SHORT PAPER

J. Chem. Research (S),
2003, 40-41

Novel stereoselective synthesis of (E)-α,β-unsaturated nitriles and ketones by the tandem reaction of deprotonation–oxidation–Wittig reaction from phosphonium salts[†]

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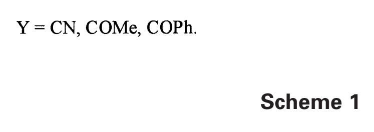
Phosphonium salt **1** and the alcohol **2** can undergo a tandem deprotonation–oxidation–Wittig reaction in the presence of sodium hydroxide and manganese dioxide, afford to an efficient method for the stereoselective synthesis of (*E*)-α,β-unsaturated nitriles and ketones **3**.

Keywords: Wittig reaction, phoshonium salts, (*E*)-α, β-unsaturated nitriles and ketones

The Wittig reaction offers an important method for the formation of carbon–carbon double bonds and has been widely used in the synthesis of natural products.[1,2] Recently it was found that alcohols can undergo the tandem reaction of oxidation–Wittig reaction with phosponium ylides to give corresponding olefination products. This showed potential use in organic synthesis.[3,4] To simplify and improve the reaction further, we have combined the deprotonation of the ylide, oxidation of alcohol and the Wittig reaction into one tandem reaction.

At the beginning of the study, potassium carbonate was used as weak base to deprotonate the phosphonium salt **1**, but the tandem reaction of deprotonation–oxidation–Wittig reaction did not proceed smoothly. The reason may be that, the concentration of phosphonium ylide **1** was too low under the condition of low concentration of aldehyde formed *in situ*. Then we used sodium hydroxide as a strong base and found that, in the presence of active manganese dioxide, the phosphonium salt **1** and the alcohol **2** underwent the tandem reaction of deprotonation–oxidation–Wittig reaction smoothly to form the desired product **3** (see Scheme 1). The tandem reaction gave a good yield of the α,β-unsaturated nitriles or ketones **3** (see Table 1). The configuration of the major products **3** are *E*-form since the coupling constants of vinyl protons range in 16-17Hz (see Experimental). The protocol has high stereoselectivity to give predominantly the (*E*)-α, β-unsaturated nitriles or ketones **3**.



Scheme 1

In conclusion, the previous tandem reaction of oxidation–Wittig reaction has been improved further in the present tandem reaction sequence of deprotonation–oxidation–Wittig reaction. This protocol has the advantages of mild reaction conditions, good yields and high stereoselectivities and affords an efficient method for the stereoselective synthesis of (*E*)-α,β-unsaturated nitriles and ketones.

Table 1 Tandem reaction of deprotonation–oxidation–Wittig reaction

Product	Y	X	R	Reaction time/h	Isolated yields/%[a]	*Z*/*E*[b]
3a	CN	Cl	4-$NO_2C_6H_4$	2	85	90/10
3b	CN	Cl	C_6H_5	3	76	80/20
3c	CN	Cl	4-$CH_3OC_6H_4$	6	71	85/15
3d	CN	Cl	$C_6H_5CH{=}CH$	3	75	95/5
3e	COMe	Br	4-$NO_2C_6H_4$	24	81	100/0
3f	COMe	Br	C_6H_5	24	71	90/10
3g	COPh	Br	4-$NO_2C_6H_4$	20	70	99/1

[a]The structure of the products are confirmed by ^1H NMR, IR, and MS.

[b]The ratioes of Z-isomer to E-isomer are determined by ^1H NMR or GC.

Experimental

All reactions were carried out in a Schlenk apparatus under nitrogen atmosphere. ^1H NMR spectra were determined in $CDCl_3$ on a Brucker Advance 400(400MHz) with TMS as internal standard. Mass spectra(EI) were obtained on a HP5989B mass spectrometer. IR spectra were taken with a Brucker Vector 22 spectrometer. Melting points were uncorrected. Cynomethylenetriphenylphosphorane, acetylmethylene triphenylphosphorane and benzoylmethylene triphenylphosphorane **1** were prepared according to the literature method.[5-7]

General procedure for the stereoselective synthesis of (E)-α,β-unsaturated nitriles and ketones **3a–g**: The mixture of phosphonium salt **1** (1.5mmol), alcohol(1.4mmol), sodium hydroxide(0.088g, 2.2mmol) and manganese dioxide (1.04g, 12mmol) in dry dichloromethane was stirred at r.t. for the time indicated in Table 1. After the reaction was complete (monitored by TLC), the mixture was filtered. The filtrate was concentrated and the crude product was subjected to preparative TLC (hexane–ethyl acetate as eluant) to give **3a–g**.

3-(4-Nitrophenyl)-2-propenenitrile **3a**: 199–200°C (Lit[8]); δ_H(ppm): 8.29(d, *J*= 8.8Hz, 2H), 7.63(d, *J*=8.8Hz, 2H), 7.47(d, *J*=16.8Hz, 1H), 6.07(d, *J*=16.8Hz, 1H); ν(cm^{-1}): 3076, 2218, 1600, 1521, 1347, 745; *m/z:* 174(M^+, 77), 101(100).

3-Phenyl-2-propenenitrile **3b:** Oil(Lit[9]); δ_H(ppm): 7.50–7.30(m, 5H), 7.12(d, *J*=16.8Hz, 1H), 5.87(d, *J*=16.8Hz, 1H); ν(cm^{-1}): 3061, 2217, 1619, 1494, 1449, 749, 689; *m/z:* 129(M^+, 100), 76(12).

3-(4-Methoxyphenyl)-2-propenenitrile **3c:** Oil(Lit[10]); δ_H(ppm): 8.29(d, *J*= 8.8Hz, 2H), 7.50–6.90(m, 3H), 5.78(d, *J*=16.4Hz, 1H), 3.95(s, 3H); ν(cm^{-1}): 3062, 2219, 1684, 1603, 1512, 1461, 768; *m/z:* 159(M^+, 100), 77(0.5).

5-Phenyl-2,4-pentadienenitrile **3d**: Oil(Lit[11]); δ_H(ppm): 7.70–7.10(m, 5H), 7.00–6.75(m, 3H), 5.44(d, *J*=16.0Hz, 1H); ν(cm^1): 3063, 2213, 1678, 1624, 1493, 748, 690; *m/z:* 155(M^+, 100), 77(13).

4-(4-Nitrophenyl)-3-buten-2-one **3e**: 114–115°C (Lit[12]); δ_H(ppm): 8.25(d, *J*= 8.4Hz, 2H), 7.68(d, *J*=8.4Hz, 2H), 7.52(d, *J*=16.4Hz, 1H),

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

6.80(d, *J*=16.4Hz, 1H), 2.41(s, 3H); ν(cm^{-1}): 3112, 1693, 1669, 1614, 1513, 1342, 747; *m/z:* 191(M$^+$, 19), 43(100).

4-Phenyl-3-buten-2-one **3f**: Oil(Lit[13]); δ_H(ppm): 7.60–7.24(m, 6H), 6.70(d, *J*=16.4Hz, 1H), 2.37(s, 3H); ν(cm^{-1}): 3028, 1668, 1610, 1495, 1450, 749, 691; *m/z:* 146(M$^+$, 61), 103(100).

3-(4-Nitrophenyl)-1-phenyl-2-propen-1-one **3g**: 158–160°C (Lit[14]); δ_H(ppm): 8.27(d, *J*=8.8Hz, 2H), 8.02(d, *J*=8.4 Hz, 2H), 7.80-7.75(m, 3H), 7.63(d, *J*=16.0Hz, 1H), 7.62-7.50(m, 3H); ν(cm^{-1}): 3080, 1658, 1609, 1518, 1341, 747, 688; *m/z:* 258(M$^+$, 43), 77(100).

We thank the National Natural Science Foundation of China for financial support of the project 29972036.

Received 5 August 2002; accepted 20 August 2002
Paper 02/1501

References

1 B.E. Maryann and A.B. Reties, *Chem. Rev.*, 1989, **89**, 863.
2 A.W. Johnson, W.C. Kaska, K.A.O. Starzewsky, D. Dixon, *Ylides and Imines of Phosphorus*, Wiley, New York, 1993.
3 X. Wei, R.J.K.Taylor, *J.Org.Chem.*, 2000, **65**, 616.
4 X. Wei, R.J.K.Taylor, *Tetrahedron Lett.*, 1998, **39**, 3815.
5 G.P. Schiemenz and H. Engelhard, *Ber*, 1961, **94**, 578.
6 D.B. Denney and S.T. Ross, *J. Org. Chem.*, 1962, **27**, 998.
7 F. Ramirez and S. Dershowitz, , *J. Org. Chem.*, 1957, **22**, 41.
8 J.H. Zheng, Y. Yu and Y.C. Sheng, *Synth. Commun.*, 1990, **20**, 3277.
9 T. Funabiki, H. Hosomi, S. Yoshida and K. Tarama, *J. Ar. Chem. Soc.*, 1982, **104**, 1560.
10 C. Palomo, J.M. Aizpurua, J.M. Garcia, I. Ganboa, F.P. Cossio, B. Lecea and C. Lopez, *J.Org.Chem.*, 1990, **55**, 2498.
11 Y.Z. Huang, Y.C. Sheng and C. Chen, *Synth. Commun.*, 1989, **19**, 83.
12 M. Nakagawa, H. Nakao and K.I. Watanabe, *Chem. Lett.*, 1985, **3**, 391.
13 H.L. Gaering, S.S. Kantner and E.P. Seitz, *J.Org.Chem.*, 1985, **50**, 5495.
14 K.I. Watanabe, A. Imazawa, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 3208.