Wittig Type Methylenation of Ketones with Bis(iodozincio)methane and Ionic Liquid

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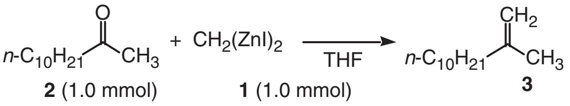
Ketones were transformed into alkenes via methylenation with bis(iodozincio)methane and ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]) in the absence of additional metal salt such as titanium chlorides.

Phosphonium ylide has been the most popular reagent for Wittig type olefination of ketones.[1] The ylide, however, was also equipped with a strong basicity which often leads to an enolization of the starting carbonyl compound. At the same time, it often suffers from a lack of nucleophilicity. For these drawbacks arose the necessity to develop the novel alkylidenation reagents. Among them, *gem*-dimetal compound showed the promising results.[2] As the carbon is substituted with a pair of electron positive metal atoms, its nucleophilicity should be increased much more than a simple organo-monometal species. In addition, careful metal tuning on *gem*-dimetal species will also solve the problem caused from strong basicity of the reagent. As such dimetal species, the organozinc reagent has played an important role.[3] Nysted reagent-Lewis acid,[3a] CH_2X_2–Zn–$TiCl_4$,[3b] the modified CH_2X_2–Zn–$TiCl_4$ by Lombardo,[3c] and $CH_2(ZnI)_2$–β-$TiCl_3$[3d] have been developed. It is supposed that *gem*-dizinc species which is activated with the added metal salt is reactive species. In all cases, the methylenation reaction proceeds at room temperature. Without an addition of titanium salt, for example, treatment of 2-dodecanone with bis(iodozincio)methane (**1**) at room temperature resulted in the sluggish reaction. Even at higher temperature, the alkene **3** was not obtained in good yield (Scheme 1).



Reaction Condition	3/%	2 (Recovery)/%
25 °C, 15 h	15	10
60 °C, 6 h	26	43
β-$TiCl_3$ (1.2 mmol), 25 °C, 0.5 h	84	<3

Scheme 1. Methylenation of **2** with **1**.

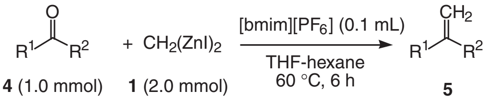
We reported a characteristic effect of tetrahydrothiophene (THT) which activates dizinc **1** to react with acyl chloride. As shown in Table 1 (run 2), an addition of small amount of THT to the reaction mixture improved the yield of methylenated product dramatically. It seems to be a good substitute for β-$TiCl_3$. As practical meaning, however, its stinking property makes the experimental procedure in large scale uncomfortable. Studying the additive, we found that an ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]) plays the same kind of role. The effect of THT to the structure of **1** was discussed previously.[4] It prevents a formation of polymethylene zinc (i.e., $(–CH_2Zn–)_n$) which is produced by the Schlenk equilibrium starting from **1**. Without THT, a solution of **1** in THF will yield polymethylene zinc at 60 °C. Bis(iodozincio)methane (**1**) is much more active for methylenation compared to polymethylene zinc. Ionic liquid may also stabilize the structure of **1** even at 60 °C to maintain its structure during the reaction at the same temperature.

Table 1. Methylenation of **2** with **1**/Additive at 60 °C

Run	Solvent	Additive[a]	Yield of 3 /%
1	THF[b]	none	43
2	THF[b]	THT (0.5 mL)	86
3	THF[b,c]	[bmim][PF_6] (0.1 mL)	56
4	THF/hexane[d]	[bmim][PF_6] (0.1 mL)	81

[a]THT: tetrahydrothiophene. [bmim]: 1-butyl-3-methyl- imidazolium. All reactions were performed at 60 °C. [b]**2** (1.0 mmol), **1** (0.5 M in THF, 2.0 mmol), and THF (1.0 mL). [c]The reaction mixture was monophase. [d]**2** (1.0 mmol), **1** (0.5 M in THF, 2.0 mmol), and hexane (1.0 mL). The reaction mixture was biphase.

Table 2. Methylenation of Various Ketones **4** with **1**/[bmim][PF_6]



Run	Ketone 4	Yield of 5 /%[a]
1	pentyl phenyl ketone	84
2	5-undecanone	47
3	cyclohexyl phenyl ketone	49
4	cyclododecanone	55
5	4-*tert*-butylcyclohexanone	74
6	3-*n*-octylcyclopentanone	20
7	α-tetralone	63
8	Methyl 10-oxoundecanoate	72[b]

[a]**2** (1.0 mmol), **1** (0.5 M THF solution, 2.0 mmol), hexane (1.0 mL), and [bmim][PF_6] were used. [b]Ester group was intact during the reaction. Methyl octanoate was also treated with **1**/[bmim][PF_6] under the same condition and recovered quantitatively.

As shown in Table 2, various ketones **4** were converted into alkenes **5** in good to moderate yields by **1**/[bmim][PF_6]. Instead of **1**, the Nysted reagent was also examined for the methylenation of **2** in the presence of ionic liquid, but did not give the corresponding alkene. Although the titanium salt is still the best additive for the effective methylenation of ketones with **1**, a use of ionic liquid shows the new possibility for an activation of *gem*-dizinc reagents.

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