A One Pot Synthesis of β-Cyanoenamines

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Orthoesters, cyanoacetic acid and secondary amines react together, in a one step procedure, to produce β-cyanoenamines.

Cyanoenamines have been already prepared in several ways: from amines and β-chloroacrylonitrile[1], cyanoacetylene[2], β-alkoxyacrylonitrile[3], 2-chlorotetramethylguanidine[4], and dicyanoethylene[5]. They can be also obtained from dimethylformamide acetal and acetonitrile[6] or dineopentylformamide acetal and cyanoacetic acid[7].

We now to report a general, effective and easy to run route to obtain secondary aliphatic and aromatic cyanoenamines of the type **4**. We have investigated the reaction of ethyl orthoformiate **1** ($R^1 = C_2H_5$; R^2 = H), cyanoacetic acid **(2)** and amine **3** which produces β-cyanoenamines **4** in a one step procedure, according to the method that we have already used for nitroenamines[8] and which has been explored by Wolfbeis with others open-chain CH_2 compounds[9].

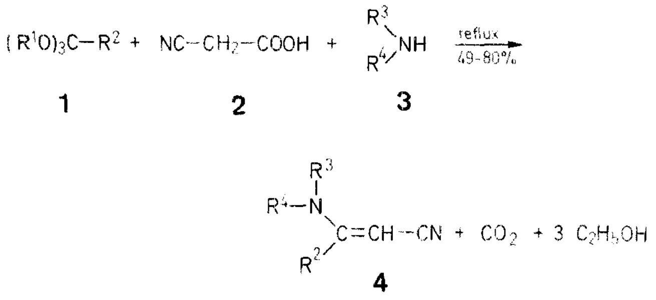
Table. Cyanoenamines **4a–l** prepared

Product No.	R^2	R^3	R^4	Yield [%][a]	b.p. [°C]/torr or m.p. [°C]	Molecular Formula[b] or Lit Data	I.R. (film/KBr) [cm⁻¹] $\nu_{C\equiv N}$	$\nu_{CH=CH}$	^{1}H-N.M.R. (CDCl$_3$/TMS) δ [ppm]
4a	H	CH_3	CH_3	68[c]	88–90°/0.4	68–70°/0.2[4]	2210	1630	2.85 (s, 6H); 3.7 (d, 1H, J = 14 Hz); 7.0 (d, 1H)
4b	H	C_2H_5	C_2H_5	49	98–102°/0.6	85–87°/0.5[1]	2195	1630	1.2 (t, 6H); 3.2 (q, 4H); 3.75 (d, 1H, J = 14 Hz); 6.9 (d, 1H)
4c	H	$—(CH_2)_4—$		54	46°	46–47°[2]	2220	1630	2.0 (m, 4H); 3.2 (m, 4H); 3.65 (d, 1H, J = 14 Hz); 7.15 (d, 1H)
4d	H	$—(CH_2)_5—$		57	56°	56°[10]	2195	1630	1.6 (m, 6H); 3.1 (m, 4H); 3.85 (d, 1H, J = 14 Hz); 6.95 (d, 1H)
4e	H	$—(CH_2)_2—O—(CH_2)_2—$		80	57°	56–57°[2]	2195	1620	3.1 (m, 4H); 3.7 (m, 4H); 3.95 (d, 1H, J = 14 Hz); 6.95 (d, 1H)
4f	H	C_6H_5	C_6H_5	52	118°	$C_{15}H_{12}N_2$ (220.3)	2200	1625	4.15 (d, 1H, J = 14.7 Hz); 7.3 (m, 10H); 7.7 (d, 1H)
4g	H	C_6H_5	CH_3	63	136–138°/0.5	$C_{10}H_{10}N_2$ (190.2)	2200	1620	3.15 (s, 3H); 4.2 (d, 1H, J = 14 Hz); 7.25 (m, 6H)
4h	H	$C_2H_5OCH_2CH_2—$	$C_2H_5OCH_2CH_2—$	68	146–148°/0.4	$C_{11}H_{20}N_2O_2$ (212.3)	2195	1625	1.15 (s, 6H); 3.5 (m, 12H); 3.85 (d, 1H, J = 14 Hz); 6.95 (d, 1H)
4i	H	$NC—CH_2CH_2—$	c-C_6H_{11}	69	55–56°	$C_{12}H_{17}N_3$ (203.3)	2195; 2210	1630	1.5 (m, 11H); 3.1 (m, 4H); 3.9 (d, 1H, J = 14 Hz); 7.0 (d, 1H)
4j	CH_3	$—(CH_2)_2—O—(CH_2)_2—$		54	40–41°	$C_8H_{12}N_2O$ (152.2)	2190	1580	2.15 (s, 3H); 3.15 (m, 4H); 3.7 (m, 4H); 3.95 (s, 1H)
4k	CH_3	$—(CH_2)_5—$		54	40–41°	$C_9H_{14}N_2$ (150.2)	2190	1580	1.5 (m, 6H); 2.15 (s, 3H); 3.2 (m, 4H); 3.85 (s, 1H)
4l	CH_3	$C_2H_5OCH_2CH_2—$	$C_2H_5OCH_2CH_2—$	51	157–159°/0.7	$C_{12}H_{22}N_2O_2$ (226.3)	2195	1580	1.2 (t, 6H); 2.2 (s, 3H); 3.5 (m, 12H); 3.75 (s, 1H)

[a] Yield of pure isolated product; checked by T.L.C. on silica gel (chloroform as solvent, ethyl acetate/pentane 80/20 as developer) and ^{1}H-N.M.R. spectrometry.

[b] Satisfactory microanalyses obtained: C ±0.3, H ±0.3, N ±0.3.

[c] The reaction is performed in a pressure bottle at 90°C.



Alkyl-substituted orthoesters can be used (e.g. $R^2 = CH_3$) with good results but with ethyl orthobenzoate ($R^2 = C_6H_5$) and morpholine only the corresponding benzamide was recovered.

Cyanoenamines 4; General Procedure:

A mixture of cyanoacetic acid (**2**; 42.5 g, 0.5 mol), orthoester **1** (0.5 mol), and amine **3** (0.5 mol) is heated under reflux during two hours. The mixture is evaporated under vacuo and the crude residue is diluted with dichloromethane (300 ml), washed with 1 molar sodium hydrogen carbonate solution (100 ml) and water (100 ml). After drying with anhydrous sodium sulfate the solution is evaporated under vacuo and the residue recrystallized from diethyl or diisopropylether.

The enamine structure of all compounds **4** was confirmed by ^{1}H-N.M.R. spectrometry. The magnitude of $J_{CH=CH}$ spin-spin coupling ($J = 14$ Hz) suggests *trans* conformation.

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