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Preparation of Polyfunctional Ketones by a Cobalt(II) Mediated Carbonylation of Organozinc Reagents.

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Abstract: Functionalized organozinc halides can be efficiently carbonylated under atmospheric pressure in the presence of cobalt(II) bromide in THF:NMP leading to polyfunctional symmetrical ketones in 56-80 % yield.

The reaction of organozincs with carbon monoxide proceeds only under strongly basic conditions and produces acyloins in modest yields.¹ The palladium catalyzed carbonylation of organozinc compounds has been reported,² but is not a general and efficient reaction and the use of a "phosgene precursor" like a chloroformate is required to obtain formally CO-insertion products.^{2a} On the other hand, aryl iodides can be coupled with carbon monoxide and alkyl iodides in the presence of zinc-copper couple and a Pd-catalyst affording unsymmetrical ketones.^{3,4} Various cobalt complexes are known to catalyze carbonylation reactions⁵ and we wish to report herein a new mild carbonylation of organozinc derivatives mediated by cobalt complexes leading to a variety of symmetrical polyfunctional ketones. In the first attempts, we treated Pent₂Zn with Co₂(CO)8 in THF at 0-20 °C for 3 h and obtained the desired ketone Pent₂CO in 45 % yield.⁶ Better results were



obtained by using inexpensive cobalt(II) bromide,^{7,8} a mixture of THF and NMP as solvent and by bubbling carbon monoxide slowly through the reaction mixture. Under these reaction conditions Pent₂Zn and Oct₂Zn were converted to the corresponding ketones Pent₂CO and Oct₂CO respectively in 44 and 50 % yield. This procedure allows the conversion of β -pinene 1 to the ketone 2 in a one-pot procedure⁹ via the intermediate dimyrtanylzinc 3 in 48 % yield (Scheme 1).

Since both alkyl groups were transferred from the zinc organometallic to the product, it implies that organozinc halides should be good substrates. Therefore, we have used the more readily available functionalized alkylzinc iodides FG-RZnI 4^{10} obtained by the direct insertion of zinc dust to the corresponding alkyl iodide 5 (Scheme 2). This procedure was very satisfactory¹¹ and provides the symmetrical ketones (FG-R)₂CO 6 in 56-80 % yield (Table 1). Interestingly, alkyl-, aryl- and benzyl-zinc halides can be used. The best yields are obtained with arylzinc iodides prepared



from the corresponding aryl iodide via an iodine-lithium exchange followed by a transmetalation with zinc bromide.¹² Functional groups such as ester or chloride are well tolerated, however using 3-cyanopropylzinc iodide,¹⁰ no carbonylation product could be isolated. Finally this method can be used to perform cyclizations, and the cobalt mediated carbonylation of the 1,4-dizinc derivative **7** prepared from the diiodide **8**¹³ provides the *trans*-cyclopentanone **9** in 63 % yield (Scheme 3).



Surprisingly under these reaction conditions, almost no homocoupling products (FG-R-R-FG) are formed, in contrast to the behavior of Grignard or lithium reagents in the presence of cobalt(II) halides.¹⁴ This may imply that organocobalt species FG-RCoX prepared from organozinc compounds may be relatively stable organometallic intermediates and be of synthetic utility for organic chemistry.

In summary, we have developed a new direct carbonylation of functionalized organozinc halides mediated by cobalt(II) bromide. Further applications involving new transition metal organometallics prepared from organozincs are currently underway in our laboratory.

entry	FG-RZnI 4	Product 5	Yield (%) ^a
1	OctZnI		59
2	PhCH ₂ ZnBr		71
3	CO ₂ Et	CO ₂ Et CO ₂ Et	58
4	CI Znl		56
5	Zni		60
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6	MeO ZnBr	мео	73
7	CI ZnBr		80

 Table 1. Symmetrical ketones 5 obtained by the carbonylation of alkylzinc halides in the presence of CoBr2 in THF:NMP (6:4).

^a Isolated yields of analytically pure products.

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- 7. One gram of cobalt(II) bromide (99 % pure) costs less than 1 DM (Aldrich).
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