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RESEARCH ARTICLE

TRANSITION METAL CATALYZED BENZYL PYRIDINE NITRATION

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ABSTRACT

Transition metal oxides (Vanadium Pentoxide and Niobium Pentoxide) Catalyzed nitration of 2-and 4-benzyl pyridine's was studied under conventional condition. Niobium Pentoxide serves as the best catalyst in regioselectivity of nitro group at para position.

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INTRODUCTION

4-(4-nitro benzyl) pyridine is an important microbiology reagent in detection of several organo phosphorous insecticides in human serum (Futagami *et al.*, 1997), detection of phosgene in air (Dangwal S.K 1994), alkylating potential in diketene (Rafael *et al.*, 2008) were as 2-(4-nitrobenzyl) pyridine is used in synthesis of 2-(2,4 dinitro benzyl) pyridine. The direct and straight forward synthesis of 4-(4-nitro benzyl) pyridine and 2-(4-nitrobenzyl) pyridines mixed acid nitration at elevated temperature (60-70°C) (Namera *et al.*, 2000 and Gilfillan *et al.*, 1994). However the elevated temperature conditions leads to the formation of undesirable side products and becomes difficult to maintain the para to ortho ratio. Thus a mild and highly selective catalyst for nitration is highly desirable. There are good quality works on nitration reported with different catalysts of different oxidation states for improvement of regioselectivity. Vanadium and Niobium are d-transition metals in group VA of the Periodic table, with ground electronic configuration [Ar]3d⁴s² and [Kr]4d⁴5s¹ respectively with versatile oxidation states. Vanadium pentoxide (V₂O₅) and

Niobium pentoxide (Nb₂O₅) are the oxides of the corresponding metals which are able to oxidize to their highest oxidation state in the reaction, thus serving as an excellent catalyst for nitration and different reactions as well by increasing the rate of reaction (Johnson *et al.*, 1985; Zhang Kaiming *et al.*, 2008; Venkatesham *et al.*, 2014 and Ignatius *et al.*, 1976).

MATERIALS AND METHODS

Each reaction was carried out under fuming hood with positive laminar flow. All the chemical and the reagents were obtained from Loba Chemie with minimum purity > 99%. Thin Layer chromatography was done on pre-coated silica gel plates Kiesegel 60 F₂₅₄ Macherey-Nagel).

NMR spectra were recorded in CDCl₃ on Agilent MR-400. All chemical shifts are reported to ppm downfield to TMS and peak multiplicities are referred to as singlet(s), doublet (d), multiplet (m). IR spectra were recorded on Thermo scientific (Nicolet is 5). GC-MS was carried out on Shimadzu. U.V_{max} was recorded on Shimadzu (UV 1800).

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Experimental

2-(4-nitrobenzyl) pyridine

To a stirred solution of 2-benzyl pyridine (10g, 59.09 mmol) in sulfuric acid (30mL) was added Niobium pentoxide (0.6g, 6% w/w) at 25-30°C. The reaction mixture was allowed to stir at the above mentioned temperature for 15 min. This was followed by the addition of 69% nitric acid (5.5mL, 59.09mmol) drop wise maintaining the temperature at 25-35°C. The reaction was maintained for 20 min and the progress of the reaction was monitored by TLC in 70:30 hexanes: ethyl acetate. The reaction mixture was quenched in ice water. The pH of the quenched mass was adjusted to pH 9-10 by addition of 50%w/w NaOH solution (35mL.). The oily suspension was extracted with methylene chloride (30mL). The organic layer was washed with water, dried over anhydrous Na₂SO₄ and concentrated in rota evaporator to give crude 12g semisolid material. The semisolid material was added in MTBE and stirred vigorously for 15 min and filtered to give crude 10.9g of 2-(4-nitrobenzyl) pyridine as pale yellow solid 1. The pale yellow solid was recrystallised with hot MTBE to give pure 9.9g as colorless crystals. Yield: 9.9 g, 78%; Solid, mp 78-80°C (lit 79-80°C); ¹H NMR (CDCl₃, 400MHz): δ 4.21 (s, 2H), δ 7.16 (m 1H), δ 7.25 (d, 1H), δ 7.41-7.43 (d, 2H), δ 7.630 (m, 1H) δ 8.14-8.16 (d, 2H), δ 8.55(d, 1H); IR(KBr,cm⁻¹): 3052(=CH), 2938(CH), 2441(NH), 1603(Pyridine derivative), 1570(NO₂), 1433(CN), 869(NH₂); GCMS: *m/z* 214; UV_{max} 257nm.

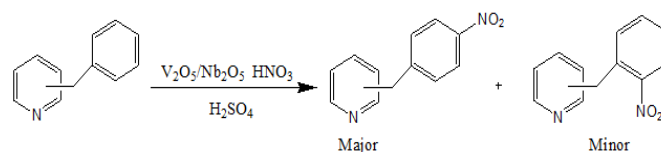
4-(4-Nitro benzyl) pyridine

To a stirred solution of 4-benzyl pyridine (10g, 59.09 mmol) in sulfuric acid (30mL) was added Niobium pentoxide (0.6g, 6% w/w) at 25-30°C. The reaction mixture was allowed to stir at the above mentioned temperature for 15 min. This was followed by the addition of 69% nitric acid (5.5mL, 59.09mmol) drop wise maintaining the temperature at 25-35°C. The reaction was maintained for 20 min and the progress of the reaction was monitored by TLC in 70:30 hexane: ethyl acetate. The reaction mixture was quenched in ice water. The pH of the quenched mass was adjusted to pH 9-10 by addition of 50%w/w NaOH solution (35mL.). The oily suspension was extracted with methylene chloride (30mL). The organic layer was washed with water, dried over anhydrous Na₂SO₄ and concentrated in rota evaporator to give crude 12.2g semisolid material. The semisolid material was added in MTBE and stirred vigorously for 15 min and filtered to give crude 11.2g of 4-(4-nitrobenzyl) pyridine as pale yellow solid 1. The pale yellow solid was recrystallised with hot MTBE to give pure 10.8g as colorless crystals. Yield: 10.8 g, 85%; Solid, mp 69-71°C (lit 70-71°C); ¹H NMR (CDCl₃, 400MHz): δ 4.09 (s, 2H), δ 7.09-7.10 (d, 2H), δ 7.33-7.35 (d, 2H), δ 8.16-8.19 (d, 2H), δ 8.53-8.55(d, 2H); IR(KBr,cm⁻¹): 3069(=CH), 2933(CH), 2450(NH), 1603(Pyridine derivative), 1557(NO₂), 1413(CN), 1348(NO₂), 1194(CN aromatic), 874(NH₂). GCMS: *m/z* 214; UV_{max} 249nm

RESULTS AND DISCUSSION

In this article (Scheme 1) we studied the effect of V₂O₅ and Nb₂O₅ concentration on the regioselectivity of para isomer of

2-benzyl pyridine and 4-benzyl pyridine under conventional condition at same temperature.



Scheme 1.

Table 1. Effect of concentration of Nb₂O₅ on nitration of 2-benzyl pyridine

Entry	Nb ₂ O ₅ (%w/w)	Ratio ^a p:o(%)	Time(h)
1	0	55:45	6
2	2	78:22	0.35
3	4	78:22	0.3
4	6	79:21	0.15

All the reactions were performed at 0-5°C.

^a Ratio were determined on the basis of integration by Gas Chromatography by comparing standards.

Table 2. Effect of concentration of Nb₂O₅ on nitration of 4-benzyl pyridine

Entry	Nb ₂ O ₅ (% w/w)	Ratio ^a p:o(%)	Time(h)
1	0	57:43	5.8
2	2	78:22	0.3
3	4	82:18	0.28
4	6	85:15	0.15

All the reactions were performed at 0-5°C.

^a Ratio were determined on the basis of integration by Gas Chromatography by comparing standards.

Table 3. Effect of concentration of V₂O₅ on nitration of 2-benzyl pyridine

Entry	V ₂ O ₅ (%w/w)	Ratio ^a p:o(%)	Time(h)
1	0	55:45	6
2	2	77:23	0.4
3	4	77:23	0.3
4	6	78:22	0.15

All the reactions were performed at 0-5°C.

^a Ratio were determined on the basis of integration by Gas Chromatography by comparing standards.

Table 4. Effect of concentration of V₂O₅ on nitration of 4-benzyl pyridine

Entry	V ₂ O ₅ (% w/w)	Ratio ^a p:o(%)	Time(h)
1	0	57:43	5.80
2	2	75:25	0.50
3	4	78:22	0.30
4	6	78:22	0.10

All the reactions were performed at 0-5°C.

^a Ratio were determined on the basis of integration by Gas Chromatography by comparing standards.

Table 5. Effect of temperature on nitration of 4-benzyl pyridine and 2-benzyl pyridine

Benzyl pyridines	Temp (°C)	Ratio ^a p:o(%)	Time(h)
2-Benzyl pyridine	0 ± 5	79:21	0.15
	25 ± 40	91:09	0.10
	50 ± 70	52:47	0.10
4-Benzyl pyridine	0 ± 5	85:15	0.15
	25 ± 40	93:07	0.10
	50 ± 70	54:46	0.10

All the reactions were performed using (6% w/w) Nb₂O₅ catalyst.

^a Ratio were determined on the basis of integration by Gas Chromatography by comparing standards.

In absence of catalyst the maximum para to ortho ratio is 55:45 and 57:43 for 2-and 4-benzyl pyridine nitration. We examined the nitration of 2-and 4- benzyl pyridine in presence of V_2O_5 and Nb_2O_5 under mild condition to ensure the catalytic activity of these polyvalent metal oxides on para to ortho ratio. Encouraged by the trial, we studied the optimization of the catalyst concentration on para to ortho ratio at same temperature. The maximum para to ortho ratio obtained for Nb_2O_5 catalyzed nitration of 2-benzyl pyridine and 4-benzyl pyridine at $0 \pm 5^\circ C$ were 79:21 and 85:15 respectively (refer Table-1 and Table-2) as compared to V_2O_5 catalyzed nitration for 2- benzyl pyridine and 4-benzyl pyridine was 78:22 (refer Table-3 and Table-4). We observed high regioselectivity ratio in Nb_2O_5 catalyzed reaction. On the basis of the optimized catalyst concentration at $0-5^\circ C$, we studied the effect of temperature on para to ortho ratio using (6.0 % w/w) Nb_2O_5 catalyst in nitration of 2 and 4-benzyl pyridines. The optimum reaction temperature for high regioselectivity is determined (refer Table 5).

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