An Efficient Microwave-Promoted Solvent-Free α-Phosphoryloxylation of Ketones

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Abstract: An efficient solvent-free α-phosphoryloxylation of ketones under microwave irradiation is reported. When ketones reacted with phosphates and (diacetoxyiodo)benzene under microwave irradiation for short time, the α-phosphoryloxylaction of ketones was easily be carried out and the corresponding ketol phosphates were prepared in moderate to good yields.

Keywords: α-Phosphoryloxylation, (Diacetoxyiodo)benzene, ketol phosphate, ketone, microwave irradiation, synthesis.

INTRODUCTION

Organic hypervalent iodine reagents have found broad application in organic chemistry and frequently used in synthesis due to their chemical properties and reactivity is similar to those of Hg (II), Tl (III) and Pb (IV), but without the toxic and environmental problems of these heavy metal congeners [1]. Among these hypervalent iodine reagents, [hydroxy(tosyloxy)iodo]benzene (Koser's reagent) is the most popular and useful reagent for the direct α-tosyloxylation of ketones, and the prepared α-tosyloxyketones are important strategic precursors for the construction of various heteroaromatics [2]. However, the analog reaction for the preparation of the important ketol phosphates by the direct α-phosphoryloxylation of ketones with hypervalent iodine reagents has been rather limited [3]. Due to many hypervalent iodine reagents have low solubility in most organic solvents and in order to extend the scope of α-phosphoryloxylation of ketones as well as to prepare more ketol phosphates, the development of solvent-free reactions and other special reactions is a big step forward and should lead to an increasing use of this chemistry.

Microwave-promoted organic syntheses have received great attention because of their fast reaction rates, high purity of products, and ease of manipulation [4]. In particular, the microwave-irradiated procedures in water medium or in the absence of solvents for organic synthesis have attracted considerable interest in recent years due to their efficient and environmentally benign conditions [5]. Our recent interest has been in the development of new synthetic methods using hypervalent iodine compounds and as part of a program, we have checked the reaction of ketones with (diacetoxyiodo)benzene (DIB) and phosphates under microwave irradiation in the absence of solvents, a good result for the direct α-phosphoryloxylation of ketones has been obtained. Now we wish to report here a rapid and efficient microwave-assisted α-phosphoryloxylation of ketones without solvents.

At the beginning, acetophenone was mixed with equal equiv of diphenyl phosphate and DIB to examine the α-phosphoryloxylation. It was found that the mixture was heated in a glass tube by a microwave irradiation at full power (650 W) for 50 seconds, the reaction provided the desired product of α-phosphoryloxyacetophenone in 45% isolated yield. Then, a series of experiments was performed on the reaction of acetophenone with DIB and diphenyl phosphate in order to determine the optimum reaction conditions. It was found that when more acetophenone was used in the reaction, the yield was increased; and when 2 equiv of acetophenone reacted with 1 equiv of diphenyl phosphate and DIB, the reaction gave the highest yield of 74% after 60 seconds microwave irradiation. However, when 3 equiv of acetophenone was added to the reaction, the yield was decreased to 65%. The influence of the reaction time was also evaluated and 60 seconds was the best choice. When the mixture of 2 equiv of acetophenone and 1 equiv of diphenyl phosphate and DIB was heated longer than 70 seconds, the product was found to be decomposed partly. So, according to our investigation, the optimal ratio of acetophenone to diphenyl phosphate and DIB was 2:1:1, and the optimal time for microwave irradiation was 60 seconds. Under the optimum reaction conditions, the α-phosphoryloxylation of ketones (**1**) with phosphates (**2**) and DIB was investigated (Scheme **1**), the good results are summarized in Table **1**.

From Table **1**, it is notable that except **1d** (entry 4), all ketones reacted with phosphates and DIB easily under microwave irradiation and gave the corresponding ketol phosphates in moderate to good yields. Ketone with electron-

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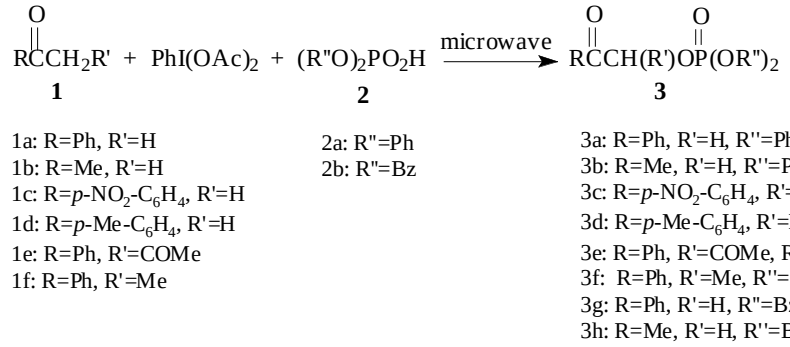

Scheme 1.

Table 1. The Result of the α-Phosphoryloxylation of Ketone

Entry	Ketone (1)	Phosphate (2)	Ketol Phosphate (3)	Time (s)	Yield (%)[a]
1	1a	2a	3a	60	74
2	1b	2a	3b	60	61
3	1c	2a	3c	60	64
4	1d	2a	3d	60	45
5	1e	2a	3e	50	81
6	1f	2a	3f	60	52
7	1a	2b	3g	60	65
8	1b	2b	3h	60	61

[a] Isolated yield

withdrawing substituent group in phenyl (1c) got product in higher yield than that with electron-donating substituent group in phenyl (1d) (entries 3-4). When β-diketone (1e) was used in the reaction, it usually needed shorter time and obtained better yield (entry 5). Due to the hinder effect of methyl group, propionylbenzene (1f) provided the corresponding product in somewhat lower yield compared with acetophenone (entry 6). Another phosphate **2b** was effective as **2a** in the reaction and resulted in the corresponding ketol phosphates in moderate yields (entries 7-8).

In summary, a rapid and efficient method for direct α-phosphoryloxylation of ketones is afforded by the microwave-promoted solvent-free reaction. It is simple, fast and affords ketol phosphates in moderate to good yields. Furthermore, the useful range of hypervalent iodine compounds in organic syntheses has been extended.

EXPERIMENTAL

IR spectra were recorded on a Thermo-Nicolet 6700 instrument, NMR spectra were measured on a Bruker ANANCE Ⅲ (500MHz) spectrometer, and Mass spectra were determined on Thermo-ITQ 1100 mass spectrometer. Microwave irradiation was carried out with a LWMC-201 microwave reactor at full power (650 W) (Nanjing, China). Wakogel B-5F was selected for preparing TLC. Ketones, (diacetoxyiodo)benzene and phosphates were commercially available.

The α-phosphoryloxylation of Ketone General Procedure

Acetophenone (1a) (120.2 mg, 1.0 mmol, 2.0 equiv) was mixed with diphenyl phosphate (2a) (125.1 mg, 0.5 mmol, 1.0 equiv) and (diacetoxyiodo)benzene (161.0 mg, 0.5mmol, 1.0 equiv) in a 10 mL glass tube. The mixture tube was placed inside an alumina bath and irradiated for 60 seconds in a microwave reactor at full power (650 W). After cooling, water (5 mL) was added. The mixture was extracted with CH_2Cl_2 (2×5 mL) and the combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give the residue. The residue was purified on a silica gel plate using (4:1 hexane-ethyl acetate) as eluant to give 136.2 mg of α-phosphoryloxyacetophenone (3a) (74% yield).

α-(Diphenylphosphoryloxy)acetophenone (3a) [3a]

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.89–7.87 (m, 2H), 7.62–7.59 (m, 1H), 7.49–7.46 (m, 2H), 7.37–7.34 (m, 4H), 7.30–7.26 (m, 4H), 7.22–7.19 (m, 2H), 5.46 (d, *J* =10.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 191.20 (d, *J* =5.0 Hz), 150.40 (d, *J* =7.5 Hz), 134.04, 133.72, 129.78, 128.88, 127.78, 125.51, 120.18 (d, *J* =5.0 Hz), 69.90 (d, *J* =5.0 Hz); IR (film, cm^{-1}): 1709, 1291; MS (EI, *m/z*, %): 369 (M+1,

3.5), 275 (100); HRMS: $C_{20}H_{17}O_5P$ calcd.: 368.0809, found: 368.0782.

α-(Diphenylphosphoryloxy)acetone (3b) [3a]

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.38–7.34 (m, 4H), 7.28–7.26 (m, 2H), 7.23–7.22 (m, 4H), 4.72 (d, *J* =9.5 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 201.39 (d, *J* =6.3 Hz), 150.17 (d, *J* = 6.3 Hz), 129.72, 125.50, 119.94 (d, *J* = 5.0 Hz), 71.54 (d, *J* = 6.3 Hz), 25.78; IR (film, cm^{-1}): 1739, 1290, 1194; MS (EI, *m/z*, %): 307 (M+1, 2.0), 250 (100); HRMS: $C_{15}H_{15}O_5P$ calcd.: 306.0657, found: 306.0624.

α-(Diphenylphosphoryloxy)-4-nitroacetophenone (3c) [3d]

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 8.31 (d, *J* = 9.0 Hz, 2H), 8.04 (d, *J* = 9.0 Hz, 2H), 7.36 (d, *J* = 7.5 Hz, 4H), 7.29–7.23 (m, 6H), 5.45 (d, *J* = 10.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 190.53 (d, *J* = 5.0 Hz), 150.78, 150.28 (d, *J* = 7.5 Hz), 138.19, 129.88, 129.10, 125.74, 124.05, 120.14 (d, *J* = 5.0 Hz), 70.02 (d, *J* = 5.0 Hz); IR (film, cm^{-1}): 1693, 1527, 1346, 1261; MS (EI, *m/z*, %): 413 (M^+, 1.9), 94 (100); HRMS: $C_{20}H_{16}NO_7P$ calcd.: 413.0664, found: 413.0632.

α-(Diphenylphosphoryloxy)-4-methylacetophenone (3d)

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.79 (d, *J* =8.0 Hz, 2H), 7.38-7.35 (m, 4H), 7.32-7.27 (m, 6H), 7.23-7.18 (m, 2H), 5.45 (d, *J* =10.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 190.79, 150.49 (d, *J* =7.5 Hz), 145.12, 131.31, 129.81, 129.61, 128.46, 125.52, 120.20 (d, *J* =7.5 Hz), 69.88 (d, *J* =6.3 Hz), 21.76; IR (film, cm^{-1}): 1700, 1288; MS (EI, *m/z*, %): 383 (M+1, 2.9), 289 (100); HRMS: $C_{21}H_{19}O_5P$ calcd.: 382.0970, found: 382.0953; HRMS: $C_{21}H_{19}O_5P$ calcd.: 382.0970, found: 382.0953.

α-(Diphenylphosphoryloxy)benzoylacetone (3e) [3d]

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.94 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.61-7.58 (m, 1H), 7.45-7.42 (m, 2H), 7.37-7.31 (m, 2H), 7.28-7.20 (m, 5H), 7.17-7.14 (m, 3H), 6.11 (d, *J* = 8.5 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 190.35 (d, *J* = 5.0 Hz), 150.22 (d, *J* = 7.5 Hz), 134.29 (d, *J* = 12.5 Hz), 133.73, 129.76 (d, *J* = 16.3 Hz), 129.42, 128.80 (dd, *J* = 10.0, 3.8 Hz), 127.50, 125.70, 120.21 (d, *J* = 5.0 Hz), 84.06 (d, *J* = 6.3 Hz); IR (film, cm^{-1}): 1730, 1688, 1218, 1024; MS (EI, *m/z*, %): 410 (M^+, 1.3), 105 (100); HRMS: $C_{22}H_{19}O_6P$ calcd.: 410.0919, found: 410.0889.

α-(Diphenylphosphoryloxy)propiophenone (3f) [3b]

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.93-7.90 (m, 2H), 7.59-7.52 (m, 1H), 7.44-7.41 (m, 2H), 7.35-7.16 (m, 10H), 5.90 (dq, *J* = 7.0, 6.5 Hz, 1H), 1.60 (d, *J* =7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 194.28 (d, *J* =5.0 Hz), 150.40 (d, *J* =7.5 Hz), 133.72, 129.73 (d, *J* =11.3 Hz), 129.10, 128.50, 125.51(d, *J* =6.3 Hz), 120.18 (d, *J* =5.0 Hz), 115.36, 76.36 (d, *J* =6.3 Hz), 19.30 (d, *J* =5.0 Hz); IR (film, cm^{-1}): 1703, 1288; MS (EI, *m/z*, %): 383 (M+1, 1.2), 289 (100); HRMS: $C_{21}H_{19}O_5P$ calcd.: 382.0970, found: 382.0947.

α-(Dibenzylphosphoryloxy)acetophenone (3g) [3d]

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.84 (d, *J* = 8.0 Hz, 2H), 7.58-7.52 (m, 1H), 7.47 (d, *J* = 8.0Hz, 2H), 7.34-7.30 (m, 10H), 5.22 (d, *J* = 10.0 Hz, 2H), 5.18 (dd, *J* = 8.0, 6.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): 191.99 (d, *J* = 5.0 Hz), 135.67 (d, *J* = 6.3 Hz), 133.89, 128.80, 128.51, 128.02, 127.68, 69.70 (d, *J* = 5.0 Hz), 68.67 (d, *J* = 5.0 Hz); IR (film, cm^{-1}): 1708, 1279; MS (EI, *m/z*, %): 397 (M^+, 1.8), 199 (100); HRMS: $C_{22}H_{21}O_5P$ calcd.: 396.1127, found: 396.1121.

α-(Dibenzylphosphoryloxy)acetone (3h)

Oil; ^{1}H NMR (500 MHz, $CDCl_3$): 7.38-7.36 (m, 10H), 5.12 (dd, *J* = 18.0, 9.0 Hz, 4H), 4.45 (d, *J* = 9.5 Hz, 2H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 202.29 (d, *J* = 6.3 Hz), 135.51 (d, *J* = 7.5 Hz), 134.44, 128.62 (d, *J* = 7.5 Hz), 128.03, 70.66 (d, *J* = 6.3 Hz) 69.75 (d, *J* = 6.3 Hz),25.85; IR (film, cm^{-1}): 1740, 1280; MS (EI, *m/z*, %): 335 (M+1, 6.0), 137 (100); HRMS: $C_{17}H_{19}O_5P$ calcd.: 334.0970, found: 334.0934.

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CONFLICT OF INTEREST

Declared none.

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