Org. Chem.* **1990**, *55*, 2943. (b) Alper, H.; Urso, F.; Smith, D. J. H. *J. Am. Chem. Soc.* **1983**, *105*, 6737. (c) Piotti. E. M.; Alper, H. *J. Am. Chem. Soc.* **1996**, *118*, 111.

(d) Calet, S.; Urso, F.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 931. (e) Spears, G. W.; Nakanishi, K.; Ohfune. Y. *Synlett.* **1991**, 91. (f) Tanner, D.; Somfai, P. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2415.

3. (a) Alper, H.; Perera, C. P.; Ahmed, F. R. *J. Am. Chem. Soc.* **1981**, *103*, 1289. (b) Alper, H.; Mahatantila, C. P. *Heterocycles* **1983**, *20*, 2025.
4. Roberto, D.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 5739.
5. Alper, H.; Delledonne, D.; Kameyama, M.; Roberto. D. *Organometallics* **1990**, *9*, 762.
6. (a) Alper, H.; Hamel, N. *Tetrahedron Lett.* **1987**, *28*, 3237. (b) Roberto, D.; Alper, H. *Organometallics* **1984**, *3*, 1767.
7. (a) Aumann, R.; Ring, H. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 50. (b) Kamiya, Y.; Kawato, K.; Ohta, H. *Chem. Lett.* **1980**, 1549. (c) Shimizu, I.; Maruyama, T.; Makuta, T.; Yamamoto, A. *Tetrahedron Lett.* **1993**, *34*, 2135. (d) Drent, E.; Kragtwijk, E. Eur. Pat. Appl. EP 577,206 (Jan 5, 1994) (e) Drent, E.; Kragtwijk, E. *Chem. Abstr.* **1994**, *120*, 191517c. (f) Alper, H.; Arzoumanian, H.; Petrignani, J. -F.; Maldonado, M. S. *J. Chem. Soc., Chem. Commun.* **1985**, 340. (g) Alper, H.; Eisenstat, A.; Satyanarayana, N. *J. Am. Chem. Soc.* **1990**, *112*, 7060.
8. (a) Nienburg, H. J.; Elschnigg, G. Ger. 1,066,572 (Oct 8, 1959) (b) Nienburg, H. J.; Elschnigg, G. *Chem. Abstr.* **1961**, *55*, 10323h. (c) Wang, M. D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20.
9. Khumtaveeporn, K.; Alper, H. *J. Org. Chem.* **1995**, *60*, 8142.
10. (a) Becker, Y.; Eisenstadt, A.; Shov, Y. *Tetrahedron Lett.* **1972**, 3183. (b) Becker, Y.; Eisenstadt, A.; Shov, Y. *Tetrahedron* **1974**, *30*, 839. (c) Becker, Y.; Eisenstadt, A.; Shov, Y. *Tetrahedron* **1978**, *34*, 799.
11. Boger. D.L.; Weinreb, S. N. " *Hetero Diels-Alder Methodology In Organic Synthesis* " Academic Press. N. Y., **1987**.
12. The following general procedure was used: A mixture of the oxazine **1** (0.5 mmol) and $Co_2(CO)_8$ (0.25 mmol) in freshly distilled benzene (10 mL) was stirred under 1000 psi of carbon monoxide at 120 °C for 24 h. The solvent was removed by rotary evaporation, and the product (**2**) was purified by chromatography on silica gel with 5:1 hexane:ether as the eluant.
13. 4,5-Dimethyl-2-(4-allylphenyl)-3,6-dihydro-2H-1,2-oxazine **1c** was synthesized as follows; 4,4-dimethyl-2-(4-iodophenyl)-3,6-dihydro-2H-1,2-oxazine, prepared from 2,3-dimethyl-1,3-butadiene and 4-iodonitrosobenzene, was treated with allyltributylstannane in the presence of $Pd(PPh_3)_4$ in benzene at 100 °C for 24 h under N_2 (50 %).[14] Similarly, **1e** was prepared in 83 % yield.
14. Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301.
15. Daniel, J.; Shukla, D.; Dhar, D. N. *Chem. Lett.* **1992**, 1575.

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