

DECHLORINATION OF SOME CHLOROPYRAZINES AND THEIR N-OXIDES

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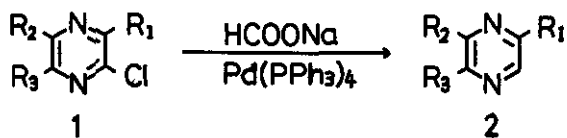
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Abstract --- By heating with sodium formate and tetrakis(tri-phenylphosphine)palladium, chloropyrazines were converted to the parent pyrazines in satisfactory yields. The chlorine atoms of chloropyrazine N-oxides could also be removed, leaving the N-O group.

Several procedures for the reduction of halogenated arenes are available.^{1a-f} In the course of the investigation on pyrazines, we once reported the reduction of 2-chloropyrazine 4-oxides via hydrazino compounds.² Since the yields in this procedure were not always good, our continued effort has led us to explore other means to achieve the removal of halogen atoms on the pyrazine ring. The Helquist's work³ on the dechlorination of halogenated arenes prompted us to apply his method to the dechlorination of 2-chloropyrazines. This report communicates that Helquist's procedure answers to our purposes and is especially useful for the reduction of 2-chloropyrazine 1- and 4-oxides without deoxygenating the N-O group.

The reactions of 2-chloropyrazines (1A-D) were carried out under the same conditions as reported, in which the substances (1 mmol) in 5 ml of N,N-dimethylformamide (DMF) were heated with sodium formate (1.5 mmol) and tetrakis(triphenylphosphine)palladium (0.05 mmol) at 100° for 2 hr under an argon stream. The reaction mixture was treated with water and extracted with hexane or ether to give the product, which was purified by column chromatography on silica gel (Wakogel C-200). As shown in Table I, all products were obtained in satisfactory yields, although the existence of a methoxyl group (1B) on the ring lowers the yields slightly. 2,5-Dichloropyrazines (1E-G) were also subjected to this reaction, using three equivalents of sodium formate and 0.01 equivalents of the palladium catalyst, and two chlorine atoms were readily removed.

Table I. Dechlorination of Chloropyrazines



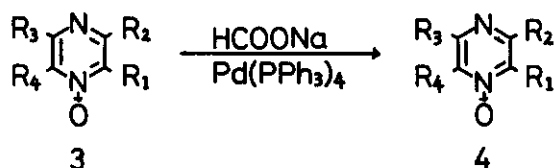
Substrate	Product	Yield (%)	mp or bp (lit. mp or bp, °C or °C/torr)
1A ⁴ R ₁ =R ₃ =isoBu, R ₂ =H	2A ^b R ₁ =R ₃ =isoBu, R ₂ =H	89	95-98/4
1B R ₁ =R ₃ =isoBu, R ₂ =OMe	2B ^b R ₁ =R ₃ =isoBu, R ₂ =OMe	50 (17) ^a	105-109/3
1C ⁵ R ₁ =C ₆ H ₅ , R ₂ =H, R ₃ =Me	2C R ₁ =C ₆ H ₅ , R ₂ =H, R ₃ =Me	94	92-93 (93-94) ⁵
1D ⁶ R ₁ =H, R ₂ =R ₃ =C ₆ H ₅	2D R ₁ =H, R ₂ =R ₃ =C ₆ H ₅	97	119-120 (112-115) ⁷
1E ⁸ R ₁ =R ₃ =CH ₂ C ₆ H ₅ , R ₂ =Cl	2E R ₁ =R ₃ =CH ₂ C ₆ H ₅ , R ₂ =H	95	68-69 (76) ⁹
1F ² R ₁ =isoPr, R ₂ =Cl, R ₃ =isoBu	2F R ₁ =isoPr, R ₂ =H, R ₃ =isoBu	91	80-85/3 (89-90/4) ²
1G ¹⁰ R ₁ =R ₃ =isoBu, R ₂ =Cl	2A	81	

a: The starting material.

b: Analytical and spectral data are consistent with the structures given.

The dechlorination of some 2-chloropyrazine 1- and 4-oxides (3A-G) was also achieved under the same conditions as the case of the reactions of 1A-D. The results are illustrated in Table II. Interestingly, the reaction of 2,5-dichloropyrazine 1-oxides (3H-I), using one equivalent of sodium formate and 0.05 equivalents of the catalyst, resulted in affording 2-chloropyrazine 1-oxides exclusively. Both chlorine atoms of 2,5-dichloropyrazine 1-oxides could barely be removed by heating with three equivalents of sodium formate and 0.01 equivalents of the catalyst at 100° for 10 hr. On the other hand, 2-chloro-3,6-diisobutylpyrazine 1,4-dioxide⁴ was not reduced under drastic conditions (prolonged heating at 100° or refluxed for 15 hr).

Table II. Dechlorination of Chloropyrazine N-Oxides



Substrate	Product	Yield (%)	mp or bp (lit. mp or bp, °C or °C/torr)
3A ⁴	4A R ₁ =R ₃ =H, R ₂ =R ₄ =isoBu	87	51
3B ¹¹	4A R ₁ =Cl, R ₂ =R ₄ =isoBu, R ₃ =H	90	
3C ¹²	4C R ₁ =R ₃ =H, R ₂ =R ₄ =isoPr	85	113-114/9
3D ²	4D R ₁ =R ₃ =H, R ₂ =isoBu, R ₄ =isoPr	90	125-130/2 (134-136/3) ²
3E ²	4E R ₁ =R ₃ =H, R ₂ =isoPr, R ₄ =isoBu	93	128-133/2 (155/7) ²
3F ⁵	4F R ₁ =R ₃ =H, R ₂ =Me, R ₄ =C ₆ H ₅	75	131-131.5 (128-129) ⁵
3G ¹³	4G R ₁ =C ₆ H ₅ , R ₂ =R ₃ =R ₄ =H	70	125-127 (132-133) ¹³
3H ^{10,a}	3B R ₁ =R ₃ =Cl, R ₂ =R ₄ =isoBu	65 (13) ^d	35-36 (33-34) ¹¹
3H ^{10,b}	3B	68	
	4A	12	
3H ^{10,c}	4A	94	
3I ^{12,a}	3C R ₁ =R ₃ =Cl, R ₂ =R ₄ =isoPr	65 (20) ^d	
3I ^{12,c}	4C	94	

a; HCOONa: 1 eq., Pd(PPh₃)₄: 0.05 eq., 100°, 2 hr.

b; HCOONa: 2.1 eq., Pd(PPh₃)₄: 0.1 eq., 100°, 2 hr.

c; HCOONa: 3 eq., Pd(PPh₃)₄: 0.1 eq., 100°, 10 hr.

d; The starting material.

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