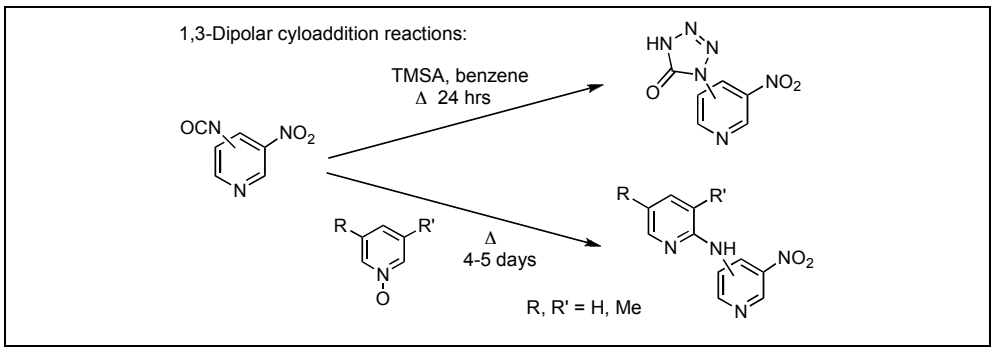
Jarle Holt and Anne Fiksdahl*

Department of Chemistry, Sem Saelands v. 8, Norwegian University of Science and Technology, NTNU, NO-7491 Trondheim, Norway

**Anne.Fiksdahl@chem.ntnu.no**

Received June 15, 2005




The reactivity of 3-nitro-4-pyridyl isocyanate (**7**) and 5-nitropyridin-2-yl isocyanate (**9**) in 1,3-dipolar cycloaddition reactions with azides and pyridine *N*-oxides has been investigated. 1,3-Dipolar cycloaddition to trimethylsilylazide (TMSA) afforded the respective tetrazolinones, 1-(3-nitropyridin-4-yl)-1*H*-tetrazol-5(4*H*)one (**8**, 50 %) and 1-(5-nitropyridin-2-yl)-1*H*-tetrazol-5(4*H*)one (**11**, 64 %). Respectively, 1,3-dipolar cycloaddition of nitropyridyl isocyanates **7** and **9** to 3,5-dimethylpyridine *N*-oxide (**14**), 3-methylpyridine *N*-oxide (**21**) and pyridine *N*-oxide (**22**) gave the substituted amines, 3,5-dimethyl-*N*-(3-nitropyridin-4-yl)pyridin-2-amine (**17**), 3,5-dimethyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**20**), *N*-(5-nitropyridin-2-yl)pyridin-2-amine (**24**), 5-methyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**23**) and 3-methyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**25**) in 65 - 80 % yield, obtained by cycloaddition, rearrangement and decarboxylation. The results demonstrate that the nitropyridyl isocyanates (**7**,**9**) readily undergo 1,3-dipolar cyloaddition reactions similar to phenyl isocyanates.

*J. Heterocyclic Chem.*, **44**, 375 (2007).

## INTRODUCTION

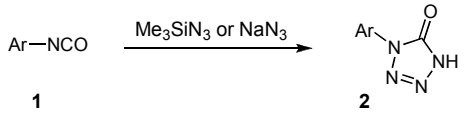
Cycloaddition reactions provide useful synthetic routes to a wide range of heterocyclic compounds, especially those containing four, five or six atoms in the ring. 1,3-Dipolar cycloaddition represents an excellent method for the construction of five-membered rings because a wide variety of 1,3-dipoles are available and these undergo addition to multiple bonds [1]. Heterocumulenes, such as isocyanates are potential dipolarophilic partners in cycloaddition reactions. Heterocyclic isocyanates are, however, mostly not suitable for syntheses due to their instability. We have recently been successful preparing the first stable nitropyridyl isocyanates [2]. The stability is caused by the electron-withdrawing effect of the nitro group. The present cycloaddition studies demonstrate some of the useful synthetic applications of nitropyridyl isocyanates as a part of our work in progress to demonstrate the synthetic potential of nitropyridyl isocyanates similar to phenyl isocyanates.

**1,3-Dipolar cycloaddition with azide.** Only a few reactions of isocyanates with organic azides have been reported. Alkyl and aryl isocyanates can be prepared from their corresponding acyl azides through the Curtius rearrangement. It is not known that the acyl azide precursors react with the resulting isocyanate products in the Curtius reaction [3]. Reaction with some other organic azides however, gives the 1,3-dipolar cycloadducts [3-5].

Aryl isocyanates have been reported to react with either sodium azide [6,7] or trimethylsilylazide (TMSA) [8,9] to form 1-aryl-5(4*H*)-tetrazolinones (**2**) (Scheme 1). TMSA behaves as a 1,3-dipole in analogy to organic azides towards acetylenes [10], olefins [4-5,11] and nitriles [11,12]. The corresponding cycloadducts are formed. Reaction of TMSA with acid chlorides [13,14], anhydrides [14-17], imides [16], esters and lactones [18] affords a variety of isocyanates. In some cases these are cyclized directly to heterocyclic compounds, like uracils [16], pyridones [14], dihydropyridines [5], triazoles [12] and aziridines [4]. The reaction of TMSA with heterocumulenes, such as isocyanates, isothiocyanates, carbodiimides and diphenylketene, has received little attention. It is, however, reported that 1,3-dipolar cycloaddition of phenyl isocyanate (**1**) to TMSA afforded 1-phenyl-5(4*H*)-tetrazolinone (**2**) in variable yields depending on the reaction conditions [8]. Equimolar amounts of TMSA gave 1,3-diphenylurea and phenylcarbamoyl-azide as byproducts in the reaction. However, using an

excess of TMSA (two equivalents), quantitative yield of **2** was obtained.

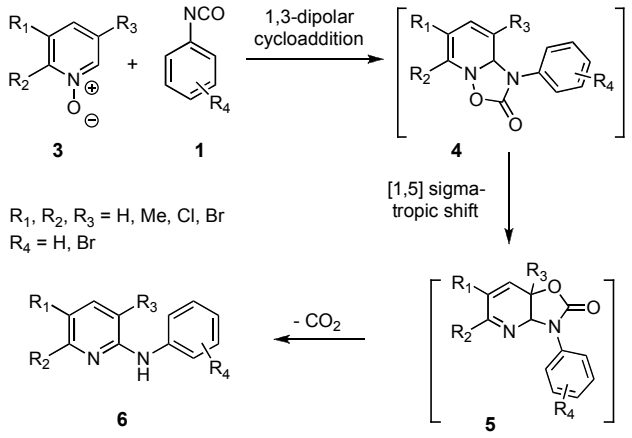
Scheme 1




Compounds which have incorporated a mono- or disubstituted tetrazolinone structure are used as herbicides [19,20], pesticides [21] and short-acting narcotic analgesics [22].

**1,3-Dipolar cycloaddition with pyridine *N*-oxides.** The 1,3-dipolar cycloaddition of aromatic isocyanates (**1**) to pyridine *N*-oxides (**3**) is a well known reaction (Scheme 2) [23-31] and has been studied since the early 1980's. The reaction has been considered to be a 1,3-dipolar cycloaddition to the nitrone function, followed by [1,5]sigmatropic rearrangement and re-aromatization by decarboxylation.

Scheme 2



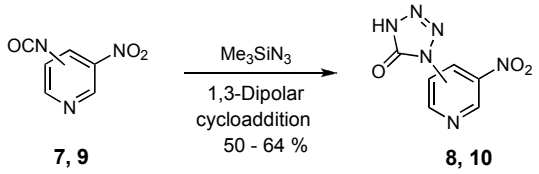

The 1,2-dihydro intermediates (**4**) are too unstable neither to be seen during the reaction nor isolated from the reaction mixtures. The 2,3-dihydro intermediates (**5**) formed from the intermediates (**4**) through a [1,5] sigmatropic shift, are more stable [23-31] and have sometimes been isolated and characterised. This is in agreement with calculations performed, which showed that the heat of formation of the rearranged compound is lower in energy than that of the adduct precursor, indicating the adduct precursor to be thermodynamically less stable [27]. After re-aromatization by decarboxylation the substituted secondary amines (**6**) are formed.

In the present work 3,5-dimethylpyridine *N*-oxide (**14**), 3-methylpyridine *N*-oxide (**21**) and pyridine *N*-oxide (**22**) have been used in cycloaddition reaction studies.

## RESULTS AND DISCUSSION

**1,3-Dipolar cycloaddition with azide.** 3-Nitropyridin-4-yl isocyanate (**7**) was prepared *in situ* in dry benzene from the corresponding acyl azide through a Curtius rearrangement [2]. The carbonyl azide precursor was made in dry diethyl ether through diazotization of the corresponding carbonyl hydrazide. For our purpose the 1,3-dipolar cycloaddition with TMSA was performed in dry benzene, since the isocyanate was generated in this solvent, in contrast to the cycloaddition with phenyl isocyanate (**1**) which could be carried out without solvent using an excess of TMSA (two equivalents) [8]. In the present work 1-(3-nitropyridin-4-yl)-1*H*-tetrazol-5(4*H*)one (**8**) was obtained in 50 % yield after reflux overnight (Scheme 3).

Scheme 3



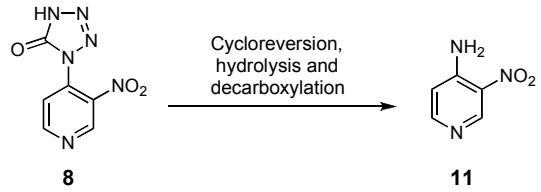

**7, 8;** 3,4-disubstituted pyridine
**9, 10;** 2,5-disubstituted pyridine

Correspondingly, in the 1,3-cycloaddition reaction of 5-nitropyridin-2-yl isocyanate (**9**) with TMSA [8] the 1-(5-nitropyridin-2-yl)-1*H*-tetrazol-5(4*H*)one (**10**) product was obtained (Scheme 3) in 64 % yield. No purification could be performed, as product **10** decomposed in solution. This will be discussed in the following.

Although retro Diels-Alder reactions are well described in the literature, only a few cycloreversions of 1,3-dipole adducts have been reported. Cycloreversion of azide 1,3-cycloaddition products have been described only once [3]. It was observed that tetrazolin-5-one products formed by cycloaddition of isocyanates and alkyl azides underwent thermal cycloreversion. The rate of cycloreversion increased with increasing electronegativity of the isocyanate moiety.

Based on the fact that increased amounts of 4-amino-3-nitropyridine **11** was observed when cycloadduct **8** was stored and left in solution, it is proposed that the tetrazolinone (**8**) prepared in this work underwent cycloreversion (Scheme 4). The aminopyridine **11** is formed by hydrolysis of isocyanate **7** formed by cycloreversion, followed by decarboxylation. The process could be followed by $^1$H NMR. 4-Amino-3-nitropyridine (**11**) was gradually formed when cycloadduct **8** was left at room temperature in solution. After a period of four weeks the **8**:**11** ratio was 15:85 %. Strong characteristic azide IR absorption frequencies (2155, 2180 cm$^{-1}$) also supported cycloreversion.

Scheme 4

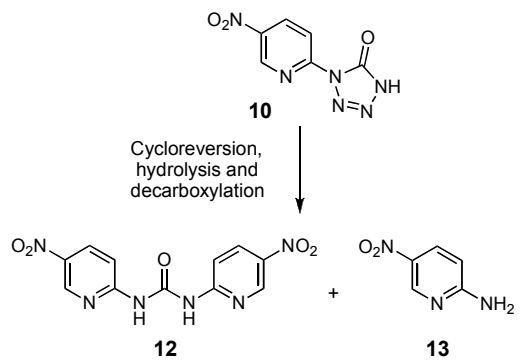



**8** **11**

A similar observation was made for tetrazolinone (**10**) (Scheme 5) when left in solution, affording 5-amino-2-nitropyridine (**13**) and the urea compound (**12**) as decomposition products [2], as shown by $^1$H NMR. The urea compound (**12**) is supposed to be a condensation product of isocyanate **9** formed by cycloreversion and the amine **13**, the isocyanate hydrolysis product.

The fact that the cycloreversion isocyanate products **7** and **9** are further hydrolysed and decarboxylated in solution, and thus removed from the thermodynamic equilibrium, may explain why the cycloaddition products **8** and **10** seem to undergo slow cycloreversion even at room temperature. It is also known [3] that electronegative groups attached to the isocyanate accelerate the cycloreversion reaction. In our present work the electron-withdrawing nitropyridyl group would therefore increase the rate of cycloreversion.

Scheme 5

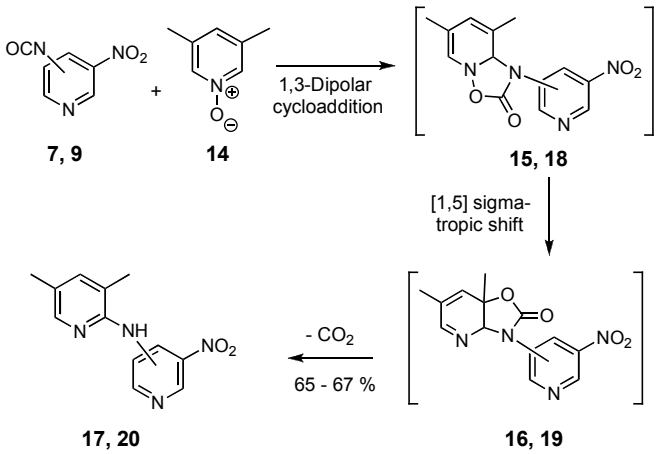



**10** **12** **13**

**1,3-Dipolar cycloaddition with pyridine N-oxides.** 3,5-Dimethylpyridine *N*-oxide (**14**), 3-methylpyridine *N*-oxide (**21**) and pyridine *N*-oxide (**22**) were used in cycloaddition reaction studies in the present work. The aromatic character of the pyridine *N*-oxides reflects its reactivity in cycloaddition reactions. The less aromatic dimethylpyridine *N*-oxide, such as **14**, with two electron donating methyl groups would be more reactive than pyridine *N*-oxide (**22**) and 3-methylpyridine *N*-oxide (**21**) [29], due to the latter's stronger aromatic character and poorer availability of the 1,3-dipole moiety, respectively.

3,5-Dimethyl-*N*-(3-nitropyridin-4-yl)pyridin-2-amine (**17**) and 3,5-dimethyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**20**) were formed through 1,3-dipolar cycloaddition of equimolar amounts of 3,5-dimethylpyridine *N*-oxide (**14**) and isocyanates **7** and **9**, respectively (Scheme 6). Isocyanate **7** and **9** were formed *in situ* in dry benzene from the corresponding acyl azide as previously described [2]. The cycloaddition reaction mixtures were refluxed for five days. The reactions proceeded according to previous reports (Scheme 2) [23] and the substituted amines (**17, 20**) were isolated in 65 – 67 % yield after purification. As expected, the less stable 1,2-dihydro intermediates (**15, 18**) were never observed by $^1$H NMR or isolated from the reaction mixtures. The crude cycloaddition product **17** consisted, however, of a mixture of the substituted amine (**17**, 80 %) and the more stable 2,3-dihydro intermediate (**16**, 20 %). The 2,3-dihydro intermediate (**16**) is formed through a [1,5]sigmatropic shift from intermediate **15** (Scheme 6), before it undergoes re-aromatization by decarboxylation to afford the substituted amine (**17**). In the reaction of isocyanate **9**, the 2,3-dihydro intermediate (**19**) could not be observed.

Scheme 6



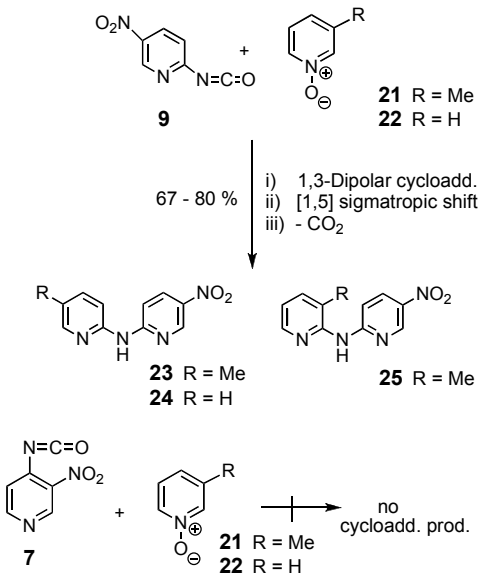

**7, 9** **14** **15, 18** **17, 20** **16, 19**

**7, 15, 16, 17;** 3,4-disubstituted pyridine
**9, 18, 19, 20;** 2,5-disubstituted pyridine

Additionally, 3-methylpyridine *N*-oxide (**21**) and pyridine *N*-oxide (**22**) were used in cycloaddition reactions with 5-nitropyridin-2-yl isocyanate (**9**) (Scheme 7). The unsymmetrical 3-methylpyridine *N*-oxide (**21**) could possibly give two products; the more and the less sterically hindered 3- and 5-methylpyridine derivatives **25** and **23**, respectively. A mixture of both products was formed in a ratio of 3:1 (**23:25**; 80 % yield in total), as shown by $^1$H NMR. The unsubstituted pyridine *N*-oxide (**22**) and isocyanate **9** afforded *N*-(5-nitropyridin-2-yl)pyridin-2-amine (**24**) in 67 % yield. The corresponding 2,3-dihydro intermediates could not be observed in any of these reactions. The isomeric 3-nitropyridin-4-yl isocyanate (**7**) failed to give cycloaddition products with

3-methylpyridine *N*-oxide (**21**) and pyridine *N*-oxide (**22**), demonstrating the lower cycloaddition reactivity of the less methyl-substituted pyridine *N*-oxides (**21**, **22**).

Scheme 7




## CONCLUSION

The 1,3-dipolar cycloaddition reactions of the nitropyridyl isocyanates **7** and **9** with azide and a pyridine *N*-oxides have been studied.

The tetrazolinones 1-(3-nitropyridin-4-yl)-1*H*-tetrazol-5(4*H*)one (**8**) and 1-(5-nitropyridin-2-yl)-1*H*-tetrazol-5(4*H*)one (**10**) were synthesized through 1,3-dipolar cycloadditions of the isocyanates (**7**) and (**9**) with TMSA in 50 % and 64 % yield, respectively. Both compounds underwent cycloreversion, hydrolysis and decarboxylation in solution in the presence of moisture to give the 4-amino-3-nitropyridine (**11**), urea (**12**) and 5-amino-2-nitropyridine (**13**) decomposition products.

The substituted amines, 3,5-dimethyl-*N*-(3-nitropyridin-4-yl)pyridin-2-amine (**17**), 3,5-dimethyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**20**), 5-methyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**23**), *N*-(5-nitropyridin-2-yl)pyridin-2-amine (**24**), and 3-methyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (**25**) were formed in 65 - 80 % yields from nitropyridyl isocyanates **7** and **9** and 3,5-dimethylpyridine *N*-oxide (**14**), 3-methylpyridine *N*-oxide (**21**) and pyridine *N*-oxide (**22**) through 1,3-dipolar cycloaddition reactions, rearrangement and decarboxylation.

The 1,2-dihydro cycloadduct intermediates, such as **15** or **18**, were unstable and could not be observed nor isolated from the reactions. The more stable 2,3-dihydro intermediate (**16**) was present in 20 % yield in the crude product of **7**. The corresponding 2,3-dihydro intermediate, such as **19**, was however never observed in the corresponding reactions with isocyanate **9**.

Our results demonstrate that the nitropyridyl isocyanates (**7**,**9**) readily undergo 1,3-dipolar cyloaddition reactions similar to phenyl isocyanates.

## EXPERIMENTAL

**Chemicals:** Trimethylsilylazide (TMSA) and 3,5-dimethylpyridine *N*-oxide, 3-methylpyridine *N*-oxide, pyridine *N*-oxide (Sigma-Aldrich). Solvents: *pro analysi* quality. Silica for flash column chromatography (sds, 60 Å, 40-63 μm). $^1$H and $^{13}$C NMR: Bruker Avance DPX 300 and 400 MHz spectrometers, chemical shifts are reported in ppm downfield from TMS. *J* values are given in Hz. MS: Finnigan MAT 95 XL mass spectrometer (EI, 70 eV). IR: Nicolet 20SXC FT-IR spectrophotometer. All melting points are uncorrected, measured by a Griffin or Stuart apparatus. Elemental analyses were done by the Laboratory of Organic Elemental Analysis at the Institute of Chemical Technology in Prague, Czech Republic. Nitropyridyl isocyanates **7** and **9** were prepared *in situ* from the respective acyl azide precursors as previously described [2].

**1,3-Dipolar cycloaddition with azide [8].**

**1-(3-Nitropyridin-4-yl)-1*H*-tetrazol-5(4*H*)one (8).** Trimethylsilylazide (TMSA, 150 mg, 0.18 mL, 1.3 mmol, 2 equivalents) was added to 3-nitropyridin-4-yl isocyanate (**7**) (110 mg, 0.65 mmol) generated *in situ* in dry benzene (5 mL) [2]. The reaction mixture was refluxed for 24 hours. Excess TMSA and solvent were removed *in vacuo* to afford 63 mg (50 %) of **8**. 4-Amino-3-nitropyridine (**11**) was gradually formed when cycloadduct **8** was left in solution. After four weeks the **8**:**11** ratio was 15:85 %, as shown by $^1$H NMR. **8:** $^1$H NMR ($d_6$-DMSO): 10.48 (br, 1H, NH), 9.09 (s, 1H, H-2'), 8.76 (d, *J* 5.6, 1H, H-6'), 7.80 (d, *J* 5.6, 1H, H-5'); $^{13}$C NMR ($d_6$-DMSO): 155.2, 154.7, 147.0, 138.7, 137.7, 117.5; MS: 208 ($M^+$, 8), 165 (100), 119 (53), 107 (15), 91 (41); IR (film); 3328 (s), 2180 (s), 2155 (s) 1717 (s), 1615 (m), 1585 (m), 1502 (s), 1446 (m), 1352 (s), 1240 (s), 1185 (m), 1052 (w), 857 (m), 764 (m) cm$^{-1}$. HRMS: Calculated for $C_6H_4N_6O_3$: 208.03449; observed for $C_6H_4N_6O_3$: 208.03521. **11 [33];** $^1$H NMR ($d_6$-DMSO): 8.96 (s, 1H, H-2), 8.13 (d, *J* 6.0, 1H, H-6), 7.95 (br, 2H, $NH_2$), 6.88 (d, *J* 6.0, 1H, H-5).

**1-(5-Nitropyridin-2-yl)-1*H*-tetrazol-5(4*H*)one (10).** Trimethylsilylazide (TMSA, 253 mg, 0.29 mL, 2.2 mmol, 2 equivalents) was added to 5-nitropyridin-2-yl carbonyl azide precursor of isocyanate **9** (212 mg, 1.1 mmol) in dry benzene (10 mL). The reaction mixture was refluxed for 24 hours. Excess TMSA and solvent were removed *in vacuo* to afford 145 mg (64 %) of **10;** $^1$H NMR ($d_6$-DMSO): 11.57 (br, 1H, NH), 9.43 (d, *J* 2.5, 1H, H-6'), 8.71 (dd, *J* 2.5 and 8.6, 1H, H-4'), 8.25 (d, *J* 8.6, 1H, H-3'); MS: 208 ($M^+$, 5), 165 (53), 139 (24), 124 (100), 119 (28), 107 (15), 91 (21), 79 (8); HRMS: Calculated for $C_6H_4N_6O_3$: 208.03449; observed for $C_6H_4N_6O_3$: 208.03385.

**1,3-Dipolar cycloaddition with pyridine N-oxides [23].** ***General method*:** The nitropyridine acyl azide precursor of the isocyanate (**7** or **9**) (100 mg, 0.52 mmol) in dry benzene (5 mL) was added drop-wise to a solution of the pyridine *N*-oxide (**14**, **21** or **22**) (0.52 mmol) in dry toluene (3 mL). The reaction mixture was refluxed under nitrogen atmosphere for five days. The solvent was removed *in vacuo*. The crude product was

purified by flash column chromatography (acetone as eluent) to afford the products **16**, **17**, **20**, **23, 24**, **25** below.

**3,5-Dimethyl-*N*-(3-nitropyridin-4-yl)pyridin-2-amine (17).** Yield: 53 mg (65 %), pure by NMR; $^1$H NMR ($CDCl_3$): 10.39 (br, 1H, NH), 9.35 (s, 1H, H-2'), 8.75 (d, *J* 6.2, 1H, H-6'), 8.47 (d, *J* 6.2, 1H, H-5'), 8.11 (s, 1H, H-4), 7.41 (s, 1H, H-6), 2.38 (s, 3H, Me), 2.32 (s, 3H, Me); $^{13}$C NMR ($CDCl_3$): 153.8, 152.8, 148.6, 145.4, 144.5, 140.2, 129.2, 122.5, 114.1, 112.3, 17.7, 17.1; IR (film): 3155 (w), 2926 (w), 1599 (s), 1522 (s), 1474 (m), 1382 (s), 904 (s) cm$^{-1}$; MS: 244 ($M^+$, 18), 198 (100), 182 (7), 170 (11), 106 (5); HRMS: Calculated for $C_{12}H_{12}N_4O_2$: 244.09602; observed for $C_{12}H_{12}N_4O_2$: 244.09634.

**6,7*a*-Dimethyl-3-(3-nitropyridin-4-yl)-3,3*a*-dihydrooxazolo-[4,5-*b*]pyridin-2(7*aH*)-one (16).** By isolation of the crude product after uncomplete conversion to **17**, the 2,3-dihydro intermediate (**16**), the precursor of intermediate **17**, was present (20 %) in the crude product, as seen by $^1$H NMR. No other spectroscopic data were available for intermediate **16**; $^1$H NMR ($CDCl_3$): 9.16 (s, 1H, H-2'), 8.81 (d, *J* 5.5, 1H, H-6'), 8.07 (d, *J* 5.5, 1H, H-5'), 7.78 (m, 1H, H-6), 5.96 (s, 1H, H-4), 5.44 (d, *J* 2.0, 1H, H-2), 2.00 (d, *J* 1.6, 3H, 5-Me), 1.77 (s, 3H, 3-Me).

**3,5-Dimethyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (20).** The product was obtained by flash column chromatography using acetone:*n*-pentane (1:2) as eluent to afford 55 mg (67 %) of **20**, pure by NMR; $^1$H NMR ($CDCl_3$): 9.08 (d, *J* 2.8, 1H, H-6'), 8.42 (d, *J* 9.6, 1H, H-4'), 8.37 (dd, *J* 2.8 and 9.6, 1H, H-3'), 8.05 (s, 1H, H-6), 7.56 (br, 1H, NH), 7.34 (s, 1H, H-4), 2.32 (s, 3H, Me), 2.29 (s, 3H, Me); $^{13}$C NMR ($CDCl_3$): 157.6, 148.6, 145.4, 145.1, 139.9, 138.0, 133.5, 128.0, 120.2, 109.9, 17.6, 17.1; IR (film): 3423 (w), 3155 (w), 2924 (w), 1589 (s), 1504 (s), 1477 (m), 1340 (s), 909 (s) cm$^{-1}$; MS: 244 ($M^+$, 38), 240 (13), 239 (22), 229 (15), 213 (11), 198 (14), 183 (13), 165 (35), 139 (100), 119 (20), 109 (22), 107 (18), 94 (28), 91 (18); HRMS: Calculated for $C_{12}H_{12}N_4O_2$: 244.09602; observed for $C_{12}H_{12}N_4O_2$: 244.09552.

**5-Methyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (23) and 3-methyl-*N*-(5-nitropyridin-2-yl)pyridin-2-amine (25).** Yield: 80 % (95 mg), which was a 3:1mixture of **23** and **25**, as shown by $^1$H NMR. **23**: $^1$H NMR ($CDCl_3$): 9.14 (d, *J* 2.6, 1H, H-6'), 8.54 (s, 1H, H-6), 8.41 (dd, *J* 7.6, 2.6, 1H, H-4'), 7.82 (d, *J* 8.1, 1H, H-4), 7.65 (br. s, 1H, NH), 7.50 (d, *J* 7.6, 1H, H-3'), 7.37 (d, *J* 8.1, 1H, H-3); $^{13}$C NMR ($CDCl_3$): 110.4, 112.8, 118.4, 123.1, 133.1, 138.8, 143.8, 145.2, 150.9, 157.4. **25**: $^1$H NMR ($CDCl_3$): 9.14 (d, *J* 2.6, 1H, H-6'), 8.65 (dd, J 2.4, 9.5, 1H, H-6), 8.41 (dd, *J* 7.6, 2.6, 1H, H-4'), 7.74 (d, *J* 9.5, 1H, H-4), 7.65 (br. s, 1H, NH), 7.50 (d, *J* 7.6, 1H, H-3'), 7.23 (m, 1H, H-5); MS: 230 ($M^+$, 52), 215 (17), 200 (5), 184 (12), 183 (26), 167 (21), 151 (24), 139 (11), 124 (58), 123 (38), 107 (4). HRMS: Calculated for $C_{11}H_{10}N_4O_2$: 230.08041; Found for $C_{11}H_{10}N_4O_2$: 230.08037.

***N*-(5-Nitropyridin-2-yl)pyridin-2-amine (24) [32].** Yield:67 % (75 mg); $^1$H NMR ($CDCl_3$): 9.14 (d, *J* 2.6, 1H, H-6'), 8.44 (br. s, 1H, NH), 8.38 (dd, *J* 8.8, 2.6, 1H, H-4'), 7.84 (d, *J* 7.5, 1H, H-6), 7.71 (dd, *J* 8.4, 6.0, 1H, H-4), 7.58 (d, *J* 8.8, 1H, H-3'), 7.36 (d, *J* 8.4, 1H, H-3), 7.02 (dd, *J* 6.0, 7.5, 1H, H-5). $^{13}$C NMR ($CDCl_3$): 110.4, 113.1, 118.4, 133.2, 138.1, 138.3, 145.5, 147.7, 152.4, 157.4. IR (film): 3066 (w), 1700 (w), 1592 (s), 1576 (m), 1506 (w), 1439 (m), 1421 (w), 1395 (w), 1335 (s), 1290 (m), 1116 (m), 1008 (w) cm$^{-1}$. MS: 216 ($M^+$, 100), 215 (87), 200 (2), 186 (7), 169 (38), 143 (6), 124 (12), 116 (3). HRMS: Calculated for $C_{10}H_8N_4O_2$: 216.06473; Found for $C_{10}H_8N_4O_2$: 216.06453.

**Acknowledgements.** Financial support from the Research Council of Norway is gratefully acknowledged

## REFERENCES

[1] Gilchrist, T. L. *Heterocyclic Chemistry*, Addison Weasley Longman Limited, Third Edition, **1997**, 91-106.

[2] Holt, J.; Andreassen, T.; Bakke, J. M.; Fiksdahl, A. *J. Heterocyclic Chem.*, **2005**, *42*, 259-264.

[3] Vandensavel, J-M.; Smets G.; L'abbe, G. *J. Org. Chem.* **1973**, *38*, 675-678.

[4] Scheiner, P. *Tetrahedron*, **1968**, *24*, 2757-2766,.

[5] Stout, D. M.; Takaya, T.; Meyers, A. I. *J. Org. Chem.* **1975**, *40*, 563-569.

[6] Horwitz, J. P.; Fisher B. E.; Tomazevski, A. J. *J. Am. Chem. Soc.*, **1959**, *81*(12), 3076-3079.

[7] Quast, H.; Nahr, U. *Chem. Ber.* **1983**, *116*, 3427-3437.

[8] Tsuge, O.; Urano S.; Oe, K. *J. Org. Chem.* **1980**, *45*, 5130-513.

[9] Toselli, M.; and Zanirato, P. *J. Chem. Soc. Perkin Trans. 1 (9)*, **1992**, 1101-1104.

[10] Birkofer L.; and Wegner, P. *Chem. Ber.*, **1966**, *99*, 2512-2517.

[11] Ettenhuber E.; Rühlmann, K. *Chem. Ber.*, **1968**, *101*, 743-750.

[12] Washburne, S. S.; Peterson, W. R. *J. Organomet. Chem.*, **1970**, *21*, 427-430.

[13] Kricheldorf, H. R. *Synthesis*, 551-553 (1972).

[14] MacMillan, J. H.; Washburne, S. S. *J. Org. Chem.* **1973**, *38*, 2982-2984.

[15] Kricheldorf, H. R. *Chem. Ber.*, **1972**, *105*, 3958-3965.

[16] Washburne, S. S.; Peterson Jr. W. R.; and Berman, D. A. *J. Org. Chem.* **1972**, *37*(11), 1738-1742.

[17] MacMillan, J. H.; Washburne, S. S. *J. Heterocyclic Chem.*, **1975**, *12*, 1215-1220.

[18] Kricheldorf, H. R. *Chem. Ber.*, **1973**, *106*, 3765-3768.

[19] Goto, T.; Seishi, I.; Watanabe, Y.; Narabu S-I.; Yanagi, A. *EP* 672663 (1995).

[20] Theodoridis, G. *US* 4909829 (1990).

[21] Covey, R. A.; Moore, R. C. *US* 4839349 (1989).

[22] Janssens, F.; Torremans, J.; Janssen, P. A. J. *J. Med. Chem.* **1986**, *29*, 2290-2297.

[23] Abramovitch, R. A.; Shinkai, I.; Van Dahm, R. *J. Heterocyclic Chem.*, **1976**, *13*(1), 171-172.

[24] Matsuoka, T.; Harano, K.; Kubo, H.; Hisano, T.*Chem. Pharm. Bull.*, **1986**, *34*(2), 572-581.

[25] Hisano, T.; Matsuoka, T.; Fukunaga, K.; Ichikawa, M. *Chem. Pharm. Bull.*, **1982**, *30*(10), 3776-3781.

[26] Harano, K.; Kondo, R.; Murase, M.; Matsuoka, T.; Hisano, T. *Chem. Pharm. Bull.*, **1986**, *34*(3), 966-974.

[27] Harano, K.; Suematsu, F.; Matsuoka, T.; Hisano, T. *Chem. Pharm. Bull.*, **1984**, *34*(2), 543-552.

[28] Hisano, T.; Matsuoka, T.; Tsutsumi, K.; Muraoka, K.; Ichikawa, M. *Chem. Pharm. Bull.*, **1981**, *29*(12), 3706-3712.

[29] Matsuoka, T.; Shinada, M.; Suematsu, F.; Harano, K.; Hisano, T. *Chem. Pharm. Bull.*, **1984,** *32*(6), 2077-2090.

[30] Matsuoka, T.; Harano, K. *Tetrahedron*, **1995**, *51*(23), 6451-6458.

[31] Hisano, T.; Harano, K.; Fukuoka, R.; Matsuoka, T.; Muraoka, K.; Shinohara, I. *Chem. Pharm. Bull.*, **1986**, *34*(4), 1485-1492.

[32] Giumanini, A.; Poiana, M.; Verardo, G.; Strazzolini, P.; Tolazzi, M.; Cerioni, G. *Bull. Chem. Soc. Jpn.*, **1994**, *67* 1465-1645.

[33] Bakke, J. M.; Riha, J, *J. Heterocyclic Chem.*, **1999**, *36*, 1143.