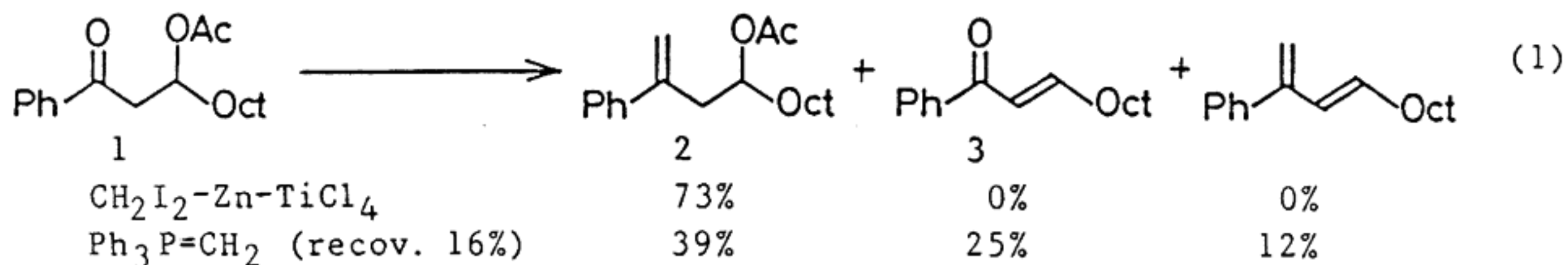


## CARBONYL METHYLENATION OF EASILY ENOLIZABLE KETONES

Jun-ichi Hibino, Takashi Okazoe, Kazuhiko Takai,\* and Hitosi Nozaki<sup>1</sup>  
 Department of Industrial Chemistry, Faculty of Engineering,  
 Kyoto University, Yoshida, Kyoto 606, Japan

Summary: An organometallic reagent prepared from  $\text{CH}_2\text{I}_2$ , Zn, and  $\text{TiCl}_4$  is effective for methylenation of the title ketones.

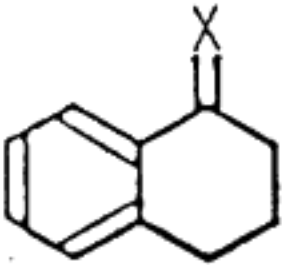
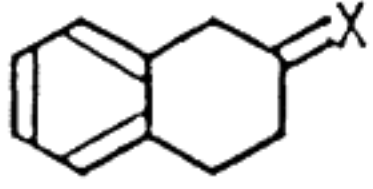
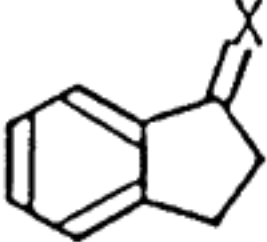
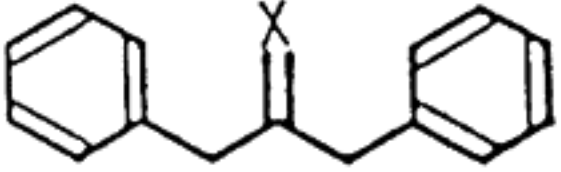
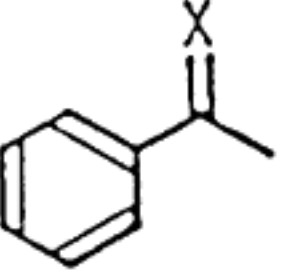
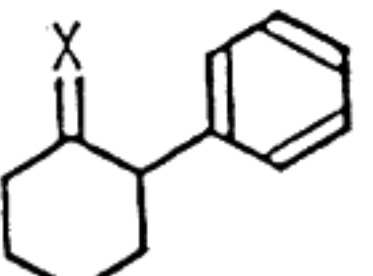


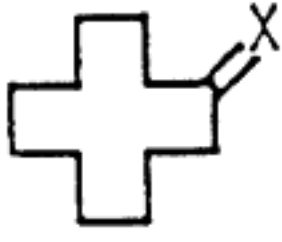
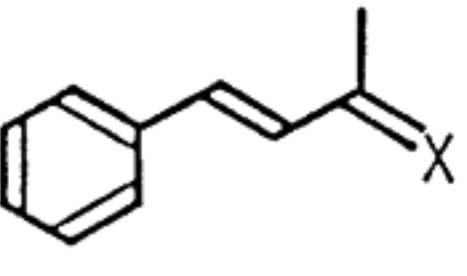
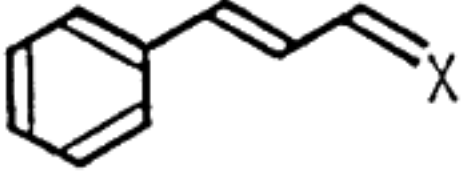
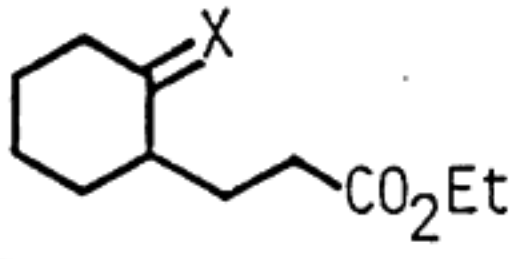
Carbonyl methylenation is commonly performed with the Wittig reagent ( $\text{Ph}_3\text{P}=\text{CH}_2$ ),<sup>2</sup> which can also function as a base to remove the  $\alpha$ -protons of carbonyl groups, especially in the case of easily enolizable ketones.<sup>3</sup> For example, treatment of  $\beta$ -acetoxy ketone **1** with 1 equiv. of the Wittig reagent gives only 39% of the desired product **2** along with an elimination product **3** (25%),<sup>4</sup> a methylenated product of enone (12%), and 16% of the unchanged ketone **1** (Eq.1). In this letter we introduce a simple method of methylenation 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  $\text{TiCl}_4$  (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** (73%) as a colorless oil.

Other results are summarized in Table 1. The  $\text{CH}_2\text{I}_2\text{-Zn-TiCl}_4$  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  $\text{CH}_2\text{I}_2$  reagent is considerably more reactive than our previously reported  $\text{CH}_2\text{Br}_2\text{-Zn-TiCl}_4$  system.<sup>7</sup> Moreover, the  $\text{CH}_2\text{I}_2$  system affords less coupling products produced by a low-valent titanium than the latter reagent containing  $\text{CH}_2\text{Br}_2$ , 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  $25^\circ\text{C}$  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

- 1) Present address: Okayama University of Science, Ridai-cho, Okayama 700, Japan.
- 2) (a) A. Maecker, *Org. React.*, **14**, 270 (1965). (b) A. W. Johnson, "Ylid Chemistry," Academic press, New York, 1966.
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- 4) T. H. Lowry, K. S. Richardson, "Mechanism and Theory in Organic Chemistry," 2nd Ed., p. 534, Harper and Row, New York, 1981.
- 5) Bp  $120^\circ\text{C}$  (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).
- 6) A. P. Uijtewaal, F. L. Jonkers, A. van der Gen, *J. Org. Chem.*, **43**, 3306 (1978). See also ref 2a, pp. 368-371.
- 7) K. Takai, Y. Hotta, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **1978**, 2417; *idem*, *Bull. Chem. Soc. Jpn.*, **53**, 1698 (1980).
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- 9) 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%).