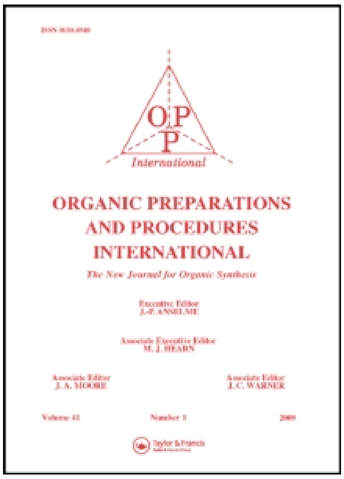

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EFFICIENCY OF THE VILSMEIER-HAACK METHOD IN THE SYNTHESIS OF *p*-AMINOBENZALDEHYDES

Ryszard Gawinecki[a]; Sylwia Andrzejak[a]; Agnieszka Puchala[b]
[a] Department of Chemistry, Technical and Agricultural University, Seminaryjna 3, Bydgoszcz, POLAND [b] Institute of Chemistry, Pedagogical University, Checinska 5, Kielce, POLAND

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EFFICIENCY OF THE VILSMEIER-HAACK METHOD IN THE SYNTHESIS OF *p*-AMINOBENZALDEHYDES

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Ryszard Gawinecki,*† Sylwia Andrzejak† and Agnieszka Puchala‡

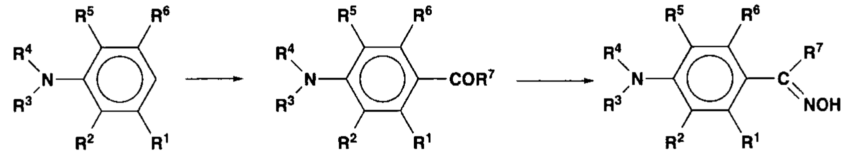
† *Department of Chemistry, Technical and Agricultural University*
Seminaryjna 3, PL-85-326 Bydgoszcz, POLAND

‡ *Institute of Chemistry, Pedagogical University*
Checinska 5, PL-25-020 Kielce, POLAND

Aromatic aldehydes[1] and their oximes[2] are important synthetic intermediates. In addition, *p*-aminobenzaldoximes show interesting chemical and biological activities.[3] It is known that only thermodynamically more stable *E*-oximes are formed by direct oximation of aromatic aldehydes,[4] thus, the product of reaction of *p*-(N,N-dimethylamino)benzaldehyde with hydroxylamine[5] is *E*-*p*-(N,N-dimethylamino)benzaldoxime[6] and it is noteworthy that Z-isomers of *p*-aminobenzaldoximes are not known.

Various methods are used to synthesize *p*-aminobenzaldehydes. The unstable parent *p*-aminobenzaldehyde has been obtained by the McFadyen-Stevens reaction of N'-benzenesulfonyl-*p*-amino-benzhydrazide,[7] by reduction of *p*-nitrobenzaldehyde[8] or from *p*-nitrotoluene.[9] N-Alkyl substituted *p*-formylanilines have been prepared by amination-dehalogenation of *p*-(formyl)halobenzenes,[10-12] by formylation of anilines,[13-15] from the reaction of formaldehyde with 4,4'-di(alkylamino)-N-benzylideneanilines[16] or *p*-(alkylamino)phenylmagnesium halide with alkyl formates.[17] A literature search for preparative procedures shows that the Vilsmeier-Haack and Duff[18] methods were most commonly used. The present paper describes the efficiency of formylation of various anilines by the

Vilsmeier-Haack method (reaction **1** → **2**). The *p*-aminobenzaldehydes obtained were subsequently transformed into respective oximes (reaction **2** → **3**), many of which being new compounds.



1 **2** **3**

	R^1	R^2	R^3	R^4	R^5	R^6	R^7		R^1	R^2	R^3	R^4	R^5	R^6	R^7
a	H	H	H	H	H	H	H	**l**	H	H	$(CH_2)_6(CH_2)_6$		H	H	H
b	H	H	Me	H	H	H	H	**m**	H	$(CH_2)_2(CH_2)_2$		Me	H	H	H
c	h	H	Me	Me	H	H	H	**n**	H	$(CH_2)_3(CH_2)_3$		H	H	H	H
d	H	H	Et	Me	H	H	H	**o**	H	$(CH_2)_3(CH_2)_3$		Me	H	H	H
e	H	H	Et	Et	H	H	H	**p**	H	$(CH_2)_4(CH_2)_4$		Me	H	H	H
f	Me	H	Me	Me	H	H	H	**q**	H	$(CH_2)_2(CH_2)_3(CH_2)_2(CH_2)_3$				H	H
g	Me	H	Me	Me	H	Me	H	**r**	H	$(CH_2)_2(CH_2)_3(CH_2)_3(CH_2)_3$				H	H
h	H	Me	Me	Me	H	H	H	**s**	H	H	H	H	H	H	Me
i	H	Me	Me	Me	Me	H	H	**t**	H	H	Me	Me	H	H	Me
j	H	H	$(CH_2)_4(CH_2)_4$		H	H	H	**u**	H	H	$(CH_2)_5(CH_2)_5$		H	H	Me
k	H	H	$(CH_2)_5(CH_2)_5$		H	H	H								

The data in Table 1 shows that most aldehydes **2** can be easily obtained from arylamines by the Vilsmeier-Haack method. The yield decreased when the number of substituents on the amine nitrogen is lower, ranging from 43-91% for tertiary amines (**1c**-**1m** and **1o**-**1r**) to 24 and 14% for secondary amines **1b** and **1n**, respectively; formylation of aniline itself by N,N-dimethylformamide and phosphorus oxychloride failed completely. 1-Formyl-1,2,3,4-tetrahydroquinoline is a self-formylating compound and its rearrangement in presence of phosphorus oxychloride gave **2n** in 21% yield. The twisted dimethylamino groups of **1h** and **1i** are weak electron-donors and this fact explains why 2,N,N-trimethyl- and 2,6,N,N-tetramethylanilines are resistant to such formylation and the less efficient Duff method has to be utilized to obtain **2h** and **2i**.

Oximes **3** were obtained by oximation of aldehydes and ketones **2** in a medium to high yield (no attempt was made to improve the reaction efficiency). The NMR spectra of all oximes obtained show there is only one isomer present.[29] Since the *p*-(N,N-dimethylamino)benzaldoxime obtained reveals the same physical data as that of *E*-*p*-(N,N-dimethylamino)benzaldoxime,[6] other oximes **3** have the same *E* configuration.

EXPERIMENTAL SECTION

Aldehydes **2c** and **2e** and ketones **2s** and **2u** are commercial products. *p*-(N,N-Dimethylamino)acetophenone (**2t**) was as a gift from Dr. Tomasz Bak (Pedagogical University, Kielce). Aldehydes **2b**, **2d**, **2f-k** and **2m-r** were obtained by the Vilsmeier-Haack[13] or Duff reaction[14,15] (see Table 1) and purified by vacuum distillation or crystallization from aqueous ethanol.

TABLE 1. Yields and Physical Constants of Aldehydes **2** and Oximes **3**

	Aldehydes **2**			Oximes **3**	
Cmpd	Reagent[a] (%, Yield)	bp. (°C/mm Hg)	mp. (°C)	Yield (%)	mp. (°C)
a	A (0)	—	—	41	126-130 (127-128)[3]
b	B (24)[b]	151-154/5 (127-130/0.04)[19]	55-56 (54)[19]	55	96.5-99
c	—	————	———	80	147-148 (145-147)[20]
d	A (52)	————	42-44 (44)[14]	77	117-121
e	—	————	———	81	89-91 (93)[14]
f	A (68)	————	65-67 (67)[14]	78	105-109 (107-109)[20]
g	A (58)	————	81-83 (83)[21]	36	134-135
h	C (63)[c]	138-141/8 (130-134/3)[20]	———	61	97-98 (97-98)[20]
i	C (24)[c]	150-165/1 (64-66/0.09)[20]	———	21	75-85[d]
j	A (91)	————	83-85 (84.5-85.5)[22]	76	190-192
k	A (61)	————	59-62 (61-62)[22]	79	161-163
l	e (72)	193-196/1	———	82	110-114
m	A (84)	————	38-40 (40.1)[23]	41	97-99
n	B (14)	165-175/4	93-95[f] (95-96)[24]	35	147-151
o	A (90)	180-195/4 (219-221/15)[25]	27-30 (30.6)[24]	51	87-88
p	A (43)	202-206/19	———	91	107-109
q	A (67)	165-167/4	36-38	82	104-106.5
r	A (80)	————	79-81 (83)[26]	85	126-128 (127-128)[26]

a) A: N,N-Dimethylformamide, phosphorus oxychloride; B: N-methylformanilide, phosphorus oxychloride; C: hexamethylenetetramine, paraformaldehyde, acetic acid (Duff). b) No aldehyde obtained when N,N-dimethyl-formamide was used. c) Starting materials were recovered when the Vilsmeier-Haack method was used. d) Crude oxime was first distilled (bp. 165-80°/1 mm Hg) and then recrystallized from aqueous ethanol. e) For reaction conditions see **Experimental Section**. f) This compound was also obtained in 21% yield by rearrangement of 1-formyl-1,2,3,4-tetrahydroquinoline in presence of phosphorus oxychloride.[24]

TABLE 2. Elemental Analyses and Chemical Shifts of α-Protons of New Compounds

Cmpd	Elemental Analysis Calcd (Found)			δ_{CHO} or $\delta_{CH=NOH}$ (ppm)[a]
	C	H	N	
2l	76.81 (76.65)	8.43 (8.59)	6.89 (6.97)	9.62[b]
2p	76.15 (76.05)	7.99 (7.86)	7.40 (7.45)	9.77[c]
2q	76.97 (77.12)	7.00 (6.94)	7.48 (7.54)	9.59[d]
3b	63.98 (64.17)	6.71 (6.66)	18.66 (18.47)	7.96
3d	67.38 (67.20)	7.92 (8.03)	15.72 (15.54)	7.99
3g	68.71 (68.90)	8.39 (8.22)	14.57 (14.39)	8.34
3i	68.71 (68.60)	8.39 (8.21)	14.57 (14.69)	8.01
3j	69.44 (69.55)	7.42 (7.56)	14.73 (14.81)	7.97
3k	70.55 (70.39)	7.90 (8.01)	13.72 (13.61)	8.00
3l	71.85 (71.65)	7.89 (7.76)	12.90 (13.01)	7.96
3m	68.15 (68.02)	6.87 (6.69)	15.90 (16.01)	7.98
3n	68.15 (68.26)	6.87 (6.99)	15.90 (15.99)	7.90
3o	69.44 (69.32)	7.42 (7.58)	14.73 (14.60)	7.93
3p	70.55 (70.39)	7.90 (7.99)	13.72 (13.59)	8.03
3q	71.26 (71.45)	6.98 (6.79)	13.85 (13.61)	7.93
3t	67.38 (67.18)	7.92 (7.96)	15.72 (15.82)	–
3u	71.52 (71.46)	8.31 (8.41)	12.84 (12.97)	–

a) In DMSO-d_6. All signals are the singlets (1H). Complete ^{1}H and ^{13}C NMR spectral data of oximes obtained is the subject of another paper.[29] b) Other ^{1}H NMR signals (δ, ppm): 7.63d (2H, **H**2 and **H**6); 6.63d (2H, **H**3 and H5); 3.47t (4H, NCH_2); 1.73m (4H, NCH_2CH_2); 1.48m (4H, $NCH_2CH_2CH_2$). IR (KBr): 1676 cm^{-1} (C=O). c) Other ^{1}H NMR signals (δ, ppm): 7.61d (1H, **H**6); 7.56s (1H, **H**2); 6.83d (1H, **H**5); 3.20t (2H, NCH_2); 2.95s (3H, NCH_3); 2.83m (2H, $NCH_2CH_2CH_2CH_2$); 1.76m (4H, NCH_2CH_2 and $CH_2CH_2CH_2$). IR (KBr): 1678 cm^{-1} (C=O). d) Other ^{1}H NMR signals (δ, ppm): 7.39s and 7.29s (1H + 1H, **H**2 and **H**6); 3.51t (2H, $NCH_2CH_2CH_2$); 3.14t (2H, NCH_2CH_2); 2.97t and 2.66t (2H + 2H, NCH_2CH_2 and $NCH_2CH_2CH_2$); 2.02m (2H, $NCH_2CH_2CH_2$). IR (KBr): 1664 cm^{-1} (C=O).

Synthesis of Aldehyde 2l.- A solution of *p*-fluorobenzaldehyde (6.21 g, 5.26 mL, 0.05 mol) and hexamethyleneimine (14.88 g, 16.91 mL, 0.15 mol) in DMSO (90 mL) was stirred for 24 h at 95°. It was then poured into water (1.75 L) and extracted with ether. Evaporation of the solvent and distillation of the residue gives **2l**.

Preparation of Oximes 3.- *p*-Aminobenzaldoxime, **3a**, was obtained in 47% yield by reduction of *p*-nitrobenzaldoxime, according to the procedure used in synthesis of *p*-aminoacetophenone oxime.[28] The product was purified by crystallization from aqueous ethanol. Aldoximes **3b**-**r** were obtained by refluxing (2h) the reaction mixture consisting of a saturated aqueous solution of hydroxylamine hydrochloride (6 g, 0.086 mol), potassium carbonate (5 g) and aldehyde (0.07 mol) in 96% ethanol (100 mL), followed by the addition of water. The precipitated products were recrystallized from aqueous ethanol. To obtain ketoximes **3s-u,** a mixture of appropriate acetophenone (0.08 mol), hydroxylamine hydrochloride (11.1 g, 0.16 mol), 96% aqueous ethanol (60 mL) and few drops of conc. hydrochloric acid was refluxed for 1.5 h. The reaction mixture was then diluted with water (150 mL) and extracted with ether. Evaporation of the solvent and crystallization of the residue from 96% ethanol gave **3s** (yield 51%, mp. 150-152°, lit.[27] mp. 155-156°), **3t** (yield 69%, mp. 218-222°) and **3u** (yield 65%, mp. 163-166°). The yields and physical data of other oximes **3** are collected in Table 1.

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IMPROVED PREPARATION OF SURFACTANTS DERIVED FROM SUCROSE WITH ULTRASOUND

Submitted by
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Jacques Besson, Catherine Fayet, J. Gelas* and Christelle Lamazzi

Ecole Nationale Supérieure de Chimie de Clermont-Ferrand
Ensemble Scientifique des Cézeaux, BP 187, Aubière, FRANCE

Sugars can constitute the hydrophilic part of a detergent, as they possess a number of hydroxy groups. For this purpose, they must be associated with a lipophilic tail, generally a linear alkyl chain. Such saccharide-derived materials have become a focus of great interest[1] because (*i*) they