Synthetic Reactions in Polyethylene Glycol. Diazotization and Sandmeyer Reactions of Anilines in Polyethylene Glycol–Methylene Dichloride

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Diazotization and the Sandmeyer reactions of representative arylamines proceed smoothly in polyethylene glycol– CH_2Cl_2 and have been found to be effective for the preparation of aryl halides and cyanides.

Chemistry in cyclic polyethers (crown ethers) has attracted widespread interest because of the rather high selectivity of many reactions of activated anion species. The properties of polyethylene glycol (PEG) make it an excellent substitute for crown ethers in many reactions,^{1,2} and its use as a co-solvent has been reported. We have now found that diazotization of arylamines and Sandmeyer substitution reactions of the resulting diazonium compounds take place with NaNO₂–HCl in PEG–CH₂Cl₂^{3,4} and with Cu₂X₂, Cu–MX, or K₂[Cu(CN)₄·NH₃] in PEG–CH₂Cl₂ systems, respectively, providing the first example of the cyano substitution of diazonium salts using the isolated solid K₂[Cu(CN)₄·NH₃] complex (Scheme 1).

$$\begin{array}{ll} \operatorname{Ar-NH}_{2} \xrightarrow{i} \operatorname{Ar-N}_{2}^{+} \operatorname{Y}^{-} \xrightarrow{ii} \operatorname{Ar-X} + \text{ other products} \\ (1) & (2) & (3) \end{array}$$

$$\begin{array}{ll} \mathbf{a}: \operatorname{Ar} = \operatorname{Ph} & \mathbf{e}: \operatorname{Ar} = p\operatorname{-MeOC}_{6}H_{4} \\ \mathbf{b}: \operatorname{Ar} = p\operatorname{-PhCOC}_{6}H_{4} & \mathbf{f}: \operatorname{Ar} = o\operatorname{-MeOC}_{6}H_{4} \\ \mathbf{c}: \operatorname{Ar} = \operatorname{\alpha-naphthyl} & \mathbf{g}: \operatorname{Ar} = m\operatorname{-MeOC}_{6}H_{4} \\ \mathbf{d}: \operatorname{Ar} = \operatorname{p-ClC}_{6}H_{4} & \mathbf{h}: \operatorname{Ar} = p\operatorname{-PhC}_{2}\operatorname{CC}_{6}H_{4} \end{array}$$

X = Cl, Br, I, or CN Y = Cl, Br, or I

Scheme 1. Reagents: i, NaNO₂-HY in PEG-CH₂Cl₂ at 0 °C; ii, MX in PEG-CH₂Cl₂ at 0 °C to room temperature.

The arylamine (1) (0.1 mmol; 10 mmol dm^{-3†}) mixed with the acid HY (0.1 cm³ of 1 mol dm⁻³: 0.1 mmol) was diazotized by addition of NaNO₂ (0.1 mmol) dissolved in PEG 200 (2 g; 1 mol dm^{-3†})–CH₂Cl₂ at 0 °C. At 0 °C the resulting diazotized solution was added to the solid reagent MX (0.1 mmol to slight excess), and the mixture set aside at room temperature. Samples were withdrawn at intervals and, for the reactions involving PEG, washed with 1M-NaOH. The products were identified by g.l.c. comparison with authentic samples and also by isolation‡ (i.r. spectroscopy). For comparison, some experiments in aqueous solution were carried out without the PEG-CH₂Cl₂ system. Table 1 shows the results.

On diazotization in PEG–CH₂Cl₂, the starting materials (1) were consumed completely in 20 min. Three equivalents of the acid were necessary.

Aniline (1a) was chlorinated quantitatively in PEG– CH₂Cl₂, whereas it did not give chlorobenzene in aqueous solution under similar conditions (Cu₂Cl₂ and/or Cu powder).⁵ Chlorination of (1b)—(1d) was accompanied by reduction to give ArH (4).⁶ Tetraglyme suppressed significantly the side reactions to give (4), when it was employed instead of PEG. Bromination proceeded in good yields with HBr, but yields were lower than in the chlorinations with HCl. The extent of iodination exceeded the consumption of the starting materials; we assume that this resulted from the

 $[\]dagger$ Final concentration in a 10 ml solution of PEG (2 g)–CH₂Cl₂–water (0.1 ml).

[‡] For isolation 100 ml of the solutions (the same concentration) were employed.

1 able 1. Diazotization and Sandmeyer reactions in PEG-CH ₂ C	indmeyer reactions in PEG-CH ₂ Cl ₂ .
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A = 1				% Yield of products (%) ^c		
Aniline (1)	HVa	of(1)(%)	MYb	$\overline{\Lambda r} = X(3)$	Ar-H(4)	Ar_Cl
	1115	O(1)(7)	MA.	AI = A(3)	$A_1 = \Pi(4)$	AI-CI
Chlorination:		0.6	P	100 [02]		
(Ia)	3M A	96		100 [93]	-	
(1a) ^d	3м А	96	D(or E)	1(1/)		
(1a) ^{a.e}	conc. Ar	100	D(or E)	/0(/4)		
(1 b)	3м А	100	D	19	78	
(1b)	5м А	100	D	20	66	
(1c)	3м А	100	D	7	25	
(1d)	3м А	99	D	35	56	
Bromination:						
(1a)	3м А	96	F	11		43
(1a)	4м В	97	F	92 [86] ^h		
(1e)	4м В	100	F	32	14	
Iodination:						
(1a)	3м А	99	G	57	_	2
(1a)	3м С	45	G	107		
(1a)	3м С ^g	56	G	163 [85] ^h		
Cyanation:						
(1a)	3м А	88	Н	15		75
(1a)	3м А	100	J/D; J/K; or J/E	0		40
(1a)	3м А	95	L	11		19
(1a)	3м А	100	М	67 [62] ^h		16
(1c)	3м А	100	М	46 [40] ⁱ	32	1
(1d)	3м А	100	М	51 [48] ⁱ	25	20
(1f)	3м А	97	М	93 [88] ⁱ	7	
(1 g)	3м А	100	М	39 [30] ⁱ	12	
(1h)	3м А	99	M	38 [35] ⁱ	53 [48] ⁱ	

^a A: HCl; B: HBr; C: HI (0.1 ml). ^b D: Cu₂Cl₂; E: copper powder; F: Cu₂Br₂; G: KI; H: Cu₂(CN)₂; J: KCN; K: Ni(NO₃)₂·6H₂O; L: 0.39 M K₂[Cu(CN)₄· \dot{N} H₃]; M: solid K₂[Cu(CN)₄· \dot{N} H₃]. ^c Based on the consumption of (1). ^d In aq. soln. ^e 333 m_M. ^f 2.5 ml. ^g 0.2 ml. ^h Isolated yield based on the starting (1). ⁱ Isolated yield after t.l.c.

known iodination of the benzene present in the PEG § by I_2 -nitric acid⁷ produced *in situ* from HI-nitrous acid (the HI used was the commercial product which showed a colour due to iodine).

Cyanation in PEG-CH₂Cl₂ did not proceed under the normal reaction conditions examined.^{8,9} Only chlorination or bromination products were obtained depending on the conditions. High yields of cyanation products were obtained when excess of the dry $K_2[Cu(CN)_4 \cdot NH_3]$ complex¹⁰ (not isolated; K_2SO_4 also present) was employed as the cyanation reagent.

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§ The PEG 200 used was dried azeotropically with benzene. A series of blank tests in the absence of aniline confirmed that only the iodination gave such a halogenation product under otherwise identical conditions; the other halogenations did not give such a product.

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