Synthesis of alkyl 2-[2-oxopyridin-1(2*H*)-yl]acrylates by nucleophilic addition of alkyl propiolates catalysed by Ph_3P

Bita Mohtat[a], Sepideh Jabbar[a], Abdollah Ghasemi[a] and Issa Yavari[b]*

[a]*Chemistry Department, Islamic Azad University, Karaj, Iran*

[b]*Chemistry Department, Science & Research Campus, Islamic Azad University, Ponak, Tehran, Iran*

2-Hydroxypyridine undergoes a smooth reaction with alkyl propiolates in the presence of triphenylphosphine (15 mol%) to produce the corresponding alkyl 2-[2-oxopyridin-1(2*H*)-yl]acrylates in good yields. When the reaction was performed by 2-hydroxyquinoline and 2-hydroxyisoquinoline similar α-substituted alkyl acrylates were obtained.

Keywords: NH-acids, 2-hydroxypyridine, 2-hydroxyquinoline, 2-hydroxyisoquinoline, alkyl acrylates, alkyl propiolates, triphenylphosphine

Organophosphorus compounds have been used in organic synthesis as useful reagents as well as ligands of a number of transition metal catalysts.[1-3] However, there are a few reactions in which organophosphorus(III) species work as catalysts.[4-8] The phosphine induced isomerisation of alkynoates and addition to the α-position of these substrates indicated the possibility of a new reactivity pattern for alkynoates-nucleophilic addition at the α-position as a new source of α-substituted alkyl acrylates.

An important point is the ability of the nucleophile to undergo Michael addition in preference to the α-attack since phosphines could also serve as general base catalysts for conjugate additions.[1-3] Alkyl propiolates should be particularly prone to undergo such Michael additions.

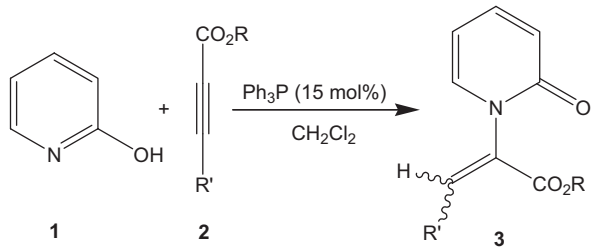
In this regard, triphenylphosphine (Ph_3P) have received increasing attention as versatile and mild reagent in many occasions for various organic transformations under neutral conditions in recent years.[9-12] The addition reaction between electron-deficient acetylenic compounds and nitrogen-containing hetrocycles has been extensively investigated.[13,14]

Recently, we reported[15] the synthesis of the *E/Z* isomers of dialkyl 2-(2-oxopyridin-1(2*H*)-yl)but-2-enedioate**s** through the reaction of 2-hydroxypyridine with dialkyl acetylenedicarboxylates in the presence of triphenylphosphine (Ph_3P). In this work, we present the nucleophilic α-addition of 2-hydroxypyridine **(1)** to alkyl propiolates **(2)** in the presence of Ph_3P under neutral conditions. Thus, alkyl propiolate undergoes a smooth reaction with the 2-hydroxypyridine in the presence of Ph_3P to produce alkyl 2-[2-oxopyridin-1(2*H*)-yl]acrylates **(3)** in good yields (Scheme 1).

The products were separated by column chromatography and identified as **3** based on their elemental analyses and their IR, ^1H, and ^{13}C NMR spectral data. The mass spectra of these compounds displayed molecular ion peaks at appropriate *m/z* values. The ^1H NMR spectrum of **3a** exhibited a single sharp line for the methyl group at δ = 3.77 ppm, together with two singlet at δ = 5.80 and 6.38 ppm for the C=CH_2 protons. The ^{13}C NMR spectrum of **3a** showed nine distinct resonances in agreement with the methyl 2-[2-oxopyridin-1(2*H*)-yl]acrylate structure. The ^1H and ^{13}C NMR spectra of **3b** and **3c** are similar to those of **3a** except for the alkoxy moieties, which exhibited characteristic resonances with appropriate chemical shifts.

NMR spectroscopy was employed to distinguish between **(*Z*)-3c** and **(*E*)-3c**. The (*Z*) and (*E*) configurations of the carbon–carbon double bonds in **3c** are based on the chemical shift of the olefinic proton.[16] The ^1H NMR spectra of **(*Z*)-3c** showed olefinic proton at 7.00 ppm, while the **(*E*)-3c** isomer exhibited the olefinic proton at 7.82 ppm.

Mechanistically, it is conceivable that the reaction involves the initial formation of a zwitterionic 1 : 1 intermediate **4** between Ph_3P and the acetylenic compound (Scheme 2).[17] The intermediate **4** is then protonated by the OH-acidic **1** to afford **5**. The latter might be attacked by the N-atom of the bidentate anion **6** to afford the ylide **7**. This intermediate undergoes a proton transfer to furnish the 1,3-diionic structure **8,** which is converted to the final product by loss of Ph_3P (Scheme 2).



2, 3	R	R'
a	Me	H
b	Et	H
c	Et	Ph

Scheme 1

When the reaction is carried out using 2-hydroxyquinoline and 2-hydroxyisoquinoline the same α-substituted alkyl acrylates **(9** and **10)** are obtained in excellent overall yields (Scheme 2). Compounds **9** and **10** were identified based on their elemental analyses and their IR, ^1H, and ^{13}C NMR spectral data.

In conclusion, we have described a convenient route to α-substituted alkyl acrylates, through nucleophilic addition to alkyl propiolate. These functionalised acrylates may be considered as potentially useful synthetic intermediates because they possess atoms with different oxidation states. The present method has the advantages that not only are the reaction performed under neutral conditions, but also the substances can be mixed without any modification. The simplicity of the present procedure makes it an interesting alternative to other approaches.

Experimental

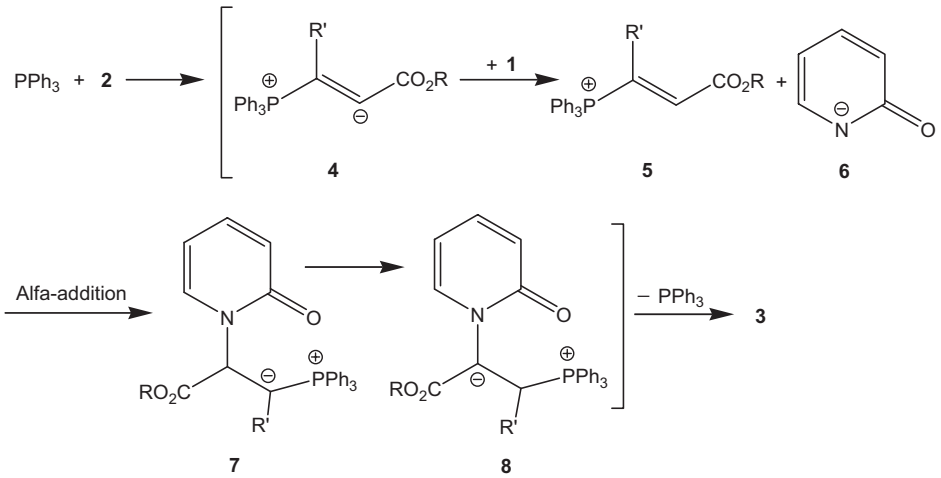
General procedure

Compounds **1**, **2** and Ph_3P were obtained from Fluka and were used without further purification. M.p. Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer. ^1H- and ^{13}C NMR spectra: Bruker DRX-500 AVANCE instrument; in $CDCl_3$ at 300 and 75 MHz, respectively; δ in ppm. EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer, in *m/z*. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyser.

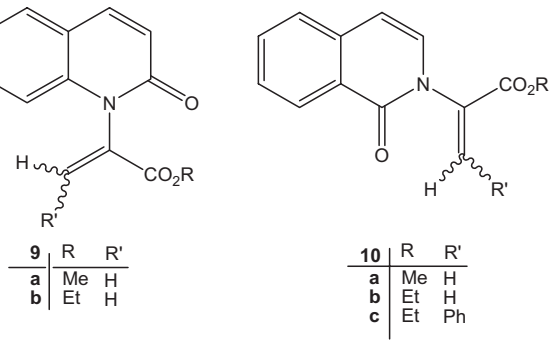
Typical procedure for preparation of **(3)**

To a stirred solution of 0.52 g of Ph_3P (2 mmol) and 0.19 g **1** (2 mmol) in 10 ml of CH_2CI_2 was added, drop wise, a mixture of **2** (2 mmol) in 4 ml of CH_2Cl_2 at –5 °C over 10 min. The reaction

* Correspondent. E-mail: yavarisa@modares.ac.ir; isayavar@yahoo.com



Scheme 2



Scheme 3

mixture was then allowed to warm up to room temperature and stirred for 24 h. The solvent was removed under reduced pressure and the residue was separated by column chromatography (SiO_2; *n*-hexane: EtOAc = 1:1) to afford the pure title compounds.

Methyl 2-[2-oxopyridin-1(2H)-yl]acrylate (**3a**): Yellow oil, yield: 0.26 g (75%). IR (KBr): 1737 and 1675 (C=O). ^{1}H NMR: 3.77 (3 H, *s*, OMe), 5.80 (1 H, s, CH), 6.19 (1 H, t, ^3J = 6.8Hz, CH), 6.38 (1 H, s, CH), 6.51 (1 H, d, ^3J = 9.3Hz, CH), 7.16 (1 H, d, ^3J = 6.8Hz, CH), 7.43 (1 H, t, ^3J = 9.3Hz, CH). ^{13}C NMR: 52.7 (OMe), 106.1 (CH), 121.3 (CH_2), 123.5, 137.2 (2 CH), 140.1 (C), 140.5 (CH), 161.9, 162.6 (2 C=O). EI-MS: *m/z* (%) = 179 (M^+, 20), 83 (87), 59 (40), 39 (75). Anal. Calcd for $C_9H_9NO_3$ (179.17): C, 60.33; H, 5.06; N, 7.82; found: C, 60.66; H, 5.15; N, 7.74%.

Ethyl 2-[2-oxopyridin-1(2H)-yl]acrylate (**3b**): Yellow oil, yield: 0.26 g (60%). IR (KBr): 1737 and 1673 (C=O). ^{1}H NMR: 1.26 (3 H, t, ^3J = 7.1Hz, Me), 4.25 (2 H, q, ^3J = 7.1Hz, OCH_2), 5.80 (1 H, s, CH), 6.18 (1 H, t, ^3J = 6.7Hz, CH), 6.39 (1 H, s, CH), 6.52 (1 H, d, ^3J = 9.3Hz, CH), 7.17 (1 H, d, ^3J = 6.7Hz, CH), 7.38 (1 H, t, ^3J = 9.3Hz, CH). ^{13}C NMR: 14.0 (Me), 62.0 (OCH_2), 106.1 (CH), 121.3 (CH_2), 123.2, 137.3 (2 CH), 140.5 (C), 140.6 (CH), 161.9, 162.2, (2 C=O). EI-MS: *m/z* (%) = 193 (M^+, 4), 164 (100), 120 (25), 96 (23), 51 (25). Anal. Calcd for $C_{10}H_{11}NO_3$ (193.2): C, 62.17; H, 5.74; N, 7.25; found: C, 62.54; H, 5.57; N, 7.68%.

Ethyl (2Z)-2-[2-oxopyridin-1(2H)-yl]-3-phenylacrylate (***Z*-3c**): Yellow oil, yield: 0.12 g (25%). IR (KBr): 1721 and 1668 (C=O). ^{1}H NMR: 1.10 (3 H, t, ^3J = 7.1Hz, Me), 4.18 (2 H, q, ^3J = 7.1Hz, OCH_2), 6.23 (1 H, t, ^3J = 6.7Hz, CH), 6.55 (1 H, d, ^3J = 9.3Hz, CH), 7.00 (1 H, s, CH), 7.15 (1 H, d, ^3J = 6.7Hz, CH),7.17–7.42 (5 H, m, 5CH) 7.44 (1 H, t, ^3J = 9.3Hz, CH). ^{13}C NMR: 13.5 (Me), 61.5, (OCH_2), 106.4, 121.1, 128.4, 128.6, 130.2, 131.5 (8 CH), 131.9 (C), 134.7, 137.9 (2 CH), 140.5 (C), 162.2, 163.4 (2 C=O). EI-MS: *m/z* (%) = 256 (M^+, 9), 164 (71), 120 (25), 96 (23), 77 (68), 73 (25). Anal. Calcd for $C_{16}H_{15}NO_3$ (256.28): C, 71.36; H, 5.61; N, 5.20; found: C, 71.66; H, 5.75; N, 5.34%.

Ethyl (2E)-2-[2-oxopyridin-1(2H)-yl]-3-phenylacrylate (***E*-3c**): Yellow oil, yield: 0.30 g (60%). IR (KBr): 1721 and 1668 (C=O). ^{1}H NMR: 1.31 (3 H, t, ^3J = 7.1Hz, Me), 4.30 (2 H, q, ^3J = 7.1Hz, OCH_2), 6.16 (1 H, t, ^3J = 6.7Hz, CH), 6.67 (1 H, d, ^3J = 9.8Hz, CH), 7.16 (1 H, d, ^3J = 6.8Hz, CH), 7.19–7.41 (5 H, m, 5 CH), 7.43 (1 H, t, ^3J = 9.3Hz, CH), 7.82 (1 H, s, CH). ^{13}C NMR: 14.1 (Me), 62.0, (OCH_2), 106.8, 121.9, 128.9, 130.0, 130.5, 132.0 (8 CH), 132.1(C), 137.4, 137.7 (2 CH), 140.7 (C), 162.4, 163.4 (2 C=O). EI-MS: *m/z* (%) = 256 (M^+, 9), 164 (71), 120 (25), 96 (23), 77 (68), 73 (25). Anal. Calcd for $C_{16}H_{15}NO_3$ (256.28): C, 71.36; H, 5.61; N, 5.20; found: C, 71.56; H, 7.35; N, 5.30%.

Methyl 2-[2-oxoquinolin-1(2H)-yl]acrylate (**9a**): Yellow oil, yield: 0.32 g (70%). IR (KBr): 1726, 1650 (C=O). ^{1}H NMR: 3.79 (3 H, s, OMe), 6.01 (1 H, s, CH), 6.71 (1 H, d, ^3J = 9.6Hz, CH), 6.96 (1 H, s, CH), 7.17 (1 H, d, ^3J = 8.1Hz, CH), 7.22 (1 H, t, ^3J = 7.6Hz, CH), 7.47 (1 H, t, ^3J = 8.1Hz, CH), 7.59 (1 H, d, ^3J = 7.6Hz, CH), 7.75 (1 H, d, ^3J = 9.6Hz, CH). ^{13}C NMR: 52.8 (OMe) 114.8 (CH), 120.4 (C), 121.6 (CH_2), 122.7, 128.8, 129.5, 130.7 (4 CH), 135.0, 139.8 (2 C), 140.4 (CH), 161.8, 163.0 (2 C=O). EI-MS: *m/z* (%) = 229 (M^+, 23), 214 (14), 201 (44), 170 (75), 128 (30), 115 (40). Anal. Calcd for $C_{13}H_{11}NO_3$ (229.23): C, 68.11; H, 4.84; N, 6.11; found: C, 68.31; H, 4.95; N, 6.24%.

Ethyl 2-[2-oxoquinolin-1(2H)-yl]acrylate (**9b**): Yellow oil, yield: 0.36 g (75%). IR (KBr): 1735, 1650 (C=O). ^{1}H NMR: 1.26 (3 H, t, ^3J = 7.1Hz, Me), 4.26 (2 H, q, ^3J = 7.1Hz, OCH_2), 6.01 (1 H, s, CH), 6.70 (1 H, d, ^3J = 9.6Hz, CH), 6.95 (1 H, s, CH), 7.17 (1 H, d, ^3J = 8.4Hz, CH), 7.23 (1 H, t, ^3J = 7.6Hz, CH), 7.48 (1 H, t, ^3J = 8.4Hz, CH), 7.56 (1 H, d, ^3J = 7.6Hz, CH), 7.75 (1 H, d, ^3J = 9.6Hz, CH). ^{13}C NMR: 14.0 (Me), 62.0 (OCH_2) 114.8 (CH) 120.4 (C), 121.7 (CH_2), 122.6, 128.7, 129.22, 130.6 (4 CH), 135.3, 139.8 (2 C), 140.3 (CH), 162.5, 163.6 (2 C=O). EI-MS: *m/z* (%) = 243 (M^+, 38), 229 (71), 214 (20), 170 (34), 73 (13). Anal. Calcd for $C_{14}H_{13}NO_3$ (243.26): C, 69.12; H, 5.39; N, 5.76; found: C, 69.34; H, 5.33; N, 5.84%.

Methyl 2-[2-oxo-isoquinolin-1(2H)-yl]acrylate (**10a**): Yellow oil, yield: 0.32 g (72%). IR (KBr): 1753 and 1659 (C=O). ^{1}H NMR: 3.80 (3 H, s, O*Me*), 5.84 (1 H, d, ^3J = 0.6Hz, CH), 6.42 (1 H, d, ^3J = 0.6Hz, CH), 6.51 (1 H, d, ^3J = 7.4Hz, CH), 7.01 (1 H, d, ^3J = 7.4Hz, CH), 7.44 (1 H, t, ^3J = 7.4Hz, CH), 7.49, (1 H, d, ^3J = 8.2Hz, CH), 7.63 (1 H, t, ^3J = 8.2Hz, CH), 8.37 (1 H, d, ^3J = 7.4Hz, CH). ^{13}C NMR: 52.7 (O*Me*), 106.8 (CH), 123.2 (CH_2), 125.9 (C), 126.1, 127.2, 127.9, 131.3, 132.8 (5 CH), 137.3, 140.4 (2 C), 161.7, 163.2 (2 C=O). EI-MS: *m/z* (%) = 229 (M^+, 12), 214 (14), 201 (44), 170 (75), 128 (30), 115 (40). Anal. Calcd for $C_{13}H_{11}NO_3$ (229.23): C, 68.11; H, 4.84; N, 6.11; found: C, 68.26; H, 4.75; N, 6.20%.

Ethyl 2-[2-oxoquinolin-1(2H)-yl]acrylate (**10b**): Yellow oil, yield: 0.38 g (78%). IR (KBr): 1735, 1667 (C=O). ^{1}H NMR: 1.28 (3 H, t, ^3J = 7.1Hz, Me), 4.27 (2 H, q, ^3J = 7.1Hz, OCH_2), 5.83 (1 H, d, ^3J = 0.8Hz, CH), 6.41 (1 H, d, ^3J = 0.8Hz, CH), 6.51 (1 H, d, ^3J = 7.4Hz, CH), 6.98 (1 H, d, ^3J = 7.4Hz, CH), 7.44 (1 H, t, ^3J = 7.4Hz, CH), 7.49 (1 H, d, ^3J = 7.1Hz, CH), 7.63 (1 H, t, ^3J = 7.1Hz, CH), 8.37 (1 H, d, ^3J = 7.4Hz, CH). ^{13}C NMR: 14.1 (Me), 61.9 (OCH_2), 106.7 (CH), 122.9 (CH_2), 126.0 (C), 126.1, 127.2, 128.1, 131.4, 132.8 (5 CH), 137.2, 140.7 (2 C), 161.7, 162.7 (2 C=O). EI-MS: *m/z* (%) = 243 (M^+, 38), 229 (71), 214 (20), 170 (34), 73 (13). Anal. Calcd for $C_{14}H_{13}NO_3$ (243.26): C, 69.12; H, 5.39; N, 5.76; found: C, 69.25; H, 5.35; N, 5.84%.

Ethyl (2Z)-2-[2-oxoquinolin-1(2H)-yl]-3-phenylacrylate (***Z*-10c**): Yellow oil, yield: 0.22 g (35%). IR (KBr): 1721 and 1668 (C=O). ^{1}H NMR: 1.09 (3 H, t, ^3J = 7.1Hz, Me), 4.21 (2 H, q, ^3J = 7.1Hz, OCH_2), 6.58 (1 H, d, ^3J = 7.4Hz, CH), 6.76 (1 H, d, ^3J = 7.4Hz, CH),7.05 (1 H,

s, CH), 7.20–7.27 (5 H, m, 5CH), 7.35 (1 H, t, ^3J = 7.4Hz, CH), 7.50 (1 H, d, ^3J = 7.1Hz, CH), 7.65 (1 H, t, ^3J = 7.1Hz, CH), 8.40 (1 H, d, ^3J = 7.4Hz, CH). ^{13}C NMR: 13.5, (Me), 61.5, (OCH_2), 107.4 (CH), 126.2 (C), 126.3, 127.0, 128.9, 130.1, 130.3, 130.4, 131.6, 131.8, 132.9 (11 CH), 137.1, 137.2, 137.4 (3 C), 162.1, 164.0 (3 C=O). EI-MS: *m/z* (%) = 319 (M^+, 10), 229 (21), 214 (20), 170 (34), 77 (60), 73 (13). Anal. Calcd for $C_{20}H_{17}NO_3$ (319.35): C, 75.22; H, 5.37; N, 4.39; found: C, 75.36; H, 5.38; N, 4.44%.

Ethyl (2E)- 2-[2-oxoquinolin-1(2H)-yl]-3-phenylacrylate (***E*-10c**): Yellow oil, yield: 0.34 g (55%). IR (KBr): 1721 and 1668 (C=O). ^{1}H NMR: 1.29 (3 H, t, ^3J = 7.1Hz, Me), 4.31 (2 H, q, ^3J = 7.1Hz, OCH_2), 6.51 (1 H, d, ^3J = 7.4Hz, CH), 6.76 (1 H, d, ^3J = 7.4Hz, CH), 7.20–7.27 (5 H, m, 5CH), 7.29 (1 H, t, ^3J = 7.4Hz, CH), 7.53 (1 H, d, ^3J = 7.1Hz, CH), 7.69 (1 H, t, ^3J = 7.1Hz, CH), 7.83 (1 H, s, CH), 8.46 (1 H, d, ^3J = 8.1Hz, CH). ^{13}C NMR: 14.1 (Me), 62.0, (OCH_2), 107.0 (CH), 125.8 (C), 126.1, 127.4, 128.2, 128.3, 128.4, 129.1, 132.1, 133.4, 133.7 (11 CH), 134.4, 137.1, 137.2 (3 C), 162.0, 164.0 (2 C=O). EI-MS: *m/z* (%) = 319 (M^+, 10), 229 (21), 214 (20), 170 (34), 77 (60), 73 (13). Anal. Calcd for $C_{20}H_{17}NO_3$ (319.35): C, 75.22; H, 5.37; N, 4.39; found: C, 75.46; H, 5.45; N, 4.45%.

We thank the Islamic Azad University of Karaj for support of this work.

Received 23 June 2008; accepted 18 August 2008
Paper 08/0015 doi: 10.3184/030823408X377771
Published online: 17 October 2008

References

1 L.D. Quin, *A Guide to organophosphorus chemistry*, Wiley-Interscience, New York, 2000.
2 R. Engel, *Synthesis of carbon–phosphorus bond*, CRC Press, Boca Raton, 1998.
3 D.E.C. Cobridge, Phosphorus: *An outline of chemistry, biochemistry and uses*, 5th edn, Elsevier, Amsterdam, 1995.
4 B.M. Trost and U. Kazmaier, *J. Am. Chem. Soc*., 1992, **114**, 7933.
5 B.M. Trost and C. Li, *J. Am. Chem. Soc*., 1994, **116**, 3167.
6 B.M. Trost and C. Li, *J. Am. Chem. Soc*., 1994, **116**, 10819.
7 C. Guo and X. Lu, *J. Chem. Soc., Perkin Trans. 1,* 1993, 1921.
8 C. Guo and X. Lu, *J. Chem. Soc., Chem. Commun*., 1993, 394.
9 I. Yavari and A. Ramazani, *Synth. Commun.,* 1997, **27**, 1449.
10 I. Yavari and H. Norouzi-Arasi, *Phosphorus, Sulfur, and Silicon,* 2002, **177**, 87.
11 I. Yavari, S. Souri, M. Sirouspour, H. Djahaniani and F. Nasiri, *Synthesis,* 2005, 1761.
12 I. Yavari and M. Bayat, *Tetrahedron,* 2003, **59**, 2001.
13 R.M. Acheson and N.F. Elmore, *Adv. Hetrocycl. Chem*., 1978, **23**, 263.
14 R.M. Acheson and J. Woolard, *J. Chem. Soc. Perkin Trans. 1*, 1975, 438.
15 I. Yavari, A.R. Alborzi and B. Mohtat, *J. Chem. Res. (S),* 2007, 401.
16 E.L. Eliel and S.H. Wilen, *Stereochemistry of organic compounds*, Wiley, New York, 1994, p. 570.
17 Y. Shen, *Acc. Chem. Res.,* 1998, **31**, 584.