

THE SELECTIVE 3- AND 5-NITRATION OF 2-PYRIDONES¹

A. G. Burton, P. J. Halls, and A. R. Katritzky

School of Chemical Sciences, University of East Anglia, Norwich, England

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2-Pyridone, and various simple derivatives, are reported, in divergent literature, as undergoing nitration to give predominantly 3-nitro-, 5-nitro-, and/or 3,5-dinitro-derivatives.² Following work on 3- and 5-methyl-2-pyridone,³ we have now investigated kinetically the nitration of 2-pyridone and 4-methyl-2-pyridone, with special attention to the proportions of 3- and 5-nitro-isomers formed. The results⁴ show that the substrates undergo reaction as the free base species over the range of conditions investigated, but that the rate constants for nitration at the 5-position increase with increasing acidity more rapidly than those for nitration at the 3-position. Other variations in the conditions influence the rates in the manner expected, considering the effect of temperature⁵ and concentration⁶ on acidity functions.

This theoretical work not only offers an explanation for the divergent preparative results already mentioned, but also allows choice of conditions for the selective nitration of 2-pyridones at the 3- and 5-positions which now makes such nitro-derivatives readily accessible in high yield. Details for three 2-pyridones are shown in the Table, and the following general procedures were used in all cases.

(i) For 3-Nitration. Premixed nitric acid (\underline{d} 1.5, 1.5 g) and sulphuric acid (0.5 g) was added dropwise at 5-10^o to the substrate (1 g) in sulphuric acid (\underline{d} 1.84, 5.0 g). The mixture was heated at 80^o for 1 hr then cooled and added to ice (20 g). Saturated aqueous sodium carbonate was added until effervescence ceased, and the precipitate was collected. The NMR spectrum of the crude product was examined (see Table); recrystallization from water gave the pure 3-nitro-derivative.

(ii) For 5-Nitration. Oleum (20% SO₃, 10 g) was added to the substrate (1 g) in sulphuric acid (20 g) and the whole cooled to 0^o. Nitric acid (\underline{d} 1.5, 1.5 g) and sulphuric acid (1 g) were mixed, cooled, and added dropwise to the oleum solution at 0-5^o. The whole was kept at 5^o for 12 hr and poured onto ice (50 g). Neutralisation with sodium carbonate gave the crude product (NMR: see Table) which was crystallized from water to give the pure 5-nitro-derivative.

2-Pyridone substituents	Method	Crude product Composition %		Pure product Yield %	m. p.	Literature m. p.
		3-NO ₂	5-NO ₂			
None	i	100	0	85 (3-NO ₂)	224-225	224-225 ^a
	ii	17	83	72 (5-NO ₂)	189-190	191 ^a
4-Methyl	i	93	7	82 (3-NO ₂)	234-235	234-235 ^b
	ii	22	78	60 (5-NO ₂)	188-190	189-190 ^b
1-Methyl	i	88	12	75 (3-NO ₂)	174-176	175-176 ^c
	ii	0	100	65 (5-NO ₂)	172-173	172 ^c

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This work illustrates the manner in which acidity, temperature and concentration may be manipulated to secure considerable selectivity in nitration, this procedure should be applicable in other series.

REFERENCES

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- (2) For literature summaries see (a) R. A. Abramovitch and J. G. Saha, Adv. Heterocyclic Chem. **6**, 254 (1966); (b) K. Schofield, Heteroaromatic Nitrogen Compounds p. 173. Butterworths, London (1967).
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