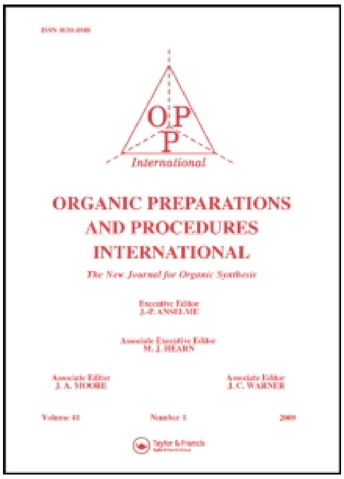

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SOLVENT EFFECT ON THE GOMBERG-BACHMANN-HEY ARYLAPON OF PYRIDINE

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SOLVENT EFFECT ON THE GOMBERG-BACHMANN-HEY ARYLATION OF PYRIDINE

Submitted by
(02/13/90)

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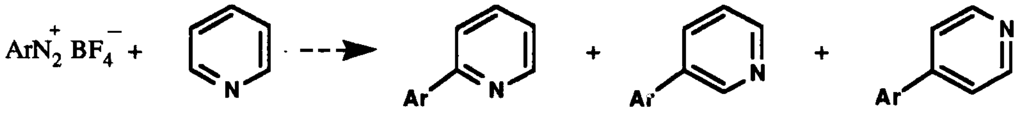
Polychlorinated (PCB) biphenyls are very stable materials of low flammability and are exceptionally persistent in the environment. This fact coupled with their carcinogenicity,[1] require that they be eliminated from several applications. Polychlorinated phenylpyridines may be considered as possible substitutes as they are less hydrophobic and more susceptible to biodegradation; indeed, the nitrogen should relatively easily be oxidized, protonated and methylated and should coordinate to metals ions. Among possible chloro derivatives of phenylpyridines, the 4-phenyl isomers seem to be most promising.



1 2 3 4

a) Ar = $4\text{-}NO_2C_6H_4$ b) Ar = C_6H_5 c) Ar = $4\text{-}EtOC_6H_4$

Biphenyl and its unsymmetrically substituted derivatives are available by the free radical arylation of benzene and its homologues with either aryldiazonium salts (Gomberg-Bachmann-Hey reaction),[2] N-nitrosoacetanilide, N-nitroso-N,N'-diphenylurea[3] or aryldiazopyridinium salts.[4] Similarly, 2-, 3- and 4-arylpyridines may also be obtained in varying overall yield but with a rather constant 6:2:1 ratio of the 2-, 3- and 4-isomer, respectively.[5a] Although difficult to change by alteration of the reaction conditions, this ratio can be modified when pyridine is coordinated to various metals.[5]

We found that the overall yield of the products as well as the ratio of isomers of arylpyridines depend on the substituents present in the aryl moiety as well as on the solvent used. 4-Nitrophenyldiazonium tetrafluoroborate (**1a**) gave higher yield of all three isomeric 2-,3- and 4-(4'-nitrophenyl)pyridines whereas 4'-ethoxyphenyldiazonium tetrafluoroborate (**1c**) was formed in lower yields (only 2- and 4-isomers were formed). All four solvents used - acetonitrile (MeCN), dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and hexamethylphosphoramide (HMPA)- favor the formation of the 4-isomers, irrespective of the substituent in the aryl radical. The preference for the formation of a given isomer decreases in the order 4 > 2 > 3; acetonitrile is the most effective solvent, providing the highest yield and selectivity (Table 1). Total yields of products in that solvent are approximately two to five times higher than those achieved by the arylation of pyridine itself by means of corresponding diazonium salts.[6] Some of the data is complicated by the reaction of the diazonium salt with some of the solvents, especially with HMPA. Such reactions, manifested by faster evolution of nitrogen and formation of tars, have already been observed in the case of DMSO.[7] The identity of each compounds was established by their IR spectra and elemental analysis for nitrogen.

TABLE 1. Yields (%) of the Arylation of Pyridine

Solvent	2a	3a	4a	2b	3b	4b	2c	3c	4c
MeCN	15	11	46	8	7	55	3	0	48
DMF	17	12	37	16	8	45	2	0	44
DMSO	16	14	37	13	10	43	0	0	30
HMPA	14	7	15	14	13	34	0	0	14

EXPERIMENTAL SECTION

General Procedure.- A solution of pyridine (0.8 mL, 0.01 mole) in 25 mL of MeCN (or DMF, DMSO, HMPA) was added with stirring to an equivalent amount of a dry aryldiazonium tetrafluoroborate[8] at room temperature. After 1 hr, the reaction mixture was neutralized with a 1.25 M solution of sodium hydroxide (8 mL) in 1:1 ethanol-water. The precipitated sodium tetrafluoroborate was filtered off and the filtrate was evaporated *in vacuo* at room temperature. The crude product mixture was treated with a hot ethanolic solution of picric acid (0.015 mole) to yield a mixture of picrates.

The picrate of each isomer was separated by fractional crystallization from acetone. The pure picrates were decomposed with aqueous sodium hydroxide (20%) to give the free bases which were extracted into ether followed by the distillation or crystallization from ethanol (Table 2).

TABLE 2. Mps of **2**, **3**, **4** and of their Corresponding Picrates

Cmpd	Total Yield^a (%)	mp.^{b} (°C)	lit. mp. (°C)	mp. (picrate (°C)	lit. mp. (°C)
2a	72	131	$131^{c,d}$	168	$168^{c,d}$
3a	—	148	$148^{c,d}$	220	$220^{c,}$
4a	—	123-124	$123\text{-}124^{c,d}$	228	$228^{c,}$
2b	70	(270-273)	$(270\text{-}273)^c$	176	176^c
3b	—	(116-118/5mm)	$(166\text{-}118/5mm)^e$	160	16
4b	—	77	$77^{c,f}$	195-196	$195\text{-}196^{c,f}$
2c	51	74-75	$74\text{-}75^f$	169	169^f
4c	—	100-102	$100\text{-}102^g$	199-200	$199\text{-}200^g$

a) Yield of picrate mixtures in acetonitrile. b) bp are in parentheses. c) J. W. Haworth, J. M. Heilbron and R. H. Hey, J. Chem. Soc., 349 (1940). d) R. Forsyth and L. E. Pyman, J. Chem. Soc., 2912 (1926). e) H. Rapoport, M. Look and G. J. Kelly, J. Am. Chem. Soc., 74, 6293 (1952). f) J. Overhoff and G. Tilman, Rec. Trav. Chim. Pays-Bas, 48, 993 (1929). g) E. C. Butterworth, J. M. Heilbron and D. H. Hey, J. Chem. Soc., 355 (1940).

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IMPROVED SYNTHESIS OF 2,4-HEXADIENOIC ACID[†]

Submitted by
(10/31/89)

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2,4-Hexadienoic acid (**1**, sorbic acid) is a useful starting material for the synthesis of 8(E), 10(E)-dodecadienol,[1] which is a sex pheromone component of many insects.[2] Compound **1** is available from natural sources (e. g. from the plant *Sorbus aucuparia*[3]) or can be prepared by the Wittig-Horner reaction[4] or by the Doebner modification[5] of the Knoevenagel from 2(E)-butenal (**2**) and malonic acid (**3**) in the presence of pyridine. Although this latter procedure involving heating a mixture of 2(E)-butenal, malonic acid in pyridine at 80° for 3 hrs (Eq. 1), uses cheaper reagents than Wittig-Horner process, it gave very low yield (28-32%). The low yield stems from the competing self-condensation of 2(E)-butenal which is faster than the condensation of **2** with **3**. This process can be followed by the deepening of the color of the reaction time. The polycondensation products can also react with **3** producing polysorbic acids. We now report our modification of this synthesis which results in a higher yield of 1 (40-70%).

$$\underset{\mathbf{2}}{CH_3CH{=}CHCHO} + \underset{\mathbf{3}}{CH_2(CO_2H)_2} \xrightarrow[80^\circ,\ 3\ \text{hrs}]{\text{pyridine}} \underset{\mathbf{1}}{CH_3CH{=}CHCH{=}CHCO_2H}$$

In order to decrease the self-condensation, **2** was added dropwise to a stirred solution of **3** in pyridine at 80°. In this case, the color of reaction mixture remained only slightly yellow and the yield was higher. We also attempted to catalyze this reaction with piperidine.[6] However, piperidine