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Reactions of Organic Anions; CXXVII[1]. Catalytic Two-phase (C.T.P.) Synthesis of α-Cyanoenamines

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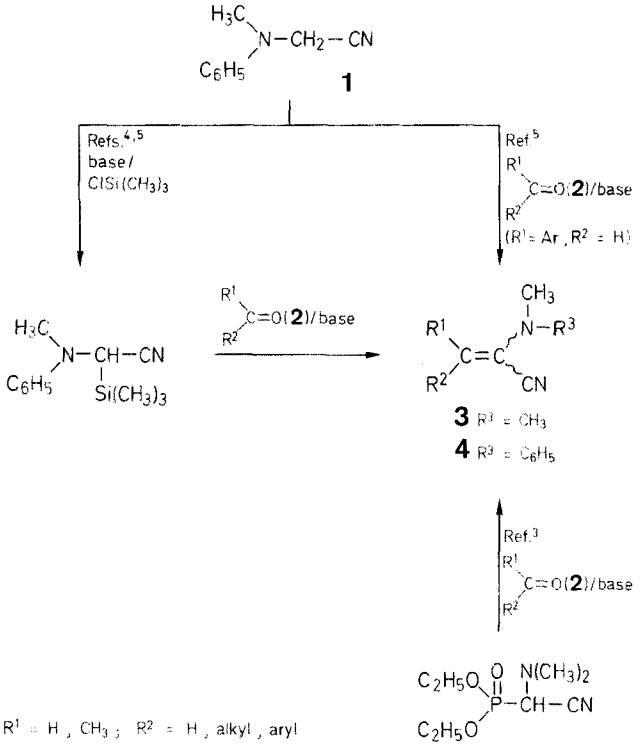
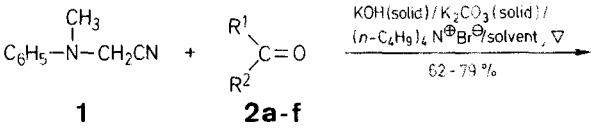
The preparation of α-cyanoenamines **4** via the condensation of carbonyl compounds **2** with α-(*N*-methylanilino)-acetonitrile (**1**) carried out in the presence of a mixture of powdered potassium hydroxide and potassium carbonate and tetra-*n*-butylammonium bromide as a catalyst (solid-liquid catalytic two-phase system) is described. This reaction comprises a useful one-carbon chain lengthening of carbonyl compounds.

The preparation and chemical transformations of α-cyanoenamines has recently become subject of increased interest[2]. Costisella and Gross[3] have prepared compounds **3** by means of the Wittig-Horner reaction of diethyl α-cyano-α-(dimethylamino)-methanephosphonate with carbonyl compounds. Ahlbrecht und Pfaff[4] described the synthesis of **4** ($R^1 = R^2 = H$) via the Peterson reaction of α-(*N*-methylanilino)-α-(trimethylsilyl)-acetonitrile [prepared *in situ* from α-(*N*-methyloanilino)-acetonitrile (**1**) and trimethylchlorosilane] with formaldehyde (**2**; $R^1 = R^2 = H$). Later Takahashi et al.[5] prepared a variety of α-cyanoenamines **4** by means of the Peterson reaction or in a straightforward manner via the condensation of carbanion of **1** with **2**.

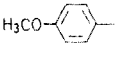


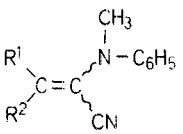
The latter reaction has been carried out with aromatic aldehydes only, in the presence of potassium hydride in tetrahydrofuran.

The recent report by Takahashi et al.[5] prompted us to publish our results on the synthesis of **4** via the condensation of **1** with **2**. Our investigations indicate that this condensation can be conveniently carried out in the presence of a mixture of powdered potassium hydroxide and potassium carbonate with tetra-*n*-butylammonium bromide as a catalyst (solid-liquid catalytic two-phase system[6,7]). The reaction is simply carried out by stirring the reactants in benzene (or in excess of aliphatic ketone) at ambient temperature for 15–30 min (Table 1).



1 **2a-f**

2,4	R^1	R^2
a		H
b		H
c	*i*-C_3H_7	H
d	$-(CH_2)_5-$	
e	CH_3	CH_3
f	CH_3	C_2H_5



4a-f

Under these unoptimized conditions, aromatic aldehydes and aliphatic ketones produced compounds **4** in moderate to high yields. However, 3-pentanone and benzophenone did not give the corresponding α-cyanoenamines, the starting materials were recovered unchanged. The reaction also fails in the case of *N,N*-dialkylaminoacetonitriles, for example diethylaminoacetonitrile did not react with benzaldehyde under the described conditions. The structures of α-cyanoenamines **4** were confirmed by ^{1}H-N.M.R., I.R. spectrometry (Table 2) and microanalyses.

In the case of aldehydes or 2-butanone, products **4** were formed as mixtures of the (*E*)- and (*Z*)-isomers. There is a discrepancy in the literature[2,3,5] concerning the (*E*)/(*Z*)-stereochemistry of α-cyanoenamines, deduced from their ^{1}H-N.M.R. spectra. According to De Kimpe et al.[2] and Costisella and Gross[3], the δ-value of the olefinic hydrogen signal of (*E*)-isomers of α-cyano-(*N,N*-dialkyl)-enamines bearing one β-substituent is 4.7–5.9 ppm while the value for the (*Z*)-isomers is higher, namely 5.3–6.3 ppm. On the other hand, Takahashi et al.[5] ascribed the signal at $\delta \approx 6.2$–7.0 ppm as that of the vinyl hydrogen for the (*E*)-isomers of **4** ($R^1 = H$; R^2 = alkyl, aryl), and the signal at $\delta \approx 5.8$–6.7 ppm as that of the corresponding hydrogen atom in the (*Z*)-isomers. We have applied the latter data[5] in order to ascribe the stereochemistry of known products **4a, b** and the former values[2,3] in the case of product **4c**.

Finally, the stereochemistry of **4f**, lacking a β-hydrogen atom was not elucidated. Concerning the I.R. spectra of α-

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Table 1. α-Cyanoenamines **4a–f** prepared

Product	Molar Ratio of **2**:**1**	Reaction Conditions solvent/temperature/time	Yield [%]	m.p. [°C] or b.p. [°C]/torr	Molecular Formula[a] or Lit. Data
4a	1	C_6H_6/~ 50 °C/15 min	78	oil	oil[5]
4b	1	C_6H_6/~ 50 °C/15 min	79	oil	oil[5]
4c	1.2	C_6H_6/~ 50 °C/20 min	44	oil	$C_{13}H_{16}N_2$ (200.3)
4d	1	C_6H_6/~ 50 °C/30 min	71	oil	$C_{15}H_{18}N_2$ (226.3)
4e	–[b]	excess **2e**/56 °C (b.p.)/30 min	70	oil	$C_{12}H_{14}N_2$ (186.2)
4f	–[b]	excess **2f**/50–55 °C/30 min	62	oil	$C_{13}H_{16}N_2$ (200.3)

[a] Satisfactory microanalyses obtained: C ±0.11, H ±0.21, N ±0.39; exception **4d**, N +0.61.
[b] Reaction performed in excess ketone **2**.

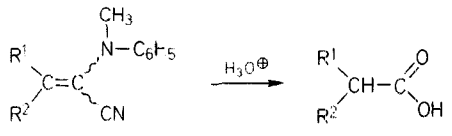
Table 2. Spectra Data for Compounds **4a–f**

Product	I.R. ($CHCl_3$)[a] $\nu_{C\equiv N}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS)[b] δ [ppm]
4a[c]	2210	(*Z*): 3.24 (s, 3H); 6.57 (s, 1H); 7.04–7.75 (m, 10H) (*E*): 3.06 (s, 3H); 6.85–7.70 (m, 11H)
4b	2210	(*Z*): 3.20 (s, 3H); 3.78 (s, 3H); 6.70–7.80 (m, 10H) (*E*): 3.05 (s, 3H); 3.74 (s, 3H); 6.70–7.80 (m, 10H)
4c[c]	2200	(*Z*): 1.00 (d, *J* = 9 Hz, 6H); 2.50–3.00 (m, 1H); 3.04 (s, 3H); 6.12 (d, *J* = 10 Hz, 1H); 6.72–6.98 (m, 3H); 7.19–7.46 (m, 2H) (*E*): 1.12 (d, *J* = 9 Hz, 6H); 2.70–3.00 (m, 1H); 3.09 (s, 3H); 5.72 (d, *J* = 10 Hz, 1H); 6.90–7.10 (m, 3H); 7.20–7.48 (m, 2H)
4d	2200	1.42–1.93 (m, 6H); 2.20–2.46 (m, 2H); 2.59 (t, *J* = 9 Hz, 2H); 3.05 (s, 3H); 6.68–6.96 (m, 3H); 7.19–7.41 (m, 2H)
4e	2200	1.84 (s, 3H); 2.15 (s, 3H); 3.05 (s, 3H); 6.67–6.98 (m, 3H); 7.17–7.42 (m, 2H)
4f[d]	2200	0.99 (t, *J* = 7.5 Hz, 3H); 1.17 (t, *J* = 7.5 Hz, 3H); 1.78 (s, 3H); 2.10 (s, 3H); 2.23 (q, *J* = 7.5 Hz, 2H); 2.47 (q, *J* = 7.5 Hz, 2H); 3.02 (s, 3H); 6.68–6.98 (m, 3H); 7.18–7.46 (m, 2H)

[a] Recorded on a Specord 71 I.R. (Carl-Zeiss, Jena).
[b] Recorded on a Jeol-JNM-100 MHz spectrometer.
[c] Samples of pure (*E*)- and (*Z*)-isomers were isolated by column chromatography.
[d] (*E*)/(*Z*)-stereochemistry was not established.

cyanoenamines there are either different bands reported[2] for the (*E*)- and (*Z*)-isomers or a single absorption band[5] for their mixtures. We have obtained the latter result. Due to the above cited divergent data, the stereochemistry of α-cyanoenamines has to be reinvestigated.

Since the conversion of **4** into carboxylic acids **5** is known[5], the reaction described above represents a useful one-carbon chain-lengthening of carbonyl compounds[8] **2** to acids **5**.



4 **5**

α-Cyanoenamines 4; General Procedure:

A mixture of powdered potassium hydroxide (~85%; 2.6 g, 39.5 mmol), anhydrous potassium carbonate (1.0 g, 7 mmol), and benzene (6 ml) is stirred at 50 °C and treated dropwise with a mixture of nitrile **1**[9] (1.0 g, 6.8 mmol) and tetra-*n*-butylammonium bromide (0.087 g, 0.27 mmol) in benzene (2 ml), followed by the addition of the aldehyde or cyclohexanone **2** (Table 1) in benzene (2 ml). For the preparation of **4e, f**, an excess of ketone **2** (5 ml) is used in place of benzene, and a mixture of tetra-*n*-butylammonium bromide in the aliphatic ketone (5 ml) is added. After the addition, the mixture in each case is stirred and heated (Table 1). After the time indicated in Table 1, it is cooled, the solid material is filtered, and washed with benzene. The filtrate is concentrated in vacuo and the products are isolated by column chromatography on silica gel using a mixture of chloroform and hexane (2:5) as eluent. The synthesis of compounds **4** are reported in Table 1 and their spectral data are given in Table 2.

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