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**A CONVENIENT SYNTHESIS OF  $\alpha$ -HYDROXYIMINOACETONITRILES  
FROM ALDOXIMES**

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**Abstract:** Aromatic  $\alpha$ -hydroxyiminoacetoneitriles can be conveniently prepared by a facile one-pot procedure in high yields involving chlorination of the corresponding aldoximes with tert-butyl hypochlorite followed by reaction with alkali cyanide.

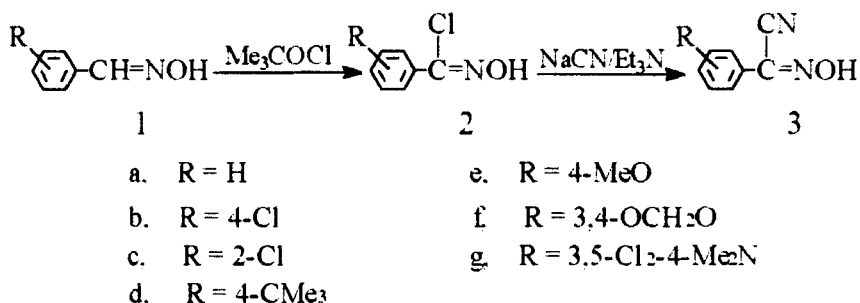
Aromatic  $\alpha$ -hydroxyiminoacetoneitriles are useful activators and carriers of amino-protecting groups in the peptide syntheses<sup>1,2</sup>, and important intermediates in the synthesis of some agricultural chemicals<sup>3,4</sup>. Compounds of this oxime class have been prepared usually from the appropriate acetonitrile and alkyl nitrite<sup>1</sup> or nitric oxide<sup>2</sup>, from  $\omega,\omega'$ -dibromoaceto compounds by action of hydroxylamine and alkali<sup>3</sup>, or by boiling the appropriate glyoxime with sodium carbonate<sup>4</sup>. In addition, a method has been described which involves chlorination of aldoximes with chlorine and following by reaction with alkali cyanide<sup>5,6</sup>. However, side

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reactions predominate in the chlorination process, hence the yield of  $\alpha$ -hydroxyiminoacetone nitriles often is low.

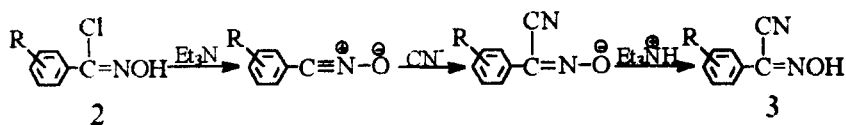
We wish to report herein a new simple and efficient method for the preparation of aromatic  $\alpha$ -hydroxyiminoacetone nitriles from aldoximes via hydroximinoyl chlorides in a single-vessel. Thus aromatic aldoximes (**1**) were allowed to react with tert-butyl hypochlorite to yield regioselectively benzohydroximinoyl chlorides (**2**), then the reaction mixture was treated with triethylamine and sodium cyanide to afford the desired products (**3**), as depicted in Scheme 1:



**Scheme 1**

The chlorination reaction of compounds **1** with tert-butyl hypochlorite in dichloroethane-isopropyl alcohol proceeded smoothly to provide the regioselective benzohydroximinoyl chlorides in good yields. This procedure normally provided an intermediates **2** of sufficient purity for the subsequent reactions.

It is noted that sodium cyanide did not react with hydroximinoyl chloride at an appreciable rate, under the conditions which we employed, if no triethylamine was added. M.H.Been<sup>12</sup>



Scheme 2

reported addition of triethylamine to a cold solution of hydroximinoyl chloride resulted in immediate precipitation of triethylamine hydrochloride and generated the nitrile oxide. Thus it is reasonable to assume the procedure for *in situ* generation of nitrile oxides from hydroximinoyl chlorides and their *in situ* conversion to  $\alpha$ -hydroxyiminoacetone nitriles (Scheme 2).

### Experimental

**General** All the melting points are uncorrected. IR spectra were obtained on a Shimadzu 435 spectrophotometer.  $^1\text{H}$ NMR spectra were recorded on a Jeol FX-90Q spectrometer and a Bruker AC-P200 instrument ( $\delta$  values are in ppm from TMS in  $\text{CDCl}_3$ ). Elemental analyses were carried out on a Yana MT-3 analyser.

#### General procedure (a single-vessel reaction)

A solution of tert-butyl hypochlorite (6.0mmol) in dichloroethane (5ml) was added dropwise at  $-12$ – $-10^\circ\text{C}$  to aromatic aldoximes (**1a–g**, 6.0mmol) in dichloroethane (10ml) and isopropyl alcohol (2.5ml) with vigorous stirring. After 30 minutes a solution of triethylamine (6.0mmol) and sodium cyanide (7.2mmol) in water (5ml) was added at  $-5$ – $0^\circ\text{C}$ . The mixture

was stirred for 4 hours at ambient temperature, diluted with dichloroethane (30ml) and separated. The organic layer was washed with water, aqueous sulphuric acid (5%) and water, then dried ( $\text{MgSO}_4$ ). The solvent was removed under reduced pressure to afford the crude products (**3a-g**), which was purified by recrystallization from dichloroethane-light petroleum.

Spectral data and elemental analyses are given as follows:

**3a**: yield 83.2%, colorless laths, m.p.122~124°C (lit.<sup>10</sup>, m.p.132~133°C), IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3317, 2263, 1634, 1600, 1560, 1377, 954.  $^1\text{H}$ NMR ( $\text{CDCl}_3$ )  $\delta$  ppm: 7.40~7.92 (m, 5H,  $\text{C}_6\text{H}_5$ ), 8.96 (s, 1H, N-O-H).

**3b**: yield 88.4%, colorless laths, m.p.102~103°C (lit.<sup>10</sup>, m.p.107~109°C), IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3320, 2254, 1614, 1595, 1580, 1370, 1010.  $^1\text{H}$ NMR ( $\text{CDCl}_3$ )  $\delta$  ppm: 7.32~7.84 (dd, 4H,  $\text{C}_2\text{H}_4$ ), 8.90 (s, 1H, N-O-H).

**3c**: yield 79.5%, colorless laths, m.p.119~120°C (lit.<sup>11</sup>, m.p.124°C), IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3330, 2276, 1638, 1587, 1470, 1396, 968.  $^1\text{H}$ NMR ( $\text{CDCl}_3$ )  $\delta$  ppm: 7.28~7.60 (m, 4H,  $\text{C}_2\text{H}_4$ ), 9.44 (s, 1H, N-O-H).

**3d**: yield 76.1%, colorless needles, m.p.104~105°C, IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3308, 2275, 1636, 1609, 1477, 1283, 961.  $^1\text{H}$ NMR ( $\text{CDCl}_3$ )  $\delta$  ppm: 1.36 (s, 9H,  $3\text{CH}_3$ ), 7.40~7.80 (dd, 4H,  $\text{C}_2\text{H}_4$ ), 8.40 (s, 1H, N-O-H). Found: C, 71.26; H, 6.89; N, 13.87 (Anal. calcd. For  $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}$ : C, 71.25; H, 6.97; N, 13.85).

**3e**: yield 80.4%, colorless plates, m.p.52~53°C, IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3356, 2232, 1604, 1512, 1435, 1285, 964.  $^1\text{H}$ NMR ( $\text{CDCl}_3$ )  $\delta$  ppm: 3.88 (s, 3H,  $\text{OCH}_3$ ), 6.88~7.84 (dd, 4H,  $\text{C}_2\text{H}_4$ ), 9.08 (s, 1H, N-O-H), (lit.<sup>12</sup>,  $^1\text{H}$ NMR( $\text{CDCl}_3$ )  $\delta$  ppm: 3.87(3H), 7.74(4H), 12.37(1H) ).

**3f**: yield 90.0%, colorless spars, m.p.76~78°C, IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 3377, 2207, 1623, 1585,

1440, 1292, 1030.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 6.05 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.84~7.23 (m, 3H,  $\text{C}_6\text{H}_5$ ).

Found: C, 56.80; H, 3.12; N, 14.57 (Anal. calcd. For  $\text{C}_9\text{H}_6\text{N}_2\text{O}_2$ : C, 56.84; H, 3.18; N, 14.73).

**3g**: yield 88.5%, colorless prisms, m.p.124~125°C, IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 3380, 2226, 1625,

1537, 1463, 1300, 1020.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.96 (s, 6H,  $2\text{CH}_3$ ), 7.72 (s, 2H,  $\text{C}_6\text{H}_2$ ), 8.96

(s, 1H, N-O-H). Found: C, 46.40; H, 3.77; N, 15.94 (Anal. calcd. For  $\text{C}_{10}\text{H}_7\text{Cl}_2\text{N}_2\text{O}$ : C, 46.53;

H, 3.51; N, 16.28).

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