Aromatic α,β-Unsaturated Nitriles via Polyethylene Glycol-Catalyzed Two-Phase Aldol-Type Condensation

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Onium salts and crown ethers[1-7] are frequently used catalysts in phase-transfer reactions. Linear oligo-polyethylene glycols (of different average molecular weights $\bar{M}$; PEG), as inexpensive compounds available on an industrial scale, have already shown in some cases their promising role in phase-transfer catalysis[8,9,10]. The efficiency of PEG-dimethyl ethers [PEG(E)] has been compared with that of crown ethers[8] in halogen displacement reactions [5-15 mol-% of PEG(E)-400], while the usefulness of unsubstituted PEG has been pointed out in some additional examples[9], e.g. in halogen displacement (40 mol-% of PEG-1500), hydrolysis (300 mol-% of PEG-400 - used as the solvent), *O*-alkylation (150 mol-% of PEG-400), and oxidation (160 mol-% of PEG-6000).

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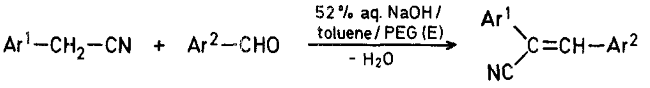
We have shown recently that PEG and their dimethyl ethers [PEG(E)] can also catalyze *C*-alkylations (10 mol-% of PEG-400) of arylacetonitriles[10]. The unreacted nitrile has usually been removed by aldol condensation[11], which was noticeably facilitated in the presence of PEG(E). This result prompted us to explore this type of reaction further and in more detail.



$$Ar^1{-}CH_2{-}CN + Ar^2{-}CHO \xrightarrow[-\,H_2O]{52\%\ aq.\ NaOH/toluene/PEG(E)} (Ar^1)(NC)C{=}CH{-}Ar^2$$

1 **2** **3**

Table 1 summarizes the syntheses of some *α,β*-diarylacrylonitriles **3**, resulting from sodium hydroxide-induced condensation of a suitable nitrile **1** with an aldehyde **2** in the two-phase system consisting of 52% aqueous sodium hydroxide/toluene in the presence of a catalytic amount of PEG(E)-400. Reaction conditions (60 min at 20 °C) and molar ratio of reactants [**1** : **2** : NaOH : PEG(E)-400 is 1 : 1 : 6 : 0.2] were chosen on the basis of experience in *C*-alkylations.

The sensitivity of the reaction to the changes in the structure of **1** and **2** is not clearly apparent, except in the cases of **3e** and **3f**, where the presence of bulky substituent groups on the aromatic ring Ar^1 affected the normal course of the reaction. On the basis of the chemical shift of the aromatic protons in the N.M.R. spectra, it can be established that the aromatic rings are coplanar with the double bond and that the configuration of **3a-h** is (*E*).

To define the catalytic activity of PEG(E)-400, the rate of condensation between phenylacetonitrile and benzaldehyde was determined in dependence of various amounts of catalyst and different molar ratios of nitrile : sodium hydroxide. At equimolecular ratio, 5 mol-% of catalyst were sufficient for isolation of the product in high yield after 60 min (Table 2). While in this case the reaction time may be shortened even to 30 min, this was not so for experiments with smaller amounts of catalyst.

Table 2. Efficiency of Different Catalysts in the Condensation of Phenylacetonitrile (**1**; $Ar = C_6H_5$) with Benzaldehyde (**2**; $Ar^2 = C_6H_5$)[a]

PT-Catalyst (PTC)[b]	mol-% of PTC	conc. of PTC (mol/l)	conc. of **1** (mol/l)	Yield [%][c]
PEG-4000	0.125	0.001	0.89	45
PEG-1500	0.5	0.004	0.87	40
PEG(E)-400	0.5	0.004	0.70	21
PEG(E)-400	1	0.009	0.87	45
PEG-1000	1	0.013	1.34	51
PEG(E)-400	2	0.027	1.34	69
PEG(E)-400	5	0.067	1.34	70
PEG-400	5	0.067	1.34	70
TEBA	5	0.037	0.74	54
PEG-200	10	0.134	1.34	40
PEG(E)-200	10	0.087	0.87	37

[a] Molar ratio of **1** : **2** : NaOH = 1 : 1 : 1.
[b] Except for PEG-1000 (Hoechst), all PEG were the products of Teol, Ljubljana. PEG(E) were prepared in our laboratory (see Ref.[13]).
[c] Yields of pure crystalline products.

Polyethylene glycols of higher $\bar{M}$ are also highly efficient in ion binding though not so convenient in application, due to thickening of reaction mixture. This effect, noticed also with benzyltriethylammonium chloride, can be diminished by diluting the reaction mixture and/or reducing the PEG quantity. In such cases we isolated the product in somewhat lower yield due to smaller concentrations of nitrile and catalyst (mol/l). However, the condensation proceeded extremely slowly when no catalyst was present (16% yield - determined by N.M.R.).

Table 1. *α,β*-Unsaturated Nitriles **3a-h**

Product No.	Ar^1	Ar^2	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr	Molecular formula[b] or Lit. data	I.R. (nujol) $\nu_{C \equiv N}$ [cm⁻¹]	¹H-N.M.R. ($CDCl_3$ or CCl_4/TMS) δ [ppm]
3a	C_6H_5	C_6H_5	71[c]	84.5-86.5°	86-87°[12]	2215	7.1-7.3 (m, 7H); 7.5 (m, 2H); 7.7 (m, 2H)
3b	$3-H_3CO{-}C_6H_4$	C_6H_5	59[c]	71.5-72.5°	$C_{16}H_{13}NO$ (235.3)	2215	3.72 (s, 3H); 6.70 (dd, 1H, *J* = 7 Hz, 1 Hz); 7.0 (m, 1H); 7.1 (m, 2H); 7.2-7.4 (m, 4H); 7.8 (m, 2H)
3c	$4-H_3CO{-}C_6H_4$	C_6H_5	64	93.5-95°	$C_{16}H_{13}NO$ (235.3)	2225	3.72 (s, 3H); 6.78 (d, 2H, *J* = 9 Hz); 7.2-7.4 (m, 4H); 7.44 (d, 2H, *J* = 9 Hz); 7.7 (m, 2H)
3d	$2,3-di-H_3CO{-}C_6H_3$	C_6H_5	69	84.5-86.5°	$C_{17}H_{15}NO_2$ (265.3)	2210	3.72 (s, 3H); 3.78 (s, 3H); 6.71 (d, 1H, *J* = 8 Hz); 6.94 (d, 1H, *J* = 1 Hz); 7.05 (dd, 1H, *J* = 8 Hz, 1 Hz); 7.2-7.3 (m, 4H); 7.7 (m, 2H)
3e	$3-F_3C{-}C_6H_4$	C_6H_5	29	80.5-81.5°	$C_{16}H_{10}F_3N$ (273.3)	2220	7.3-7.5 (m, 6H); 7.7-7.9 (m, 4H)
3f	$3-C_6H_5{-}CO{-}C_6H_4$	C_6H_5	11	114.5-115.5°; 259-266°/0.2	$C_{22}H_{15}NO$ (309.4)	2210	7.1-7.4 (m, 8H); 7.5-7.8 (m, 6H); 7.9 (m, 1H)
3g	C_6H_5	$2,6-di-Cl{-}C_6H_3$	62[c]	110.5-112°	$C_{15}H_9Cl_2N$ (274.2)	2205	7.0-7.4 (m, 7H); 7.6 (m, 2H)
3h	$4-H_3CO{-}C_6H_4$	$2,6-di-Cl{-}C_6H_3$	55	130.5-132°	$C_{16}H_{11}Cl_2NO$ (304.2)	2215	3.78 (s, 3H); 6.9 (m, 2H); 7.1-7.4 (m, 4H); 7.5 (m, 2H)

[a] Yield of product recrystallized twice from methanol.
[b] Satisfactory microanalyses obtained: C ±0.12, H ±0.1, N ±0.13.
[c] Same yield obtained using molar ratio of **1** : **2** : NaOH : PEG(E)-400 = 1 : 1 : 1 : 0.05.

The results obtained indicate that apparently there is no significant difference in the catalytic activities of PEG(E) and benzyltriethylammonium chloride as well as PEG and PEG(E) in some cases.

The method described herein represents a convenient condensation/dehydration sequence for obtaining α,β-unsaturated nitriles in good yields under mild reaction conditions.

α-(4-Methoxyphenyl)-β-phenylacrylonitrile (3c); Typical Procedure: 4-Methoxyphenylacetonitrile (7.63 g, 50 mmol) in toluene (30 ml), PEG(E)-400 (4 g, 10 mmol) and 52% aqueous sodium hydroxide (10.73 g in 12.4 ml water) are placed in a flask equipped with a magnetic stirrer. Benzaldehyde (5.31 g, 50 mmol) in toluene (7 ml) is added dropwise. The mixture is stirred for 1 h at 20 °C and then diluted with water (30 ml). The organic layer is separated, washed with water (3 × 40 ml), and dried with sodium sulfate. The solvent is removed under reduced pressure and the residue is recrystallized twice from methanol; yield: 7.53 g (64%); m.p. 93.5–95 °C.

$C_{16}H_{13}NO$	calc.	C 81.68	H 5.57	N 5.95
(235.3)	found	81.74	5.63	6.08

^{1}H-N.M.R. ($CDCl_3$): $\delta=3.72$ (s, 3H); 6.78 (d, 2H, $J=9$ Hz); 7.2–7.4 (m, 4H); 7.44 (d, 2H, $J=9$ Hz); 7.7 ppm (m, 2H).

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