

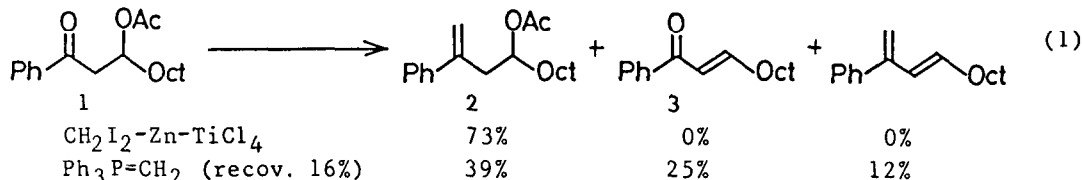
CARBONYL METHYLENATION OF EASILY ENOLIZABLE KETONES

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Summary: An organometallic reagent prepared from CH<sub>2</sub>I<sub>2</sub>, Zn, and TiCl<sub>4</sub> is effective for methylenation of the title ketones.

Carbonyl methylenation is commonly performed with the Wittig reagent (Ph<sub>3</sub>P=CH<sub>2</sub>),<sup>2</sup> which can also function as a base to remove the α-protons of carbonyl groups, especially in the case of easily enolizable ketones.<sup>3</sup> For example, treatment of β-acetoxy ketone 1 with 1 equiv. of the Wittig reagent gives only 39% of the desired product 2, along with an elimination product 3.

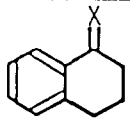
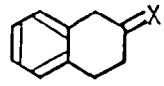
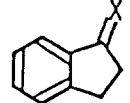
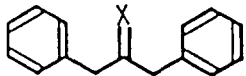
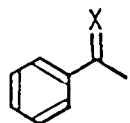
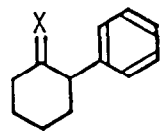


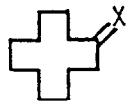
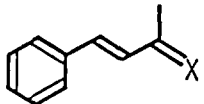
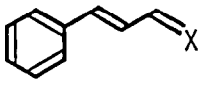
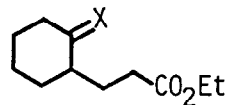
tion which is particularly useful for easily enolizable ketones.



Diiodomethane (0.80 mL, 10 mmol) is added at 25°C to a stirring suspension of zinc (1.2 g, 18 mmol) in THF (20 mL) under an argon atmosphere. After 30 min, a dichloromethane solution of TiCl<sub>4</sub> (1.0 M, 2.0 mmol) is added at 0°C and the resulting dark brown mixture is stirred at 25°C for 30 min. A solution of ketone 1 (0.30 g, 2.0 mmol) in THF (4 mL) is added dropwise at 25°C. After being stirred at 25°C for 15 min, the mixture is diluted with ether (10 mL) and the organic layer is washed with 1 M HCl solution (20 mL) and brine. The concentrated crude product is purified by chromatography on a silica gel column to give 0.22 g of 2<sup>5</sup> (73%) as a colorless oil.

Other results are summarized in Table 1. The CH<sub>2</sub>I<sub>2</sub>-Zn-TiCl<sub>4</sub> system has the following features. (1) The reagent is also effective for the methylenation of aldehydes (runs 8 and 11). (2) An ester group remained unchanged,<sup>6</sup> while ketone methylenation proceeded (run 12). (3) The CH<sub>2</sub>I<sub>2</sub> reagent is considerably more reactive than our previously reported CH<sub>2</sub>Br<sub>2</sub>-Zn-TiCl<sub>4</sub> system.<sup>7</sup> Moreover, the CH<sub>2</sub>I<sub>2</sub> system affords less coupling products produced by a low-valent titanium than the latter reagent containing CH<sub>2</sub>Br<sub>2</sub>, especially in the case of phenyl ketone derivatives.<sup>8,9</sup>

Table 1. Methylenation of carbonyl compounds by means of  $\text{CH}_2\text{I}_2\text{-Zn-TiCl}_4$  system<sup>a</sup>

			
① (15 min, 88%)	② (1 h, 64%)	③ (30 min, 63%)	④ (15 min, 79%)
			⑦ (20 min, 86%)
⑤ (30 min, 90%) <sup>b</sup>	⑥ (3 h, 88%)		⑧ (30 min, 72%)
			
⑨ (20 min, 90%)	⑩ (15 min, 78%)	⑪ (30 min, 52%)	⑫ (30 min, 72%)

a) A carbonyl compound ( $\text{X}=\text{O}$ , 2.0 mmol) was treated at 25°C with the reagent prepared from  $\text{CH}_2\text{I}_2$  (10 mmol), Zn (18 mmol), and  $\text{TiCl}_4$  (2.0 mmol) in THF. Reaction time and isolated yields of methylenated products ( $\text{X}=\text{CH}_2$ ) are shown in parentheses. b) GLPC yield.

## References and Notes

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- Bp 120°C (bath temp, 2 Torr); IR (neat): 2920, 2850, 1740, 1370, 1240, 700  $\text{cm}^{-1}$ ; NMR ( $\text{CCl}_4$ ):  $\delta$ 0.87 (t,  $J=7$  Hz, 3H), 1.21-1.30 (m, 12H), 1.51-1.55 (m, 2H), 1.89 (s, 3H), 2.68 (dd,  $J=6, 14$  Hz, 1H), 2.83 (dd,  $J=7, 14$  Hz, 1H), 4.94 (ddt,  $J=6, 6, 7$  Hz, 1H), 5.11 (d,  $J=1$  Hz, 1H), 5.33 (d,  $J=1$  Hz, 1H), 7.30-7.41 (m, 5H).
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- Methylenation of  $\alpha$ -tetralone (run 1,  $\text{X}=\text{O}$ ) using the  $\text{CH}_2\text{Br}_2$  system<sup>7</sup> afforded only 11% of the methylenated product and the major products were the tetrasubstituted olefin (53%) and the pinacol-type diol (13%).

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