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## Highly Chemo- and Stereoselective Fe-Catalyzed Alkenylation of Organomanganese Reagents.<sup>1</sup>

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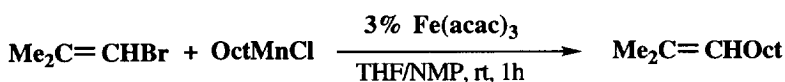
**Abstract:** Organomanganese chlorides react with alkenyl iodides, bromides and chlorides in the presence of 3% Fe(acac)<sub>3</sub>. The reaction takes place under very mild conditions (THF-NMP, rt, 1h) to afford the substituted olefin in excellent yields with a high stereo- and chemoselectivity. Thus an unprotected keto alkenyl chloride selectively gives the corresponding keto olefin. From a preparative point of view, this procedure is the first real alternative to the Pd- and Ni-cross coupling reaction used until now.

Numerous cross-coupling reactions between alkenyl halides and organometallic compounds have been reported. They generally take place under Pd- or Ni-catalysis<sup>2</sup> and are very convenient on a laboratory scale. However, it is often difficult to use them for large scale applications since the Pd- or Ni-complexes used as catalyst are expensive (Pd) or toxic (Pd, Ni). In 1971, Kochi<sup>3</sup> showed that alkenyl bromides are alkylated by Grignard reagents in the presence of iron (III) acetylacetonate. This report is very interesting since iron salts are very cheap and not toxic, unfortunately, the preparative interest of this reaction is limited since, as a rule, a large excess of alkenyl bromide (3 to 5 equiv.) is required to obtain satisfactory yields of substituted olefins.<sup>3,4</sup>

Since a few years, we have undertook to develop new selective C-C bond forming reactions *via* organomanganese reagents under transition metal catalysis. Thus, we have recently shown that the Cu-catalyzed alkylation of organomanganese reagents<sup>5</sup> can be advantageously compared to the other classical related procedures (*i. e.* cuprate and Cu-catalyzed Grignard alkylation). In this communication, we now report the Fe-catalyzed alkenylation of organomanganese reagents. This new reaction is clearly more efficient than the corresponding Fe-catalyzed Grignard procedure mentioned above and offers an efficient alternative to the Pd- and Ni-catalyzed procedures<sup>2</sup> used until now.

As evidenced below, prenyl bromide reacts with octylmanganese chloride at room temperature in the presence of 3% iron acetylacetonate as catalyst to give the substitution product in excellent yield.

The reaction has been carried out in THF with NMP (*N*-methyl 2-Pyrrolidinone) as cosolvent. It is interesting to note that all our attempts to perform the reaction in THF alone or by replacing the NMP by another polar cosolvent resulted in lower yields (Table 1). Such a beneficial influence of NMP has already been demonstrated for the Cu-catalyzed alkylation of organomanganese reagents.<sup>5</sup>

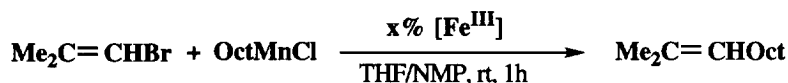


**Table 1.** Fe-Catalyzed Alkenylation of RMnCl: Influence of the Solvent.

| Solvent   | THF | DME | THF-AcOEt <sup>a</sup> | THF-MeCN <sup>a</sup> | THF-Sulfolane <sup>a</sup> | THF-NMP <sup>a</sup> |
|-----------|-----|-----|------------------------|-----------------------|----------------------------|----------------------|
| Yield (%) | 12  | 12  | 13                     | 15                    | 24                         | 76                   |

<sup>a</sup>/ 50 ml of cosolvent for 50 mmoles of prenyl bromide (see typical procedure, note 6).

Various iron salts can be used as catalyst provided that they are soluble in the reaction mixture (Table 2). Generally, the best yields were obtained by using 3% of the readily available iron (III) acetylacetonate .

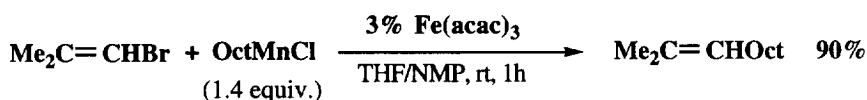
**Table 2.** Fe-Catalyzed Alkenylation of RMnCl: Nature and Percentage of the Iron (III) salt used as Catalyst.

| Catalyst  | 1% Fe(acac) <sub>3</sub> | 3% Fe(acac) <sub>3</sub> | 6% Fe(acac) <sub>3</sub> | 3% Fe(DBM) <sub>3</sub> | 3% FeCl <sub>3</sub> | 3% FeCl <sub>3</sub> •thiopy <sup>a</sup> |
|-----------|--------------------------|--------------------------|--------------------------|-------------------------|----------------------|---|
| Yield (%) | 62                       | 76                       | 76                       | 70                      | 67                   | 77  |

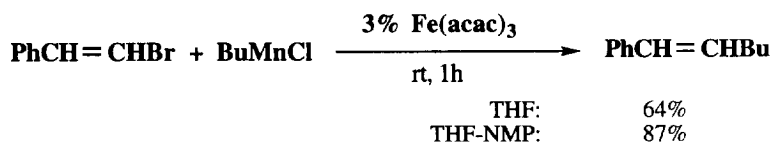
<sup>a</sup>/ thiopy = 2-thiophenyl 2-pyridine.

The reaction described above can be performed with octylmanganese chloride prepared from either octylmagnesium chloride or octyllithium. However, the yield is better when the organomanganese compound is obtained by transmetallation from the corresponding Grignard (76% instead of 68%).

All our efforts to get more than 76% yield from a stoichiometric amount of reactants (OctMnCl:Me<sub>2</sub>C=CHBr= 1.05:1) resulted in failure. In all cases, a part of the prenyl bromide (10 to 20%) was recovered at the end of the reaction. The only way to drive the reaction to completion is to employ an excess of octylmanganese chloride (1.4 equiv.). As expected an excellent yield was thus obtained.



It should be noted that, in THF alone, the yield of substituted olefin is clearly better when the reaction is performed from a more reactive alkenyl bromide such as styryl bromide. Nevertheless, even in this case the best result was obtained in the presence of NMP.



The reaction has a very large scope (Table 3). Thus, alkenyl iodides, bromides and even chlorides (entries 1 to 3) were used successfully. The excellent yields obtained from the chlorides (entries 3 and 6) must be underlined since these compounds are generally poor reactants in the Pd- or Ni-catalyzed cross coupling reactions.<sup>2</sup>

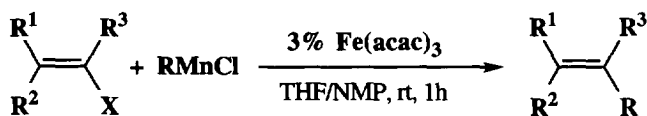


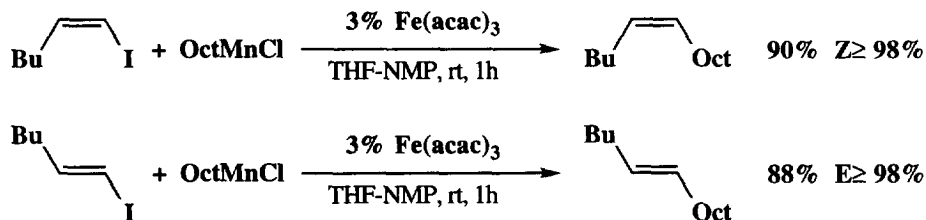
Table 3. Fe-Catalyzed Alkenylation of RMnCl.

| Entry | R   | Alkenyl Halide | Yield (%) <sup>a</sup> | Entry | R                    | Alkenyl Halide | Yield (%) <sup>a</sup> |
|-------|-----|----------------|------------------------|-------|----------------------|----------------|------------------------|
| 1     | Oct |                | 90                     | 6     | Bu                   |                | 80                     |
| 2     | "   |                | 89                     | 7     | c-Hex                |                | 84                     |
| 3     | "   |                | 88                     | 8     | Ph                   |                | 71                     |
| 4     | "   |                | 90                     | 9     | t-Bu                 |                | 30                     |
| 5     | Bu  |                | 89                     | 10    | Me <sub>2</sub> C=CH |                | 25                     |

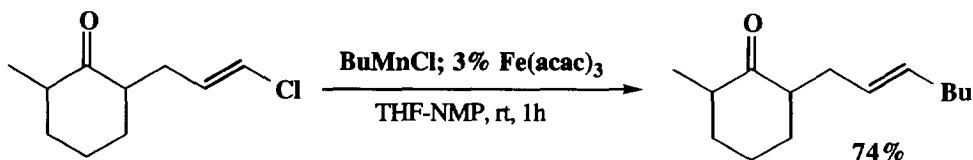
a/ Yield of isolated product. All the reactions were performed on a 50 mmoles scale. For a typical procedure see note 6.

The alkenyl halides can indifferently bear substituents at the  $\alpha$ - or  $\beta$ -position (entries 3 to 6). Aryl as well as *n*- and *sec*-alkylmanganese chlorides gave good yields of substituted olefins (entries 6 to 8). On the other hand, *tert*-alkylmanganese chlorides mainly led to the  $\beta$ -elimination products (entry 9) whereas vinylic organomanganese chlorides afforded moderate yields of 1,3-dienes (entry 10). The vinyl-vinyl coupling reaction is currently studied to improve the yields.

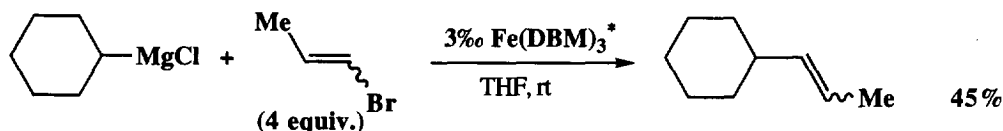
This new Fe-catalyzed procedure is very interesting for its selectivity. Thus, as shown below, the reaction occurs highly stereoselectively.



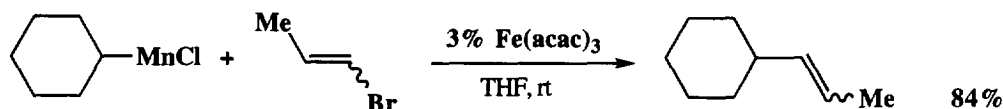
In addition, it should be noted that the cross coupling reaction also takes place with a remarkable chemoselectivity. As an example, it is possible to alkylate selectively an  $\omega$ -ketoalkenyl chloride without protecting the keto group.



In conclusion, the procedure described herein has a large scope of application and can be easily carried out. As mentioned above, it compares very favorably with the Fe-catalyzed alkenylation of Grignard reagents previously described in the literature.<sup>3,4</sup> Indeed, it gives higher yields and does not require an excess of alkenyl bromide.



\* DBM = dibenzoylmethido.



Moreover the Fe-catalyzed organomanganese reaction is much more chemoselective and can even be performed with alkenyl chlorides in spite of their low reactivity.

Finally, it should be pointed out that it is the first example of Fe-catalyzed alkenylation of organometallics of real interest for preparative organometallic chemistry. It is also the first real alternative to the Pd- and Ni-catalyzed procedures<sup>2</sup> used until now to perform such a cross-coupling reaction.

## References and Notes.

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- a/ Tamura, M. and Kochi, J.K. *J. Am. Chem. Soc.* **1971**, *93*, 1487-1489. b/ Neumann, S.M. and Kochi, J.K. *J. Org. Chem.* **1975**, *40*, 599-606. c/ Smith, R.S. and Kochi, J.K. *J. Org. Chem.* **1976**, *41*, 502-509.
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- Typical Procedure:** To a solution of  $\text{RMnCl}^7$  (70 mmoles) in 80 ml of THF are added, at room temperature, 50 ml of distilled NMP, 3%  $\text{Fe(acac)}_3$  (1.5 mmoles) then a solution of alkenyl halide (50 mmoles) in 10 ml of THF. The reaction mixture was stirred for 1 to 2 hours at room temperature then hydrolyzed with 80 ml of aqueous hydrochloric acid (1M) at  $-10^\circ\text{C}$ . After classical work up (extraction with ether), the desired product was isolated by distillation.
- For the preparation of  $\text{RMnCl}$  see: Cahiez, G. and Alami, M. *Tetrahedron* **1989**, *45*, 4163-4176. Cahiez, G. *Butyl Manganese Chloride and Related Reagents in Encyclopedia of Reagents for Organic Synthesis*, L. Paquette Ed., Wiley, Chichester **1995**, in press. b/ Cahiez, G. *Manganese (II) Chloride in Encyclopedia of Reagents for Organic Synthesis*, L. Paquette Ed., Wiley, Chichester **1995**, in press.