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Highly regioselective conversion of epoxides to β-hydroxy nitriles using metal(II) Schiff base complexes as new catalysts under mild conditions

Hossein Naeimi *, Azam Karshenas

Department of Organic Chemistry, Faculty of Chemistry, University of Kashan, Kashan 87317, Iran

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ABSTRACT

Epoxides undergo efficient ring opening with potassium cyanide in acetonitrile in the presence of metal Schiff base complexes as catalysts. This method was carried out under neutral and mild conditions with both high yields and high regioselectivity within a short period of time. Thus, several β-hydroxy nitriles, useful intermediates for the synthesis of biologically active molecules, were easily obtained at room temperature.

1. Introduction

Epoxides are versatile intermediates in organic synthesis. They can be easily prepared and cleaved with different nucleophiles, leading to the formation of regio- and stereoselective ring opened products. β-Hydroxy nitriles are important reagents as well as technical products in organic chemistry. They have been extensively investigated and employed for the preparation of intermediates of many naturally occurring bioactive compounds [1–4].

β-Hydroxy nitriles can be prepared by the reaction of epoxides with the toxic volatile HCN [5], NaCN [6,7], KCN [8], LiCN [9], cyanide exchange resin [10b] and TBAF-TMSCN in CH_3CN [11–13]. The reaction of epoxides with NaCN, KCN or HCN usually requires extended times [6,7b,c,8c], protic solvents [5–7,8a,b] or additives [7a,8c], e.g., the Zr-catalyzed one-pot synthesis of β-cyanohydrins from olefins via epoxidation of the olefins and nucleophilic ring opening of the epoxides [10a]. By using trimethylsilylcyanide (TMSCN) in the preparation of β-hydroxy nitriles, the iso-nitrile has been formed [12,13d] as the main product.

In the literature, ring opening of epoxides with the cyanide ion as a nucleophile has been carried out by employing non-volatile alkali cyanides in the presence of perchlorate salts [8c] or $Yb(CN)_3$ [12,8c]. Some methods employ acetone cyanohydrin in the presence of various bases [14], lanthanide alkoxides [15] or alkyl aluminum cyanides [16]. In most methods referred to in the literature, the reaction conditions are usually severe; some reagents are commercially unavailable and have to be prepared from alkali cyanides. In addition, the use of alkyl aluminum cyanides presents difficulties in large scale reactions.

To overcome these limitations, we developed a new approach to oxirane ring opening with potassium cyanide in acetonitrile as a solvent, using Schiff base metal (II) complexes as homogeneous and especially effective catalysts [17] at room temperature. In this study, we have reported a mild, simple and efficient method for the synthesis of β-hydroxy nitriles.

2. Experimental section

2.1. Materials

All commercially available reagents were used without further purification and were purchased from the Merck Chemical Company in high purity. The epoxides and used solvents were purified by standard procedures.

2.2. Apparatus

IR spectra were recorded using a Perkin Elmer FT-IR 550 spectrometer and values are reported as ν in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded with a 400 MHz spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal reference. Melting points were determined in open capillaries using an Electrothermal Mk3 apparatus. Mass spectra were recorded on a Finnigan MAT 44S with an ionization voltage of 70 eV. The elemental analyses (CHN) were obtained on a Carlo ERBA Model EA 1108 analyzer or a Perkin Elmer 240c analyzer. The chromatography was carried

* Corresponding author. Tel.: +98 3615912388; fax: +98 3615912397.
E-mail address: naeimi@kashanu.ac.ir (H. Naeimi).

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out on silica gel 60 (70–230 mesh). The purity determination of the substrates and reactions were monitored by thin layer chromatography (TLC).

2.3. General procedure

2.3.1. General procedure for the synthesis of the Schiff base ligands

All the tetradentate Schiff base ligands were prepared by the condensation between diamines and 2,5-dihydroxybenzaldehyde in methanol. The Schiff base ligands were prepared by dissolving 2,5-dihydroxybenzaldehyde (0.35 g, 2.5 mmol) and diamine (0.1 g, 1.4 mmol) in methanol with stirring. The stirring was continued until completion of the reaction. The progress of the reaction was monitored by thin layer chromatography (TLC). After the completion of the reaction, a colored substance was obtained. The solid product was filtered off and washed with cold MeOH and the pure Schiff base was obtained in high yield after leaving the solid for the appropriate time to dry. The Schiff base products were identified by physical and spectroscopic data [18].

2.3.1.1. 2,2′-[1,2–Ethanediyl-bis(nitrilomethylidene)]-bis(4-hydroxyphenol). Yellow solid; Yield: 95%; M.p: 286–288 °C. *Anal.* Calc.: C, 64; H, 5.3; N, 9.3. Found: C, 64.3; H, 5.3; N, 9.2%. IR (KBr)/ν(cm^{-1}): 3190–3385 (s, br, 2OH), 1640 (s, C=N), 1596, 1507 (Ar), 1217 (s, C–O). ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 12.5 (br, 2OH, intramolecular hydrogen bonding), 8.97 (br, 2OH), 8.47 (s, 2CH imine), 6.67–6.78 (m, 6H, Ar), 3.87 (s, 4H, $2CH_2$). ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 167.08, 153.50, 149.75, 120.37, 118.96, 117.93, 116.98, 59.50. MS *m*/*z*: 300 (M^+, 2), 165 (4), 150 (18), 136 (24), 123 (88), 109 (28), 80 (65), 56 (100), 67 (87).

2.3.1.2. 2,2′-[1,7–Heptanediyl-bis(nitrilomethylidene)]-bis(4-hydroxyphenol). Yellow solid; Yield: 90%; M.p: 215–217 °C. *Anal.* Calc.: C, 68.1; H, 7.02; N, 7.6. Found: C, 68.1; H, 6.9; N, 7.4%. IR (KBr)/ν(cm^{-1}): 3373–3500 (s, br, 2OH), 1646 (s, C=N), 1503, 1457 (Ar), 1239 (s, C–O). ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 12.7 (br, 2OH, intramolecular hydrogen bonding), 8.90 (br, 2OH), 8.42 (s, 2CH imine), 6.78 (d, 2H, Ar), 6.76 (dd, 2H, Ar), 6.69 (d, 2H, Ar), 3.54 (t, 4H, $2CH_2$), 1.58 (m, 8H, $4CH_2$), 1.33 (m, 2H, CH_2). ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 165.77, 153.62, 149.70, 120.12, 119.01, 117.25, 116.90, 59.02, 30.83, 28.88, 27.03. MS *m*/*z*: 370 (M^+, 4), 235 (6), 220 (22), 206 (28), 193 (90), 179 (32), 150 (68), 137 (92), 126 (100).

2.3.1.3. 2,2′-[1,2–Phenylenediyl-bis(nitrilomethylidene)]-bis(4-hydroxyphenol). Red solid; Yield: 96%; M.p: 270–272 °C. *Anal.* Calc.: C, 68.9; H, 4.6; N, 8.04. Found: C, 68.7; H, 4.9; N, 7.7%. IR (KBr)/ν(cm^{-1}): 3250–3500 (s, br, 2OH), 1619 (s, C=N), 1572, 1488 (Ar), 1289 (s, C–O). ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 12.13 (br, 2OH, intramolecular hydrogen bonding), 9.10 (br, 2OH), 8.79 (s, 2CH imine), 7.40 (dd, 2H, Ar), 7.37 (dd, 2H, Ar), 7.02 (d, 2H, Ar), 6.86 (dd, 2H, Ar), 6.78 (d, 2H, Ar). ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 164.28, 153.73, 150.04, 142.98, 128.03, 121.77, 120.28, 119.88, 117.38, 117.27. MS *m*/*z*: 348 (M^+, 3), 212 (10), 129 (14), 92 (78), 93 (14), 80 (42), 77 (47), 65 (100).

2.3.1.4. 2,2′-[1,9–Nonanediyl-bis(nitrilomethylidene)]-bis(4-hydroxyphenol). Yellow solid; Yield: 85%; M.p: 186–189 °C. *Anal.* Calc.: C, 69.3; H, 7.5; N, 7.03. Found: C, 69.4; H, 7.2; N, 7.1%. IR (KBr)/ν(cm^{-1}): 3325–3525 (s, br, 2OH), 1646 (s, C=N), 1545, 1460 (Ar), 1240 (s, C–O). ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 12.73 (br, 2OH, intramolecular hydrogen bonding), 8.90 (br, 2OH), 8.42 (s, 2CH imine), 6.79 (d, 2H, Ar), 6.77 (dd, 2H, Ar), 6.69 (d, 2H, Ar), 3.53 (t, 4H, $2CH_2$), 1.56 (m, 4H, $2CH_2$), 1.28 (m, 10H, $5CH_2$). ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 165.78, 153.57, 149.72, 120.10, 119.01, 117.22, 116.88, 59.03, 30.86, 29.38, 29.12, 27.04. MS *m*/*z*: 398 (M^+, 8), 263 (5), 248 (24), 234 (28), 221 (95), 207 (30), 178 (70), 165 (94), 154 (100).

2.3.1.5. 2,2′-[3,6-Dioxo-1,8-octanediyl-bis(nitrilomethylidine)]-bis(4-hydroxyphenol). Yellow solid; Yield: 80%; M.p: 158–160 °C. *Anal.* Calc.: C, 61.3; H, 6.5; N, 7.03. Found: C, 61.8; H, 6.2; N, 7.2%. IR (KBr)/ν(cm^{-1}): 3300–3450 (s, br, 2OH), 1649 (s, C=N), 1544, 1452 (Ar), 1235 (s, C–O). ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 12.75 (br, 2OH, intramolecular hydrogen bonding), 8.90 (br, 2OH), 8.42 (s, 2CH imine), 6.78 (d, 2H, Ar), 6.74 (dd, 2H, Ar), 6.67 (d, 2H, Ar), 3.60 (s, 4H, $2CH_2$), 3.53 (t, 4H, $2CH_2$), 3.50 (t, 4H, $2CH_2$). ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 167.05, 153.56, 149.71, 120.27, 119.05, 117.30, 116.93, 76.80, 70.36, 58.79.

2.3.2. General procedure for the preparation of the Schiff base metal (II) complexes

$M(O_2CCH_3)_2$ (1 mmol) was dissolved in MeOH (10 mL) and the solution was filtered and added drop-wise into a methanolic solution of the ligand (1 mmol). The reaction mixture was stirred until completion of the reaction. The progress of the reaction was monitored by TLC. After the completion of complex formation, a colored substance was obtained. The solid product was filtered off and washed with MeOH, and the pure Schiff base complex was obtained.

*2.3.2.1. 2,2′-(1,2-Ethanediylbisnitrilomethylidine)-bis(4-hydroxyphenolato) nickel(II) (**A**).* Brown solid, Yield: 90%, M.p: 312–314 °C; IR (KBr)/ν(cm^{-1}): 3350–3408 (br, OH), 1618 (s, C=N), 1554, 1451 (s, Ar C=C), 1299 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 8.55 (br, 2H, 2 OH), 7.77 (s, 2CH imine), 6.52–6.73 (m, 6H, Ar), 3.15 (s, 4H, 2 CH_2); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 162.41, 158.66, 146.20, 124.45, 120.45, 119.60, 115.61, 64.10; *Anal.* Calc.: C, 53.9; H, 3.9; N, 7.9. Found: C, 54.1; H, 3.8; N, 8.02%. MS *m*/*z*: 356 (M^+, 6), 131 (4), 107 (10), 91 (100), 77 (70), 51 (95).

*2.3.2.2. 2,2′-(1,7-Heptanediylbisnitrilomethylidine)-bis(4-hydroxyphenolato)nickel(II) (**B**).* Light green solid, Yield: 80%, M.p: 310–312 °C; IR (KBr)/ν(cm^{-1}): 3400–3430 (br, OH), 1632 (s, C=N), 1552, 1470 (s, Ar C=C), 1292 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 8.9 (br, 2H, 2 OH), 8.42 (s, 2CH imine), 6.78 (dd, 2H, Ar), 6.76 (dd, 2H, Ar), 6.69 (d, 2H, Ar), 3.54 (t, 4H, 2 CH_2), 1.58 (m, 8H, 4 CH2), 1.33 (m, 2H, CH2); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 165.77, 153.62, 149.70, 120.12, 119.01, 117.25, 116.90, 59.02, 30.83, 28.88, 27.03; *Anal.* Calc.: C, 59.2; H, 5.6; N, 6.6. Found: C, 59.1; H, 5.6; N, 6.4%. MS *m*/*z*: 426 (M^+, 4), 201 (6), 174 (14), 91 (100), 77 (72).

*2.3.2.3. 2,2-(1,2-Phenylenediylbisnitrilomethylidine)-bis(4-hydroxyphenolato) nickel(II) (**C**).* Dark red solid, Yield: 98%, M.p: 330–332 °C; IR (KBr)/ν(cm^{-1}): 3360–3418 (br, OH), 1604 (s, C=N), 1535, 1468 (s, Ar C=C), 1211 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 8.83 (br, 2H, 2 OH), 8.71 (s, 2CH imine), 7.28–8.13 (m, 4H, Ar), 6.76–6.89 (m, 6H, Ar); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 160.77, 155.72, 146.80, 142.82, 127.59, 127.25, 121.07, 119.55, 116.46, 115.20; *Anal.* Calc.: C, 59.3; H, 3.5; N, 6.9. Found: C, 59.2; H, 3.7; N, 6.7%. MS *m*/*z*: 404 (M^+, 2), 343 (5), 289 (2), 135 (22), 109 (11), 91 (28), 77 (62), 65 (74), 51 (100).

*2.3.2.4. 2,2′-(1,9-Nonanediylbisnitrilomethylidine)-bis(4-hydroxyphenolato) zinc(II) (**D**).* Light green solid, Yield: 85%, M.p: 298–300 °C; IR (KBr)/ν(cm^{-1}): 3350–3415 (br, OH), 1624 (m, C=N), 1546, 1469 (s, Ar C=C), 1283 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 8.53 (br, 2H, 2 OH), 8.30 (s, 2CH imine), 6.48–6.77 (m, 6H, Ar), 3.5 (t, 4H, $2CH_2$), 1.3–2.4 (m, 14H, $7CH_2$); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 171.53, 164.13, 145.88, 124.71, 123.09, 117.71,

60.23, 30.24, 28.91, 27.04, 26.45; *Anal.* Calc.: C, 59.9; H, 6.07; N, 6.07. Found: C, 59.8; H, 5.9; N, 6.07%. MS: *m*/*z*: 461 (M^+, 4), 236 (8), 209 (14), 91 (100), 77 (74), 51 (94).

*2.3.2.5. 2,2′-(3,6-Dioxo-1,8-octanediylbisnitrilomethylidine)-bis-(4-hydroxyphenolato) zinc (II) (**E**).* Yellow solid, Yield: 82%, M.p: 302–303 °C; IR (KBr)/ν(cm^{-1}): 3350–3400 (br, OH), 1621 (s, C=N), 1555, 1435 (s, Ar C=C), 1280 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 8.51 (br, 2H, 2 OH), 8.27 (s, 2CH imine), 6.76 (dd, 2H, Ar), 6.59 (d, 2H, Ar), 6.49 (d, 2H, Ar), 3.73 (s, 4H, $2CH_2$), 3.59 (t, 4H, $2CH_2$), 3.47 (t, 4H, 2 CH_2); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 172.34, 164.65, 145.74, 124.69, 123.16, 119.14, 117.13, 70.79, 69.63, 60.17; *Anal.* Calc.: C, 53.2; H, 4.9; N, 6.2. Found: C, 53.3; H, 4.9; N, 6.1%. MS: *m*/*z*: 451 (M^+, 5), 386 (8), 238 (18), 91 (100), 77 (47).

*2.3.2.6. 2,2′-(1,2-Ethanediylbisnitrilomethylidine)-bis(4-hydroxyphenolato) uranyl(II) (**F**).* Dark red solid, Yield: 89%, M.p: 340–342 °C; IR (KBr)/ν(cm^{-1}): 3350–3418 (br, OH), 1627 (s, C=N), 1560, 1442 (s, Ar C=C), 1275 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 9.30 (br, 2H, 2 OH), 8.7 (s, 2CH imine), 7.05 (dd, 2H, Ar), 6.95 (d, 2H, Ar), 6.75 (d, 2H, Ar), 4.41 (s, 4H, $2CH_2$); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 168.68, 163.10, 147.98, 123.69, 123.28, 121.08, 118.53, 79.63; Anal. Calc.: C, 59.2; H, 5.6; N, 6.6. Found: C, 59.1; H, 5.6; N, 6.4%. MS *m*/*z*: 568 (M^+, 4), 343 (4), 316 (6), 107 (12), 91 (100), 77 (68), 51 (96).

*2.3.2.7. 2,2′-(1,2-Phenylenediylbisnitrilomethylidine)-bis(4-hydroxyphenolato) uranyl(II) (**G**).* Dark red, Yield: 90%, M.p: 350–352 °C; IR (KBr)/ν(cm^{-1}): 3350–3434 (br, OH), 1602 (m, C=N), 1548, 1472 (s, Ar C=C), 1275 (s, C–O); ^{1}H NMR (400 MHz/DMSO-d_6)/δ ppm: 9.45 (br, 2H, 2 OH), 8.82 (s, 2CH imine), 7.50–7.51 (m, 4H, Ar), 6.79–7.13 (m, 6H, Ar); ^{13}C NMR (100 MHz/DMSO-d_6)/δ ppm: 166.50, 164.17, 148.38, 147.22, 129.09, 125.59, 123.83, 121.47, 120.66, 119.29; *Anal.* Calc.: C, 38.9; H, 2.3; N, 4.5. Found: C, 38.6; H, 2.3; N, 4.4%. MS *m*/*z*: 616 (M^+, 4), 555 (6), 501 (4), 347 (25), 109 (18), 91 (100), 77 (64), 65 (78).

2.3.3. General procedure for the cleavage of an epoxide into a β-hydroxy nitrile

To a solution of the epoxide (20 mmol) in acetonitrile (30 mL), KCN (22 mmol) was added and the mixture was stirred for 5 min at room temperature. Then, catalyst **C** (2.0 mmol) was added, and stirring was continued until completion of the reaction, as indicated by TLC. Then, 100 mL water and 20 mL CH_2Cl_2 were added to the reaction mixture whilst stirring. The organic phase was then collected and concentrated until dry under reduced pressure. The product was washed with brine and dried at room temperature. The crude products were purified over column chromatography with *n*-hexane/ethyl acetate (9/1) as the eluente. The β-hydroxy nitriles were identified by spectroscopic data.

2.3.3.1. 3-Hydroxy-3-phenylpropanenitrile. Yellow liquid, B.p: 68 °C; IR (KBr)/ν(cm^{-1}): 3063–3438 (br, OH), 2925–3033 (s, Ar C–H), 2255 (s, C≡N), 1493–1615 (s, Ar C=C), 1054, 1216, 1320, 1412 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$)/δ ppm: 7.33–7.41 (5H, m), 4.98 (1H, t), 3.73 (1H, br s), 2.71 (2H, d); ^{13}C NMR (100 MHz/$CDCl_3$)/δ ppm: 141.1, 128.8, 128.7, 125.5, 117.4, 69.8, 22.8; *Anal.* Calc.: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.17; H, 6.13; N, 9.24%.

2.3.3.2. 3-Hydroxy-4-phenoxybutanenitrile. Yellow solid, B.p: 73–77 °C; IR (KBr)/ν(cm^{-1}): 3034–3400 (br, OH), 2933 (s, Ar C–H), 2271 (s, C≡N), 1049–1244 (s, Ar C=C), 1028, 1329, 1412 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$) δ ppm: 7.27–7.38 (2H, m), 6.91–7.03 (3H, m), 4.34 (1H, br s), 4.03–4.06 (2H, m), 2.96 (1H, m), 2.73–2.82 (2H, m); ^{13}C NMR (100 MHz/$CDCl_3$)/δ ppm: 158.1, 129.8, 121.7, 117.8, 114.7, 69.9, 66.0, 22.7; *Anal.* Calc.: C, 67.79; H, 6.21; N, 7.9; Found: C, 67.59; H, 6.1; N, 7.6%.

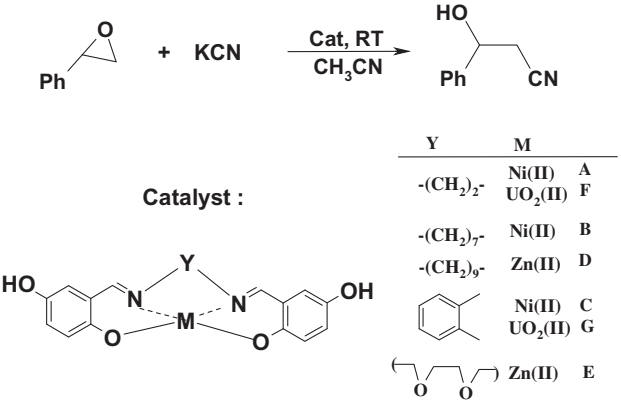
2.3.3.3. 3-Hydroxy-4-(4-chlorophenoxy)butanenitrile. Yellow solid, B.p: 73–76 °C; IR (KBr)/ν(cm^{-1}): 3068–3440 (br, OH), 2931 (s, Ar C–H), 2255 (s, C≡N), 1096–1243 (s, Ar C=C), 1043–1096 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$) δ ppm: 7.30 (2H, m), 6.88 (2H, m), 4.33 (1H, br s), 4.02–4.06 (2H, m), 2.96 (1H, m), 2.70–2.80 (2H, m); ^{13}C NMR (100 MHz/$CDCl_3$)/δ ppm: 156.6, 129.7, 129.4, 126.4, 121.6, 70.1, 69.8, 22.7; *Anal.* Calc.: C, 56.87; H, 4.74; N, 6.64; Found: C, 56.72; H, 4.64; N, 6.39%.

2.3.3.4. 3-Hydroxy-4-(4-methylphenoxy)butanenitrile. Yellow solid, M.p: 61–65 °C; IR (KBr)/ν(cm^{-1}): 3031–3445 (br, OH), 2927 (s, Ar C–H), 2254 (s, C≡N), 1046–1178 (s, Ar C=C), 1046 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$) δ ppm: 7.11 (2H, m), 6.82 (2H, m), 4.34 (1H, br s), 4.03 (1H, m), 3.68–3.81 (2H, m), 2.72–2.84 (2H, m), 2.22 (3H, s); ^{13}C NMR (100 MHz/$CDCl_3$) δ ppm: 155.8, 131.0, 130.1, 117.4, 114.4, 70.0, 66.2, 22.6, 20.5; *Anal.* Calc.: C, 69.11; H, 6.8; N, 7.33; Found: C, 68.91; H, 6.75; N, 7.06%.

2.3.3.5. 3-Hydroxy-4-(4-nitrophenoxy)butanenitrile. Yellow solid, M.p: 84–88 °C; IR (KBr)/ν(cm^{-1}): 3023–3401 (br, OH), 2838 (s, Ar C–H), 2274 (s, C≡N), 1102–1240 (s, Ar C=C), 1052 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$) δ ppm: 8.24 (2H, m), 7.27 (2H, m), 4.42 (1H, br s), 4.18 (1H, m), 3.78–3.89 (2H, m), 2.74–2.85 (2H, m); ^{13}C NMR (100 MHz/$CDCl_3$)/δ ppm: 155.0, 139.1, 132.6, 125.3, 117.7, 74.2, 68.1, 22.5; Anal. Calc.: C, 54.06; H, 4.54; N, 12.61; Found: C, 54.02; H, 4.49; N, 12.49%.

2.3.3.6. 2-Hydroxy-1-cyclohexanecarbonitrile. Yellow liquid, B.p: 58 °C; IR (KBr)/ν(cm^{-1}): 2960–3425 (br, OH), 2885 (s, Ar C–H), 2254 (s, C≡N), 1082–1189 (s, Ar C=C), 1038 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$) δ ppm: 3.6–3.8 (1H, m), 2.5 (1H, m), 2.4 (1H, s), 2. 3 (1H, m), 2.15 (1H, m), 1.7–1.9 (3H, m), 1.2–1.4 (3H, m); ^{13}C NMR (100 MHz/$CDCl_3$)/δ ppm: 118.6, 60.03, 33.4, 26.9, 24.1, 23.3, 20.6; *Anal.* Calc.: C, 67.17; H, 8.86; N, 11.19; Found: C, 67.05; H, 8.81; N, 10.94%.

2.3.3.7. 2-Hydroxy-1-cyclooctanecarbonitrile. Yellow liquid, B.p: 60 °C; IR (KBr)/ν(cm^{-1}): 2985–3400 (br, OH), 2875 (s, Ar C–H), 2252 (s, C≡N), 1082–1169 (s, Ar C=C), 1040 (s, C–O); ^{1}H NMR (400 MHz/$CDCl_3$) δ ppm: 3.6–3.9 (1H, m), 2.4 (1H, m), 2.3 (1H, s), 2.2 (2H, m), 2.1 (2H, m), 1.8–1.9 (4H, m), 1.2–1.4 (4H, m); ^{13}C NMR (100 MHz/$CDCl_3$)/δ ppm: 119.4, 62.3, 34.3, 26.7, 25.1, 24.6, 23.5, 22.6, 20.2; *Anal.* Calc.: C, 70.58; H, 9.80; N, 9.15; Found: C, 70.48; H, 9.75; N, 8.9%.



Scheme 1. Synthesis of propanenitriles.

Table 1
The reaction of styrene oxide with KCN in the presence of various complex catalysts in acetonitrile.

Entry	Catalyst	Time (min)	Yield[a] (%)[b]
1	**A**	70	90
2	**B**	65	70
3	**C**	25	98
4	**D**	35	45
5	**E**	90	55
6	**F**	75	60
7	**G**	40	50
8	–	Overnight	20

Note: The reactions were carried out at room temperature.
[a] GC yield based on epoxide.
[b] Only 3-hydroxy-3-phenylpropanenitrile was regioselectively formed.

Table 2
Ring cleavage of styrene oxide by KCN in the presence of 0.1 mol of catalyst **C** in various solvents at room temperature.

Entry	Solvent	Time (min)	Yield[a] (%)
1	CH_3CN	25	98
2	CH_2Cl_2	40	90
3	$CHCl_3$	50	85
4	CH_3COCH_3	–	–

[a] GC yields.

3. Results and discussion

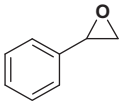
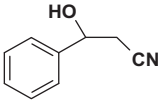
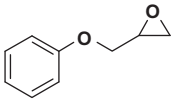
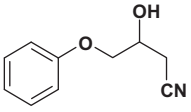
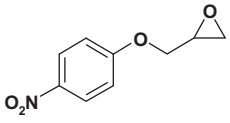
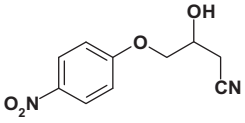
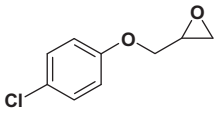
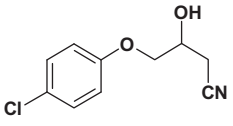
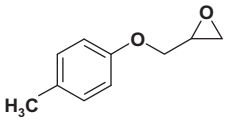
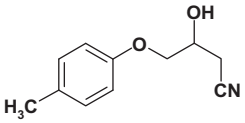
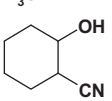
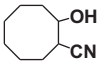
Metal(II)-salen complexes are promising catalysts for various reactions. These complexes have shown wide applicability and have recently been used as catalysts for a variety of enantioselective reactions, such as oxidation [19], aziridination [20], cyclopropanation [21], the Diels–Alder reaction [22] and conversion of epoxides to haloethanols [23]. In this study, the reaction of styrene oxide with potassium cyanide in the presence of some Schiff base metal (II) complexes was carried out (Scheme 1).

The preparation and characterization of these complexes were carried out according to the procedure reported in the literature [23–25]. On this basis, the syntheses of these metal complexes were essentially the same and involved heating and stirring of stoichiometric amounts of the appropriate tetradentate ligand and metal acetate in a suitable solvent, such as methanol, ethanol or water–methanol mixtures. The desired complexes crystallized upon cooling and were recrystallized from chloroform. The complexes were easy to prepare and are cheap. All of the used metal chelates in this study are insoluble in water, but soluble in most organic solvents. They are stable in water, even at high pH and temperature.

The IR spectra of the Schiff bases contain a band in the range 1619 to 1649 cm^{-1}, which is assigned to ν(C=N) of the azomethine group [25]. This band shifts to a lower wavenumber by about 15–20 cm^{-1} on chelation of the ligand to a metal ion. In the IR spectra, the appearance of two or three bands in the low frequency region (between 420 and 540 cm^{-1}) indicates the coordination of the phenolic oxygen in addition to the azomethine nitrogen [24].

In the ^{1}H NMR spectra of the Schiff bases [26], the broad signals around 12.1–12.7 ppm are assigned to the protons of the hydroxyl groups in the free ligands. Protons of CH=N group have the chemical shifts in the range 8.4–8.8 ppm. The signals around 6.7–7.80 ppm are assigned to the protons of aromatic rings (CH=CH). In the ^{1}H NMR spectra of the Schiff base complexes, the signals typically exhibit a shift to lower field and the broad signal around 12.5–13.1 ppm disappears.

Table 3
Reaction of various epoxides with cyanide in the presence of 0.1 mol of catalyst **C** in acetonitrile at room temperature.

Entry	Substrate	Product	Time (min)	Yield[a] (%)
1			25	98
2			60	90
3			40	90
4			50	90
5			60	85
6			45	80
7			55	75

[a] Isolated yields based on epoxide.

To examine the effects of the ligands on the catalyst, a variety of ligands were employed in the reaction (Scheme 1). After a solution of styrene oxide and the catalyst (molar ration is 10:1) in acetonitrile was stirred at room temperature, 1.2 mol of potassium cyanide was added to the flask. In this reaction, 3-hydroxy-3-phenyl propanenitrile was obtained as the product and its yield was determined by GC and TLC analysis. The results of the reactions of styrene oxide with potassium cyanide in the presence of the catalysts are given in Table 1. As shown in Table 1, in these reactions, the β-hydroxy nitrile was prepared as the product in good to excellent yields with high regioselectivity. In each case, cleavage of the epoxide ring occurs. After completion of the reaction, by addition of water and work-up with CH_2Cl_2, the propanenitrile was obtained.

In comparison, the cleavage behavior of styrene oxide with potassium cyanide in the absence of the catalyst is given in entry 8, Table 1. This reaction in acetonitrile in the absence of a catalyst afforded the product with a very low yield and low regioselectivity, even with an extended reaction time to overnight. As can be seen in Table 1, the yields of the reactions with this new method are quite fair, and the reaction time is short. It is of great importance that the reaction is considerably affected by the various ligands of the complexes. The complex catalysts **A** and **C** are the most effective ones in this reaction (Table 1, entries 1 and 3), while the complex catalysts **B**, **E**, **F** and **G** show a lower catalytic performance. This could be due to the electronic structures of the metal complexes as well as the nature of metal centers. In this reaction, the Ni(II)-salen complex **C** was the best catalyst (see Table 1).

To study the solvent effect on the reaction, nucleophilic cleavage of styrene oxide with potassium cyanide by catalyst **C** has been carried out in various solvents. The results shown in Table 2 indicated that acetonitrile is the most convenient solvent for this reaction. It was found that these reactions appeared to be largely dependent on the nature of the solvent.

The results of the reactions of some representative epoxides in the presence of complex **C** as a catalyst are summarized in Table 3. In these reactions, the optimum amount of catalyst used for all of the epoxides was 0.1 mol for 1 mol of epoxide. As can be seen, with the same amount of catalyst, the ring opening of various epoxides has been carried out with 80%-90% yields, and the reaction time was 25–60 min.

As shown in Table 3, the reactions are completely anti-stereoselective. As for the regioselectivity, an attack of the nucleophile preferentially occurs at the less-substituted oxirane carbon. An anti-Markovnikov type regioselectivity is generally observed in these reactions. In many cases, this type of regioselectivity appears to be the opposite of that observed in ring opening of the same epoxides with aqueous hydrogen cyanide under classic acidic conditions. The previously mentioned regiochemical mode can be viewed as occurring via a nucleophilic attack by a cyanide ion on the less sterically hindered oxirane carbon. This mechanism closely resembles the S_N2 model for aliphatic nucleophilic displacement.

The structures of the β-hydroxy nitrile products have been assigned by spectroscopic data. In the IR spectra, the CN stretching vibrations of the nitrile groups appear in the region between 2250 and 2274 cm^{-1}. The hydroxyl group O–H band stretching frequency is found in the region between 3400 and 3477 cm^{-1} as a strong broad band. The C–H stretching vibration of the alkyl groups appear in the region between 2880 and 2930 cm^{-1}. In the ^1H NMR spectra, OH protons have chemical shifts between 4.20–4.55 ppm as a singlet broad peak. The signals around 6.5–8.3 ppm are assigned to the protons of CH=CH of the aromatic rings.

4. Conclusion

This new method for the preparation of β-hydroxy nitriles has some advantages, such as high regioselectivity, high yields, short reaction times relative to other procedures, and work-up simplicity. The nucleophilic attack by the cyanide ion on the epoxides occurs at the primary carbon atom.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.poly.2012.10.019.

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