# Elimination of the Nitrile Group from Carbocyclic *o*-Hydroxynitriles

Janusz Sepioł, Julian Mirek

Department of Organic Chemistry, Jagiellonian University, 30-060 Krakow, Karasia 3, Poland

Ring closure of ethyl ylidenecyanoacetates to carbocyclic *o*-hydroxynitriles is a well investigated reaction. This cyclization proceeds spontaneously during distillation of crude ylidenecyanoacetates[1–5] or is performed by heating these compounds in the presence of acetamide[3,6], glycerol[7], and also on irradiation with U.V. light[8]. However, the *o*-hydroxynitriles easily obtained by these routes have been of very little synthetic value due to high resistance of the nitrile group to further transformations. Linstead et al.[2] reported the unsuccessful hydrolysis of an analog of **6**, 10-cyano-9-hydroxy-1,2,3,4-tetrahydrophenanthrene by various hydrolytic methods. The same difficulty has been encountered in the attempted hydrolyses of **3b**[4], and 9-cyano-10-hydroxyphenanthrene[9]. Cope et al.[6] reported that heating of **9** with a mixture of sodium chloride, zinc chloride, and zinc dust gave **10** with moderate yield. In contrast to this observation, application of the same method for the elimination of the nitrile function from **3b** afforded **4b** only in trace amounts[3].

A variety of methods have been reported previously for the preparation of the hydroxy-compounds **4b**, **7**, and **10**. Thus, **4b** has been synthesized by catalytic hydrogenation of 9-phenanthrol[2], cyclization of an unsaturated dienic acid[3] or from *sym*-octahydrophenanthrene[2]. A rather elaborate synthesis of **7** involves rearrangement of spiro derivatives of naphthalene[10,11]. The naphthol **10** has been obtained in several steps from the parent hydrocarbon[7], methyltetralone[12,13] or from benzyne and a dienolate anion[14].

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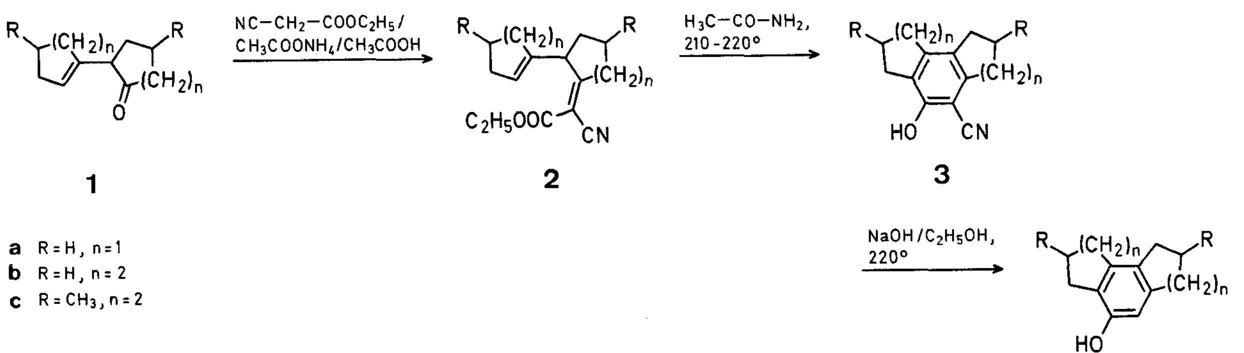

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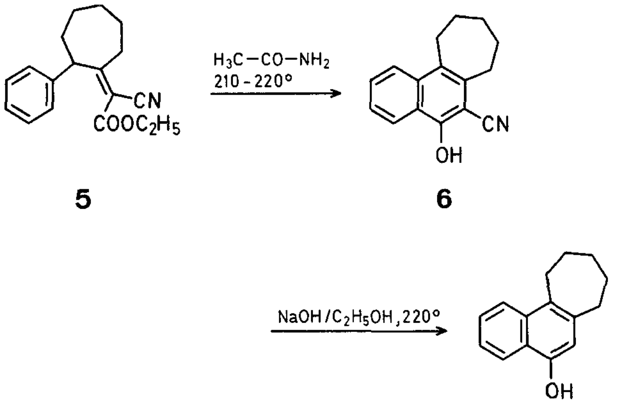

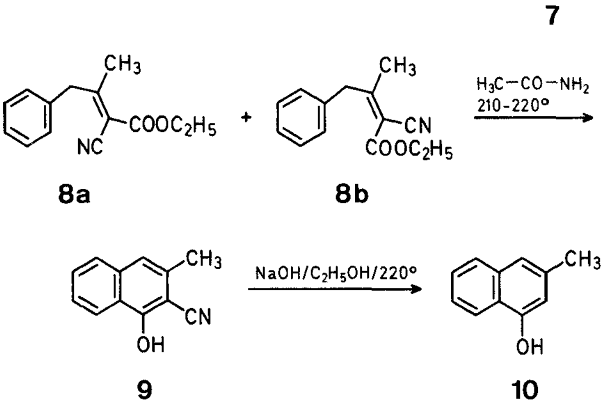

We now report a simple, three-step synthesis of phenols **4, 7**, and **10** from unsaturated ketones **1**[15], 2-phenylcycloheptanone, and phenylacetone, respectively. These ketones are condensed with ethyl cyanoacetate to afford the ylidenecyanoacetates **2, 5**, and **8**[16] which are then cyclized to the *o*-hydroxynitriles **3, 6**, and **9** by heating in acetamide. The essential transformation in this synthetic sequence is the one-step elimination of the nitrile group which is performed by heating the *o*-hydroxynitriles in an ethanolic solution of sodium hydroxide at 220° (autoclave) for several hours. We assume that at high temperature and pressure the decyanylation reaction proceeds via decarboxylation of intermediate products of hydrolysis or alcoholysis. This method of preparation of the hydroxy-compounds **4, 7**, and **10** seems to be advantageous over previously reported syntheses and affords these compounds in moderate to good yields (42–87%) and of satisfactory purity.

**Ethyl Ylidenecyanoacetates 2, 5, and 8; General Procedure:**
The ketone **1a**[17], **1b**[18], **1c**[19], 2-phenylcycloheptanone[20], or phenylacetone (0.05 mol), ethyl cyanoacetate (5.7 g, 0.05 mol), ammonium acetate (0.75 g, 0.01 mol), acetic acid (2.4 g, 0.04 mol), and benzene (40 ml) are heated under reflux with a Dean-Stark water trap until separation of water is complete (6–8 h). The solution is

Table 1. Preparation of Ethyl Ylidenecyanoacetates **2, 5**, and **8**

| Product | Yield [%] | b.p./torr (Lit. data) | $n_D^{22}$ | Molecular formula[a] | I.R. (neat) [cm⁻¹] $\nu_{C=O}$ | $\nu_{CN}$ |
|---|---|---|---|---|---|---|
| **2a** | 44 | 147–150°/3 | 1.5318 | $C_{15}H_{19}NO_2$ (245.3) | 1718 | 2215 |
| **2b** | 75 | 168–173°/3 (146–148°/1.5)[3] | 1.5175 | $C_{17}H_{23}NO_2$ (273.4) | 1740 | 2220 |
| **2c** | 45 | 170–173°/3 | 1.5108 | $C_{19}H_{27}NO_2$ (301.4) | 1724 | 2220 |
| **5** | 51 | 170–174°/4 | 1.5471 | $C_{18}H_{21}NO_2$ (283.4) | 1734 | 2220 |
| **8** | 76 | 147–152°/4 (126°/0.05)[8] | 1.5343 | $C_{14}H_{15}NO_2$ (229.3) | 1740 | 2224 |

[a] The microanalyses for the new compounds **2a, 2c**, and **5** were in satisfactory agreement with the calculated values (C ±0.34%, H ±0.14%, N ±0.30%).

Table 2. Preparation of *o*-Hydroxynitriles **3, 6**, and **9**

| Product | Yield [%] | m.p. (Lit. data) | Molecular formula[a] | I.R. (KBr) [cm⁻¹] $\nu_{CN}$ | $\nu_{OH}$ | ¹H-N.M.R. (DMSO-$d_6$) $\delta_{OH}$ [ppm] |
|---|---|---|---|---|---|---|
| **3a** | 54 | 200° (196°)[5] | $C_{13}H_{13}NO$ (199.3) | 2220 | 3290 | 3.90 |
| **3b** | 68 | 220–221° (215–216°)[3] | $C_{15}H_{17}NO$ (227.3) | 2215 | 3330 | 3.97 |
| **3c** | 65 | 175–176° | $C_{17}H_{21}NO$ (255.4) | 2218 | 3330 | 3.95 |
| **6** | 49 | 205–206° | $C_{16}H_{15}NO$ (237.3) | 2220 | 3340 | 4.13 |
| **9** | 43 | 202° (202°)[8] | $C_{12}H_9NO$ (183.2) | 2220 | 3280 | 4.55 |

[a] The microanalyses for the new compounds **3c** and **6** were in satisfactory agreement with the calculated values (C ±0.38%, H ±0.15%, N ±0.27%).

**Table 3.** Preparation of Hydroxy Compounds **4**, **7**, and **10**

| Product | Yield [%] | m.p. (Lit. data) | Molecular formula[a] | I.R. (KBr) $\nu_{OH}$ [cm$^{-1}$] | $^1$H-N.M.R. ($CDCl_3$/TMS) $\delta$ [ppm] |
|---|---|---|---|---|---|
| **4a** | 42 | 107–108° | $C_{12}H_{14}O$ (174.2) | 3340 | 6.53 (s, 1 $H_{arom}$); 4.95 (s, 1H, OH); 2.82 (t, 4H); 2.72 (t, 4H); 2.30–1.93 (m, 4H) |
| **4b** | 82 | 134–135° (134–135)[3] | $C_{14}H_{18}O$ (202.3) | 3350 | 6.35 (s, 1 $H_{arom}$); 4.65 (s, 1H, OH); 2.77–2.35 (m, 8H); 1.97–1.60 (m, 8H) |
| **4c** | 62 | 119–120° | $C_{16}H_{22}O$ (230.3) | 3350 | 6.36 (s, 1 $H_{arom}$); 4.73 (s, 1H, OH); 2.88–2.45 (m, 8H); 2.05–1.63 (m, 6H); 1.06 (d, 6H) |
| **7** | 58 | 136–137° (139–140)[10] | $C_{15}H_{16}O$ (212.3) | 3280 | 8.18–7.90 (m, 2 $H_{arom}$); 7.47–7.25 (m, 2 $H_{arom}$); 6.55 (s, 1 $H_{arom}$); 4.75 (s, 1H, OH); 3.25–3.05 (m, 2H); 2.93–2.75 (m, 2H); 1.93–1.55 (m, 6H) |
| **10** | 87 | 91° (92°)[7] | $C_{11}H_{10}O$ (158.2) | 3330 | 8.15–7.27 (m, 4 $H_{arom}$); 7.15 (s, 1 $H_{arom}$); 6.50 (s, 1 $H_{arom}$); 5.40 (s, 1H, OH); 2.40 (s, 3H) |

[a] The microanalyses for the new compounds **4a** and **4c** were in satisfactory agreement with the calculated values.

washed with water and saturated sodium hydrogen carbonate solution and is then dried with anhydrous magnesium sulfate. Benzene is removed on a rotary evaporator and the residue is fractionated under reduced pressure affording a viscous oil as the main fraction. During the preparation of **2a** after 4 h of refluxing a second portion of ammonium acetate (1.5 g) is added and heating is continued for 5 h (see Table 1).

**o-Hydroxynitriles 3, 6, and 9; General Procedure:**
Ethyl ylidenecyanoacetate **2**, **5**, or **8** (5.0 g) and freshly distilled acetamide (6.0 g) are heated at 210–220° for 2 h in a flask fitted with short air condenser. The hot solution is poured with stirring into water (250 ml). The precipitated brown solid is isolated by suction, washed with water, dried, sublimed in vacuo, and then recrystallized from ethanol (see Table 2).

**Hydroxy Compounds 4, 7, and 10; General Procedure:**
The *o*-hydroxynitrile **3**, **6**, or **9** (2.0 g) and sodium hydroxide (2.5 g) are dissolved in ethanol (60 ml) and heated at 220° for 7 h in an 250 ml autoclave. The mixture is diluted with water (40 ml) and ethanol is distilled off. The solution is filtered and then neutralized with dilute sulfuric acid. Precipitated solid is filtered off, washed with water, sublimed in vacuo, and recrystallized from *n*-hexane.

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[15] The widely accepted structure for the self-condensation product of cyclopentanone is 2-cyclopentylidenecyclopentanone, therefore **1a** should be presented as an α,β-unsaturated ketone. The $^1$H-N.M.R. spectrum of the ylidenecyanoacetate obtained from this ketone shows, however, resonance of olefinic protons attributed to the presence of **2a**.

[16] The $^1$H-N.M.R. spectrum of ethyl 2-cyano-3-methyl-4-phenyl-2-butenoate (**8**) revealed that this product consists of two geometrical isomers **8a** and **8b** in the ratio 5:4, respectively (see Ref. [8]). We have found that the characteristic $^1$H-N.M.R. spectral patterns of ylidenecyanoacetates **2** and **5** indicate that these compounds also consist of two geometrical isomers. Due to the complexity of these spectra we have not attempted to estimate their isomer ratio and for the reasons of clarity only one isomer of **2** and **5** is presented in the reaction scheme. Resonances of the olefinic protons of **2b**, **2c**, and also **2a** appeared at $\delta = 5.40$ ppm (in $CDCl_3$).

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