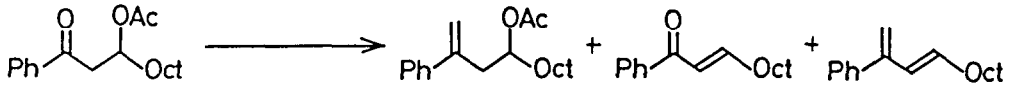
Tetrahedron Letters,Vol.26,No.45,pp 5579-5580,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

CARBONYL METHYLENATION OF EASILY ENOLIZABLE KETONES

Jun-ichi Hibino, Takashi Okazoe, Kazuhiko Takai,* and Hitosi Nozaki[1]
Department of Industrial Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Kyoto 606, Japan

Summary: An organometallic reagent prepared from CH_2I_2, Zn, and $TiCl_4$ is effective for methylenation of the title ketones.

Carbonyl methylenation is commonly performed with the Wittig reagent ($Ph_3P{=}CH_2$),[2] which can also function as a base to remove the α-protons of carbonyl groups, especially in the case of easily enolizable ketones.[3] 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** (25%),[4] 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.



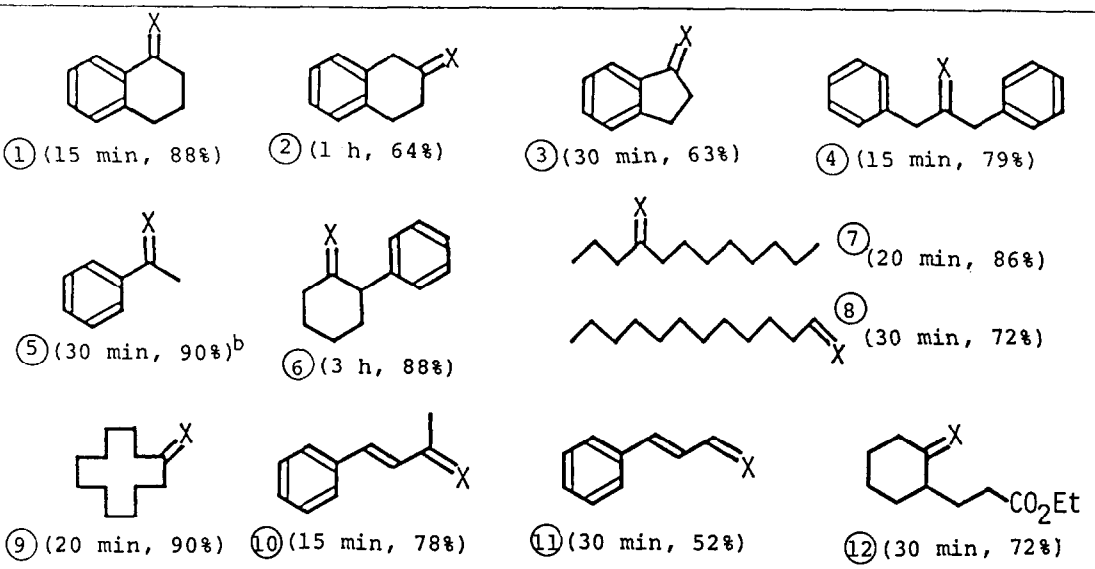
(1)

1		2	3	
CH_2I_2-Zn-$TiCl_4$		73%	0%	0%
$Ph_3P{=}CH_2$ (recov. 16%)		39%	25%	12%

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 $TiCl_4$ (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**[5] (73%) as a colorless oil.

Other results are summarized in Table 1. The CH_2I_2-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,[6] while ketone methylenation proceeded (run 12). (3) The CH_2I_2 reagent is considerably more reactive than our previously reported CH_2Br_2-Zn-$TiCl_4$ system.[7] Moreover, the CH_2I_2 system affords less coupling products produced by a low-valent titanium than the latter reagent containing CH_2Br_2, especially in the case of phenyl ketone derivatives.[8,9]

Table 1. Methylenation of carbonyl compounds by means of CH_2I_2-Zn-$TiCl_4$ system[a]



a) A carbonyl compound (X=O, 2.0 mmol) was treated at 25°C with the reagent prepared from CH_2I_2 (10 mmol), Zn (18 mmol), and $TiCl_4$ (2.0 mmol) in THF. Reaction time and isolated yields of methylenated products (X=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.
3) For methylenation of enolizable ketones, see: (a) E. Murayama, T. Kikuchi, K. Sasaki, N. Sootome, and T. Sato, Chem. Lett., **1984**, 1897. (b) L. Clawson, S. L. Buchwald, and R. H. Grubbs, Tetrahedron Lett., 25, 5733 (1984).
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°C (bath temp, 2 Torr); IR (neat): 2920, 2850, 1740, 1370, 1240, 700 cm^{-1}; NMR (CCl_4): δ0.87 (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. Uijttewaal, 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).
8) T. Mukaiyama, T. Sato, J. Hanna, Chem. Lett., **1973**, 1041.
9) Methylenation of α-tetralone (run 1, X=O) using the CH_2Br_2 system[7] afforded only 11% of the methylenated product and the major products were the tetrasubstituted olefin (53%) and the pinacol-type diol (13%).

(Received in Japan 8 August 1985)