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A NEW GENERATION OF YLIDE BY USE OF ACTIVIATED MAGNESIUM

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Abstract: A new method for the generation of ylide under neutral condition by use of activated magnesium is described and it would be expected to be used in the synthesis of alkenes in base sensitive substrates

Olefination of carbonyl compounds is one of the most useful methods and has been found widespread application in synthetic organic chemistry, particularly for the synthesis of natural products.[1] The Wittig reaction is a well known methods for achieving olefination in which a base is necessary to convert the phosphonium salts into the ylides and many kinds of bases have been chosen.[2] But in the base sensitive substrates the Wittig reaction was unsuccessful. Therefore to develop an effective method for the generation of ylide under neutral condition would be valuable. It has been reported[3] that a variety of metals such as zinc, cadnium, mercury can be used in the

dehalogenation of halophosphonium salts to generate the ylides. However, to the best of our knowledge, dehydrohalogenation of phosphonium salts by metal to generate the ylides has not been reported previously. We now wish to report a new method for the generation of ylide under neutral condition by use of magnesium activated by iodine.

The reaction sequence is as follows:

$$\underset{\mathbf{1}}{Ph_3\overset{+}{P}CH_2E\overset{-}{X}} \xrightarrow{Mg/I_2(cat)} \underset{\mathbf{2}}{Ph_3P{=}CHE} \xrightarrow{RCHO} \underset{\mathbf{3}}{RCH{=}CHE}$$

The results are summarized in Table 1.

Table 1. Substituted alkenes **3** prepared.

Compound	E	X	R	Reaction Time (h)	Yield [a] (%)	E:Z[b]
3a	CO_2CH_3	Br	C_6H_5	23	80	100:0
3b	CO_2CH_3	Br	4-$CH_3C_6H_4$	20	68	100:0
3c	CO_2CH_3	Br	4-ClC_6H_4	17	74	100:0
3d	CO_2CH_3	Br	n-C_6H_{13}	34	56	100:0
3e	CN	Cl	C_6H_5	21	88	71:29
3f	CN	Cl	4-FC_6H_4	51	92	65:35
3g	CN	Cl	2-Thienyl	5	69	51:49
3h	CN	Cl	4-$CH_3C_6H_4$	36	81	70:30
3a[c]	CO_2CH_3	Br	C_6H_5	35	73	100:0

[a] Isolated yields. [b] On the basis of ^{1}H NMR data.

[c] No iodine was added.

In this reaction a catalytic amount of iodine is necessary to be added. Otherwise the reaction time should be longer and the yield was low (see Table 1 last case). Therefore the role of iodine may be to activate the magnesiun.[4]

It is noteworthy that the characteristic feature of this reaction is no base is needed and the reaction is of wide scope. The aldehydes may be aliphatic, aromatic or heterocyclic. In the synthesis of α,β-unsaturated esters **(3a-3d)** E-isomer was obtained exclusively as judged on the basis of their NMR data, while in the synthesis of α,β-unsaturated nitriles a mixture od E- and Z-isomers were obtained.

Thus, this new method for the generation of ylide would be expected to be used in the synthesis of alkenes in base sensitive substrate, particularly in the synnthesis of natural products with base sensitive moiety.

Experimental

All melting and boiling points are uncorrected. IR spectra were recorded on Shimadzu IR-440 spectrometer. ^{1}H NMR spectra were carried out on Varian EM-360 (60 MHz) or Jeol FX90Q (90 MHz) spectrometers with tetramethylsilane as reference; $CDCl_3$ was used as solvent. *J* Values are given in Hz.

General Procedure for the Preparation of Substituted Alkenes Magnesium chips (0.5 mmol), several crystals of iodine, and phosphonium halide (1.1

mmol) were added in turn with stirring to a solution of dried N,N-dimethylformamide (1.5 ml) and aldehyde (1.0 mmol) at 20°C under nitrogen. The reaction mixture was stirred and heated at 120°C for several hours (see Table 1). After cooling, 20 ml of water was added and the mixture was extracted with petroleum ether (60-90°C). The organic layer was washed with saturated sodium chloride solution and dried. Evaporation of the solvent gave a residue which was purified by chromatography eluting with petroleum ether (bp 60-90°C)-ethyl acetate (95:5 v/v) to give the product **3.**

***Methyl 3-phenyl-2E-propenoate* 3a:**

E:Z=100:0, bp 120°C at 5 mmHg (lit.[5] bp 263°C). IR (film) υ 2950, 1720, 1640, 1450, 1370, 1280, 1200, 1160, 770 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 7.54(d, 1H, *J* 16Hz), 7.20(m, 5H), 6.20(d, 1H, *J* 16Hz), 3.55(s, 3H).

***Methyl 3-methylphenyl-2E-propenoate* 3b:**

E:Z=100:0, bp 125°C at 5 mmHg (lit.[6] bp 164-5°C at 32 mmHg). IR(film) υ 2950, 1720, 1640, 1440, 1320, 1280, 1160, 820 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 6.80-7.60(m, 5H), 6.10(d, 1H, *J* 16Hz), 3.57(s, 3H), 2.15(s, 3H).

***Methyl 3-(4-chlorophenyl)-2E-propenoate* 3c:**

E:Z=100:0, mp 74°C(lit.[7] mp 72-3°C). IR (KCl) υ 3000, 1710, 1640, 1490, 1320, 1270, 820 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 7.40(d, 1H, *J* 16Hz), 7.20(m, 4H), 6.13(d, 1H, *J* 16Hz), 3.53(s, 3H).

***Methyl 2E-nonenoate* 3d:**

E:Z=100:0, bp 80°C at 5 mmHg (lit.[8] bp 67-8°C at 3 mmHg). IR (film) υ 2900, 2850, 1730, 1660, 1460, 1380, 1270, 1040 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 6.75(dt, 1H, *J* 7, 16Hz), 5.60(d, 1H, *J* 16Hz), 3.55(s, 3H), 2.00(m, 2H), 1.10(m, 8H), 0.82(m, 3H).

***3-Phenyl-2-propenenitrile* 3e:**

E:Z=71:29, bp 90°C at 2 mmHg (lit.[5] bp 134°C at 12 mmHg). IR (film) υ 3050, 2200, 1620, 1500, 970, 750 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 7.35(m, 6H), 5.80(d, 0.71×1H, *J* 17Hz), 5.37(d, 0.29×1H, *J* 12Hz).

***3-(4-Fluorophenyl)-2-propenenitrile* 3f:**

E:Z=65:35, mp 69°C (lit.[9] mp 69-69.5°C). IR (KCl) υ 3050, 2900, 2200, 1670, 1600, 1510, 970, 850 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 6.75-7.75(m, 5H), 5.62(d, 0.65×1H, *J* 17Hz), 5.23(d, 0.35×1H, *J* 12Hz).

***3-(2-Thienyl)-2-propenenitrile* 3g:**

E:Z=51:49, bp 120°C at 10 mmHg (lit.[10] bp 154°C at 30 mmHg). IR (film) υ 3100, 2200, 1680, 1600, 1420, 1220, 1050, 960, 860 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 6.90-7.60(m, 4H), 5.40(d, 0.51×1H, *J* 16Hz), 5.03(d, 0.49×1H, *J* 12Hz).

***3-(4-Methylphenyl)-2-propenenitrile* 3h:**

E:Z=70:30, mp 67°C (lit.[6] mp 69-80°C). IR (KCl) υ 3050, 2950, 2200,

1610, 1520, 1270, 1180, 980, 800, 740 cm^{-1}. ^1H NMR ($CDCl_3$/TMS) δ 7.20(m, 5H), 5.70(d, 0.7×1H, *J* 16Hz), 5.25(d, 0.3×1H ,*J* 12Hz), 2.30(s, 3H)

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