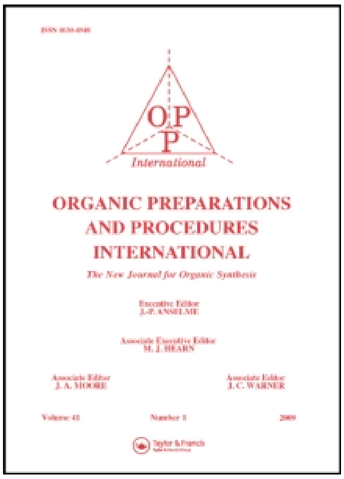

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ALKYLATION OF PHENAZINE WITH N-CHLOROAMINES

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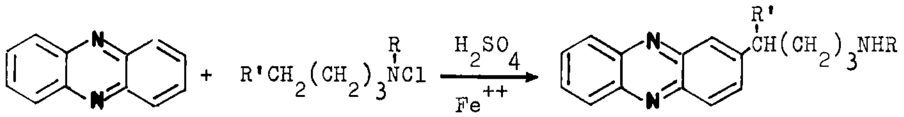
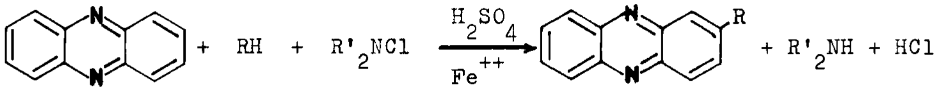
2-Alkyl substituted phenazines are obtained from phenazine and long chain alkyl N-chloroamines in conc. sulfuric acid under the conditions of the Hofmann-Loffler-Freytag reaction (Eq. 1)[1,2] and from phenazine, an aliphatic substrate and N,N-dialkyl-N-chloroamines in conc. sulfuric acid (Eq. 2).[3] Under these conditions the reactive species was the diprotonated form of phenazine (pK_2 = -5.1).[4]



(1)

I a) $R = \underline{n}\text{-}C_4H_9$, R' = H

I b) R = H , R' = CH_3



(2)

II a) R = $CH(CH_3)(CH_2)_4NH_2$

II b) R = $CH(CH_3)(CH_2)_3COOH$

II c) R = $CH(CH_3)(CH_2)_4OCH_3$

II d) R = Cyclohexyl

The products were contaminated by 5% of the 1-substituted isomers and by 1-2% of blue colored materials. Products IIa-c were further contaminated by 5-10% of other isomers on the alkyl chain. Crystallization from low boiling petroleum ether gave pure 2-isomers.

The distribution of alkyl isomers was very sensitive to the acidity (Table 2). Cyclohexyl radicals, generated in trifluoroacetic acid by hy-

TABLE 1.- Alkylation of Phenazine by N-Chloroamines in conc. Sulfuric Acid

Cmpd	N-Chloroamine	RH	Conversion (%)	Yield on converted base (%)
Ia	$(\underline{n}\text{-}C_4H_9)_2NCl$		33	82
Ib	$\underline{n}\text{-}C_5H_{11}NHCl$		12	81
IIa	$(i\text{-}C_4H_9)_2NCl$	hexylamine	32	80
IIb	"	hexanoic acid	35	85
IIc	"	hexyl-methyl-ether	28	86
IId	$(CH_3)_2NCl$	cyclohexane	31	85

drogen abstraction from cyclohexane by N-chloroamine or by catalytic decomposition[6] of hexahydrobenzyl peroxide with copper(I) acetate in CH_3COOH/CH_3CN (3:2) with 10% H_2SO_4, attack positions 1 and 2 to the same extent. In neutral medium (CH_3CN with 5% CH_3COONa), the same radical generated from the diacylperoxide, attacks position 1 seven times more rapidly than position 2, confirming the sensitivity of the reaction between alkyl radicals and heteroaromatic bases to polar effects.[5]

TABLE 2.- Isomer Distribution in Cyclohexylation of Phenazine at Different Acidity

	conc. H_2SO_4	CF_3COOH	$CH_3COOH\text{-}CH_3CN$ 10% H_2SO_4	CH_3CN CH_3COONa(5%)
1-Isomer	9	47	44	86
2-Isomer	91	53	56	14

EXPERIMENTAL

General Procedure.- In a three-necked 150 ml flask equipped with a mechanical stirrer, dropping funnel and gas inlet, the phenazine (2 g, 0.011 mole) and alkyl derivative (0.055 mole) was cautiously added to conc. H_2SO_4 (30 ml) with stirring and cooling [acetic acid (5 ml) was added for insoluble materials, most of which remain out of solution]. $FeSO_4 \cdot 7H_2O$ (1 g, 0.004

mole) was then added and the solution flushed for 15 min. with N_2. A solution of N-chloroamine (0.025 mole) in conc. H_2SO_4 (20-30 ml) was added over a period of 1-2 hrs to the vigorously stirred heterogeneous mixture. The HCl evolved was absorbed into a NH_3 solution. The reaction mixture was stirred for 4 hrs, then poured on to ice (200 g), extracted with $CHCl_3$ (2x 50 ml) to remove unreacted phenazine and all basic products. The acidic layer was made alkaline (pH = 10) with 3N NaOH and extracted with $CHCl_3$ (2 x 100 ml). The combined extracts were washed twice with water, dried over Na_2SO_4 and evaporated. The residue was analyzed by column chromatography on silica gel eluting with hexane-ethyl acetate (8:2) for weakly basic products and with ethyl acetate-methanol (5:5) for basic products. The yields and the conversions were determined on the isolated products. Isomer distribution was completely carried out only for the cyclohexyl derivatives.

The reactions at different acidity were carried out by the procedure described for cyclohexylation in trifluoroacetic acid or as published elsewhere[6] for catalytic decomposition of diacyl peroxide by cuprous acetate. The analytical data for all compounds isolated are reported in Table 3.

TABLE 3.- Analytical Data of Alkylphenazines

Cmpd	mp. (°C)	NMR (δ, $CDCl_3$) H_3	H_1	H_4	Ar^3	-CH-Ar	MS. m/e
Ia	63	7.65	7.99	8.14	7.7-8.3	2.88	307,208,194,193,181
Ib	55	7.55	8.00	8.10	7.6-8.3	3.01	265,248,222,207,181
IIa	--	7.52	7.95	8.12	7.6-8.4	2.95	279,221,207,195,181
IIb	75	7.60	7.90	8.15	7.6-8.3	2.98	294,235,221,207,181
IIc	39	7.58	8.02	8.14	7.6-8.4	2.95	294,279,221,207,181
IId	157	7.64	8.03	8.15	7.6-8.4	2.75	262,261,233,219,194
1-cyclohexylphenazine:							
	140	7.78	-	8.08	7.4-8.3	4.16	262,261,233,220,219

TABLE 4.- Elemental Analyses

Cmpd	Formula	Calcd			Found		
		C	H	N	C	H	N
Ia	$C_{20}H_{25}N_3$	78.13	8.20	13.67	78.05	8.10	13.80
Ib	$C_{17}H_{19}N_3$	76.94	7.22	15.84	76.80	7.29	15.59
IIa	$C_{18}N_{21}N_3$	77.38	7.58	15.04	77.51	7.80	14.92
IIb	$C_{18}H_{18}N_2O_2$	73.45	6.16	9.52	73.30	6.22	9.69
IIc	$C_{19}H_{22}N_2O$	77.52	7.53	9.52	77.35	7.62	9.70
IId	$C_{18}H_{18}N_2$	82.40	6.92	10.68	82.61	7.03	10.55
1-cyclohexylphenazine:	$C_{18}H_{18}N_2$	82.40	6.92	10.68	82.50	7.11	10.80

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