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We hereby report the first preparation of 3-nitro-4-pyridyl isocyanate **9** and 5-nitro-2-pyridyl isocyanate **18**. They were formed by Curtius rearrangement of the corresponding acyl azides **8** and **17**, prepared from methyl 3-nitro-4-pyridinecarboxylate **6** *via* the hydrazide **7** and 5-nitro-picolinic acid **16**, respectively. The substrates **6** and **16** were generated by nitration of methyl 4-pyridinecarboxylate **5** and nitration and oxidation of 2-picoline **14**. 3-Nitro-4-pyridyl isocyanate **9** can be stored in dry solution and is stable at room temperature for several weeks while 5-nitro-2-pyridyl isocyanate **18** was less stable and should be used for synthetic purposes immediately.

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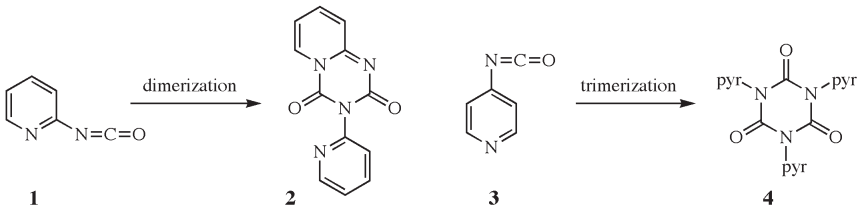
Introduction.

Isocyanates constitute an important class of compounds in organic chemistry. They undergo a series of reactions to yield a variety of interesting products including heterocyclic derivatives. Heterocyclic isocyanates have however not been given the same attention as the respective aromatic compounds in synthesis and reactivity studies. A reason for this is their instability and their high reactivity [1]. Some of the heterocyclic isocyanates have been generated *in situ*, and a spontaneous di- or trimerization process can be circumvented by trapping the isocyanate with suitable reagents. Of the three possible pyridyl isocyanates only the 3-isomer has been successfully isolated [2]. Attempts to generate 2-pyridyl isocyanate (**1**) led to the formation of its dimer (**2**), formed by a [2+4] cycloaddition, while the 4-isomer (**3**) trimerizes to an isocyanurate (**4**).



1 **2** **3** **4**

Our experience with the preparation, reactivity and instability of 2-pyridyl isocyanate (**1**) is based on a previous study of preparation and thermal cycloreversion/decomposition of the dimer (**2**) of 2-pyridyl isocyanate **1** and the cycloaddition products of **1** with ketenes [3,4]. The decomposition products were characterized by ir/Ar matrix after sublimation, flash vacuum thermolysis (FVT) and argon matrix deposition.

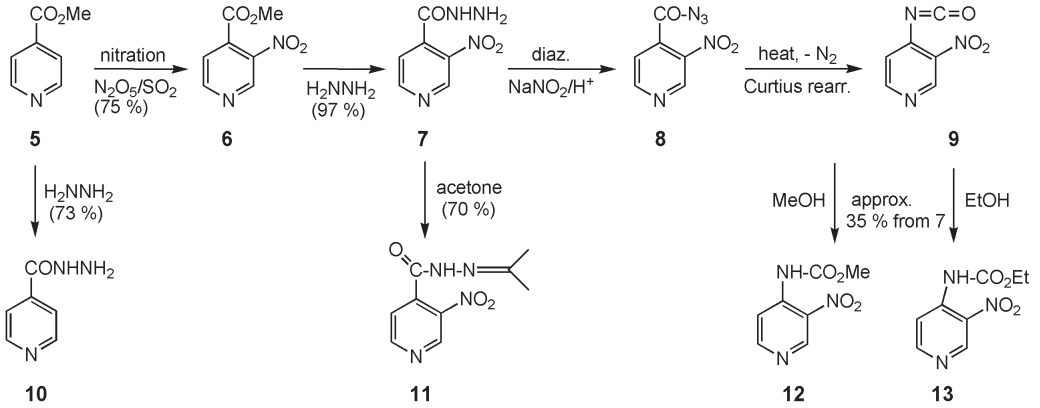
The introduction of an electronegative substituent like the nitro group was expected to reduce the basisity of the pyridine nitrogen, hence retarding the di- or trimerization, but also increase the reactivity of the isocyanate carbon towards nucleophiles. Because of this we wanted to study the preparation, stability and reactivity of nitropyridyl isocyanates. A number of substituted 3-nitropyridines have now become readily available through an improved nitration method [5,6] and some of these derivatives are suitable substrates for the preparation of 3-nitropyridyl isocyanates. We hereby report the preparation of 3-nitro-4-pyridyl isocyanate (**9**) and 5-nitro-2-pyridyl isocyanate (**18**).

Results and Discussion.

The preparation of 3-nitro-4-pyridyl isocyanate (**9**) from methyl 4-pyridinecarboxylate (**5**) was carried out by the four-step procedure shown in Scheme 1.

The nitropyridine substrate **6** was generated by nitration [5,6] of the methyl ester **5**. In contrast to the formation of hydrazide **10** based on general methods and previous reports [3], the preparation of the hydrazide **7** had to be carried out at room temperature since heating of the hydrazine reaction mixture yielded several by-products. Methanol had to be avoided as solvent for the reaction, in the work-up and as eluent in the following flash chromatography since two unidentified di-*N*-methylated by-products easily were formed, as demonstrated by ms and nmr. The acetone hydrazone derivative **11** was formed by addition of acetone to the 3-nitropyridine-4-carbonylhydrazide (**7**) reaction mixture. The hydrazone **11** was characterised as a 70:30 mixture of two tautomers, as shown by ^{1}H and ^{13}C nmr.

Scheme 1



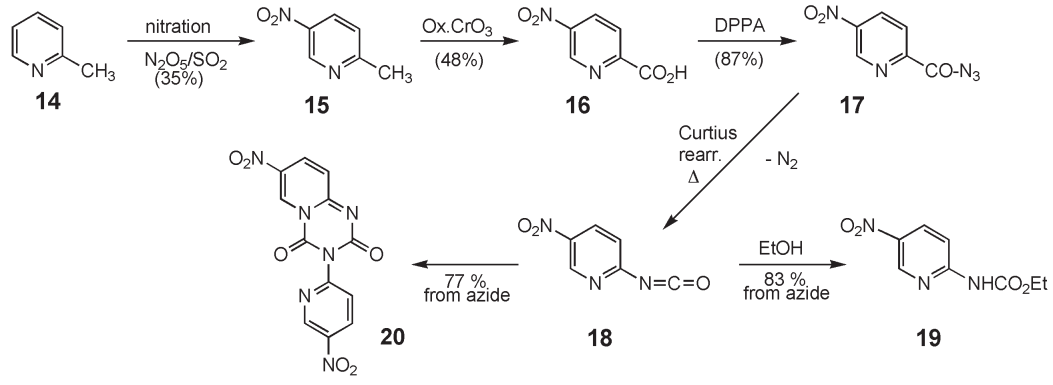
The acyl azide **8**, characterised by the strong azide ir frequency of 2180 cm^{-1}, was prepared by diazotization of the hydrazide **7**. The acyl azide **8** easily decomposed in ms and by Curtius rearrangement in solution to the isocyanate **9**, demonstrated by the minor molecular ion of the azide (0.4 %) and hence the presence of the isocyanate molecular ion of *m/z* 165 as the base peak. The exact yield of the azide was not measured since this potential unstable product was always kept in a dry diethyl ether solution and stored in the freezer.

Curtius rearrangement of the acyl azide **8**, carried out in a refluxing dry benzene solution until nitrogen gas evolution ceased, afforded the isocyanate **9**. The reaction was followed by frequent ^1H nmr analysis indicating a gradual conversion of the azide **8** into the isocyanate **9**, demonstrated by the increased shielding effect and lower frequency values of especially H-5. More than 93 % conversion of the azide and respectively 93 % purity and yield of the isocyanate **9** were obtained after 15 min. No trimer isocyanurate (see structure **4** above) or other by-products could be observed. The presence of the isocyanate group was demonstrated by the characteristic strong ir frequency of 2274 cm^{-1}. 3-Nitro-4-pyridyl isocyanate (**9**) could be stored in dry diethyl ether or benzene solutions and was stable at room temperature for several weeks. The yield of isocyanate **9** was not measured since the product was always kept in solution or directly transformed into the corresponding carbamates. The carbamates **12** and **13** were prepared directly from the acyl azide in the presence of methanol or ethanol *via* the isocyanate formed *in situ* by heating.

Correspondingly, 5-nitro-2-pyridyl isocyanate (**18**), was prepared by a Curtius rearrangement of the respective acyl azide precursor (**17**, Scheme 2). Nitration and oxidation of the easily available 2-picoline (**14**) afforded the 5-nitropicolinic acid (**16**). Diphenyl phosphoryl azide (DPPA) transforms carboxylic acids directly and conveniently to acyl azides in high yields, as demonstrated for compound **17**.

The 5-nitro-2-pyridyl isocyanate (**18**) monomer was characterized by nmr and ir, showing the characteristic isocyanate absorption (2280 cm^{-1}). However, isocyanate **18** was less stable than the 3,4-isomer (**9**) and should be used for synthetic purposes immediately. The presence of the isocyanate was also confirmed by trapping the product with alcohol. The ethyl carbamate (**19**) was afforded in 87 % yield from azide **17**, demonstrating the ability of this isocyanate to be trapped by other reagents, despite its unstability. In the absence of a trapping reagent the isocyanate

Scheme 2



monomer formed the dimer (**20**) which was isolated in 77 % yield after 2 hrs heating of the acyl azide (**17**). The dimer is formed by a [2+4] cycloaddition reaction [4].

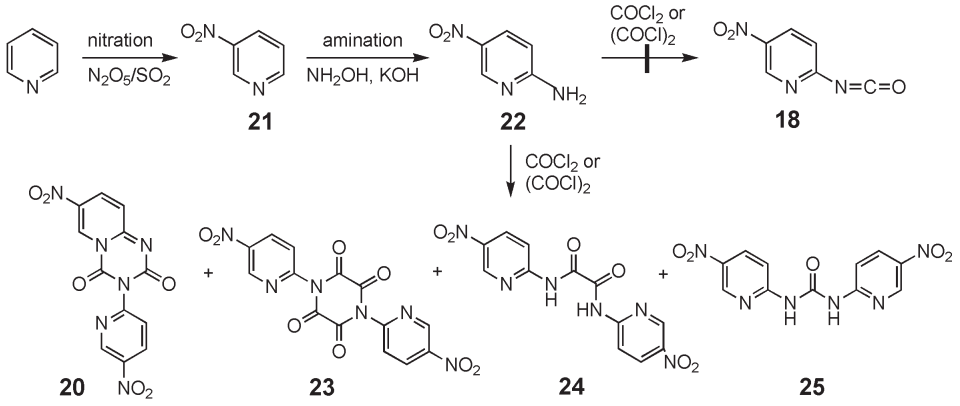
Standard phosgene reaction or alternatively oxalyl chloride [7] reaction of 2-amino-5-nitropyridine (**22**) failed to give 5-nitro-2-pyridyl isocyanate (**18**), as shown in Scheme 3. The reactions yielded several other products depending on the reagent. The phosgene reaction yielded mainly the isocyanate dimer (**20**) and minor amounts of the urea compound (**25**). The tetrone (**23**) was isolated and identified after reaction with oxalyl chloride. The latter reaction seems to proceed *via* the *N*,*N*'-dipyridylethanediamide (**24**). Indications of **24** and **25** are only based on limited spectroscopic data (ir, ^{1}H and ^{13}C nmr). The fact that no carbamate trapping product could be isolated from the reaction mixtures after addition of methanol also demonstrates the absence of isocyanate. 2-Amino-5-nitropyridine (**22**) was generated by nitration of pyridine [5,6] followed by amination [8].

alcohols. Quantitative yield of the methyl carbamate (**29**) was isolated after heating of the trimer (**28**) in methanol. The trimer decomposed by flash chromatography or tlc to give 4-aminopyridine. The observed reactivity of the trimer towards nucleophiles like methanol and moisture demonstrates that the trimer may be used as a stable and protected version of the unstable isocyanate for synthetic purposes.

Conclusion.

In conclusion, 3-nitro-4-pyridyl isocyanate (**9**) and 5-nitro-2-pyridyl isocyanate (**18**) have been prepared from methyl 4-pyridinecarboxylate (**5**) and 2-picoline (**14**), respectively, by a four-step procedure including Curtius rearrangement of the corresponding acyl azides (**8**, **17**). 3-Nitro-4-pyridyl isocyanate (**9**) was stable in dry solution at room temperature for several weeks while 5-nitro-2-pyridyl isocyanate (**18**) could be spectroscopically characterised before trapped as the dimer or as the

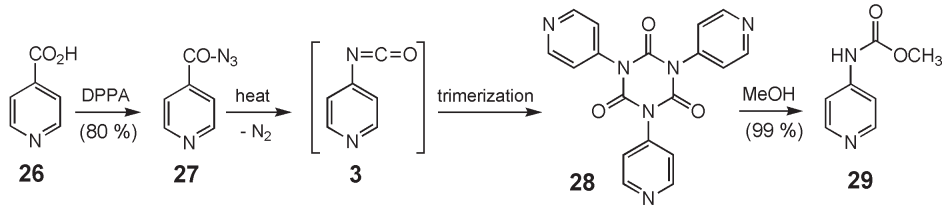
Scheme 3



The trimer isocyanurate (**28**) [9,10] of the unstable non-nitro 4-pyridyl isocyanate (**3**) was synthesized for reference purposes. Characteristic orange crystals were obtained after reaction of 4-picolinic acid (**26**) with DPPA followed by Curtius rearrangement of acyl azide (**27**) [12] as shown in Scheme 4. The trimer was less stable than previously reported and the amine or carbamate decomposition products were observed in the presence of moisture or carbamate. Treatment of isocyanates **9** and **18** with methanol or ethanol afforded the corresponding carbamates **12**, **13** and **19**.

Our results thus demonstrate that the introduction of the nitro group in the pyridyl ring stabilises the otherwise unstable heterocyclic isocyanate. This may make the nitropyridyl isocyanates available as a new and interesting group of compounds similar to aromatic isocyanates.

Scheme 4



Investigation of the chemistry of nitropyridyl isocyanates as substrates for syntheses of a series of heterocycles is now in progress in our laboratories.

EXPERIMENTAL

Chemicals: Hydrazine hydrate, NaN_3 and $NaNO_2$ (Merck), DPPA and isopicolinic acid (Acros). Solvents: *pro analysi* quality. ^1H / ^{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 (EI / 70 eV). ir: Nicolet 20SXC FT-IR spectrophotometer. All melting points are uncorrected, measured by Griffin apparatus. Flash chromatography: Silica (sds, 60 A, 40-63 μm). Compound **16** was prepared from 5-nitropicoline (**15**) [11] according to the literature [15].

3-Nitropyridine-4-carbonylhydrazide (**7**).

This compound was prepared (97%) from methyl 3-nitro-4-pyridinecarboxylate (**6**) [5,6] according to the literature [3]. mp 153-154 °C, ir (KBr) 1647s, 1534s, 1344s, 1189m, 1098w, 1041w, 851s, 717s, 661s, 569m cm^{-1}; ^1H nmr (300 MHz, DMSO-d_6): δ 4.64 (s, br, 2H), 7.64 (d, J 4.9, 1H, H-5), 8.96 (d, J 4.9, 1H, H-6), 9.25 (s, 1H, H-2), 9.96 (s, br, 1H); ^{13}C nmr (75 MHz, DMSO-d_6): δ 124.1, 139.1, 143.7, 146.0, 155.6, 163.6; ms: *m/z* 182 (M^+, 1 %), 152 (100), 135 (23), 122 (72), 105 (7), 94 (27); HRMS (ESI): calcd for $C_6H_6N_4O_3$, M+1; 183,0512; observed 183,0513.

Anal. Calcd. for $C_6H_6N_4O_3$: C, 39.57; H, 3.32; N, 30.76. Found: C, 39.50; H, 3.39; N, 30.76.

3-Nitropyridine-4-carbonyl azide (**8**).

This compound was prepared from 3-nitropyridine-4-carbonylhydrazide (**7**) by diazotization according to the literature [3]. The product which was pure by ^1H nmr was kept under N_2 atmosphere in the freezer in an approx. 100 mg/25ml dry diethyl ether solution which was used for the preparation of isocyanate **9** and the corresponding carbamates **12** and **13**; ir (film) 3084w, 3056w, 2180s, 2133m, 1696s, 1527s, 1344s, 1246s, 1154m, 1000w, 844w, 661w cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 7.64 (d, J 4.9, 1H, H-5), 9.0 (d, J 4.9, 1H, H-6), 9.25 (s, 1H, H-2) (corresponding shift values in d_6-benzene; δ 6.62, 8.13, 8.62); ^{13}C nmr (100 MHz, d_6-C_6H_6): δ 121.4, 133.8, 144.5, 153.5, 168.8, 175.6; ms: *m/z* 193 (M^+, 0.4 %), 165 (71), 151 (100), 119 (42), 91 (33).

3-Nitro-4-pyridyl isocyanate (**9**).

An aliquot of the dry diethyl ether solution of 3-nitropyridine-4-carbonyl azide above (**8**, approx. 10 mg in 2.5 ml ether) was repeatedly added d_6-benzene (3 x 0.5 ml) and the diethyl ether was removed each time carefully by N_2-flush. The d_6-benzene solution was refluxed under N_2-atmosphere. Gas evolution was observed. The reaction was followed by frequent ^1H nmr analysis indicating a gradual conversion of the azide **8** into the isocyanate **9**. More than 93 % purity of isocyanate **9** was obtained after 15 min. showing no by-products. This reaction was carried out for preparative purposes in a regular dry benzene solution. The isocyanate **9** could be stored in dry diethyl ether or benzene solutions and was stable at room temperature for several weeks; ir (film) 3224w, 2915w, 2852w, 2380w, 2274s, 2264m, 1612m, 1450m, 1323s, 1154m, 900s, 802m cm^{-1}; ^1H nmr (300 MHz, d_6-benzene): δ 6.55 (d, J 4.9, 1H, H-5), 8.08 (d, J 4.9, 1H, H-6), 8.58 (s, 1H, H-2);); ^{13}C nmr (75 MHz, d_6-C_6H_6): δ 120.8, 133.2, 144.1, 152.7, 168.5; glc-ms: *m/z* 165 (M^+, 100 %), 121 (55), 119 (78), 109 (4), 107 (17), 104 (10), 94 (42); HRMS (ESI): calcd for $C_6H_3N_3O_3$, M+1;166.0247; observed 166.0249.

Pyridine-4-carbonylhydrazide (**10**).

This compound was prepared (73 %) according to the literature [3], mp 153-154 °C; ^1H nmr (300 MHz, d_4-MeOD): δ 4.87 (s, br, 3H), 6.59 (dd, J 1.7, 4.5, 2H, H-3 and H-5), 7.52 (dd, J 1.7, 4.5, 2H, H-2 and H-6); ms: *m/z* 137 (M^+, 62 %), 122 (12), 106 (100), 104 (26), 84 (13), 79 (17), 78 (90).

Propanone 3-nitropyridine-4-carbonylhydrazone (**11**).

To the hydrazide product (**7**) reaction mixture above was added acetone (5 ml) before work-up. Tlc indicated formation of the hydrazide derivative which formed off-white crystals (approx. 70 %); mp 170-179 °C (acetone). ^1H nmr showed a 70:30 mixture of two acetone adducts as isomers/tautomers **11a** and **11b** and no other products; ^1H nmr (400 MHz, DMSO-d_6), **11a** (70 %): δ 1.67 (s, 3H), 1.85 (s, 3H), 7.63 (d, J 4.8, 1H, H-5), 8.95 (d, J 4.8, 1H, H-6), 9.26 (s, 1H, H-2), 11.15 (s, br, 1H); **11b** (30 %): δ 1.86 (s, 3H), 2.0 (s, 3H), 7.72 (d, J 4.8, 1H), 8.98 (d, J 4.8, 1H), 9.31 (s, 1H), 10.84 (s, br, 1H); ^{13}C nmr (75 MHz, DMSO-d_6) **11a**/**11b** (70/30): δ 17.7, 18.3, 18.8, 25.1, 123.4, 124.0, 139.1, 139.8, 142.5, 142.6, 144.7, 145.5, 154.0, 155.1, 155.2, 159.8, 160.4, 166.5; glc-ms: *m/z* 222 (M, 8 %), 207 (47), 183 (3), 176 (3), 151 (14), 135 (93), 122 (32), 105 (17), 94 (35), 71 (100); HRMS: (ESI); calcd for $C_9H_{10}N_4O_3$, M+1; 223.0825; observed 223.0826.

Anal. Calcd. for $C_9H_{10}N_4O_3$: C, 48.65; H, 4.54; N, 25.21. Found: C, 48.62; H, 4.66; N, 25.26.

Methyl 3-nitropyridyl-4-carbamate (**12**) [13].

The dry diethyl ether solution of 3-nitropyridine-4-carbonyl azide above (**8**, approx. 10 mg in 2.5 ml ether), dry methanol (1 ml) and dry benzene (4 ml) was refluxed under N_2 until gas evolution ceased (1 hr) and tlc showed full conversion of the azide **8** to the carbamate. Crystalline methyl carbamate **12**, pure by ^1H nmr, was obtained after flash chromatography (4 mg, approx. 37 % yield from **7**); mp 147-148 °C (acetone/hexane); ir (KBr) 3270m, 2915w, 1731s, 1600s, 1485s, 1443m, 1408m, 1344s, 1253s, 1234w, 1168m, 1048m, 865w, 759w, 724w cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 3.9 (s, 3H), 8.55 (d, J 6.0, 1H, H-5), 8.66 (d, J 6.0, 1H, H-6), 9.37 (s, 1H, H-2), 10.04 (s, br, 1H, NH); ^{13}C nmr (75 MHz, $CDCl_3$): δ 53.4 (OCH_3), 113.5 (C-5), 131.9 (C-3), 141.9 (C-4), 148.0 (C-2), 152.8, (C=O), 155.2 (C-6); ms: *m/z* 197 (M^+, 19 %), 165 (2), 151 (37), 94 (4), 88 (10), 86 (57), 49 (100); HRMS (ESI): calcd for $C_7H_7N_3O_4$, M+1;198.0509; observed 198.0508.

Ethyl 3-nitropyridyl-4-carbamate (**13**) [14].

This compound was prepared from 3-nitro-4-pyridyl isocyanate (**9**) as described above for the preparation of methyl carbamate **12**, replacing dry methanol with dry ethanol. Crystalline carbamate **13**, pure by ^1H nmr, was obtained (4.1 mg, approx. 36 % yield from hydrazide **7**); mp 59-60 °C (diethyl ether/hexane), ir (KBr) 3344m, 2971w, 2915w, 1739s, 1598s, 1570s, 1492s, 1436m, 1344s, 1253s, 1234w, 1177m, 1048m, 858w, 759w cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 1.37 (t, J 7.1, 3H), 4.34 (q, J 7.1, 2H), 8.55 (d, J 6.0, 1H, H-5), 8.65 (d, J 6.0, 1H, H-6), 9.44 (s, 1H, H-2), 10.0 (s, br, 1H, NH); ^{13}C nmr (75 MHz, $CDCl_3$): δ 14.3

(CH_3), 62.8 (CH_2), 113.3 (C-5), 131.8 (C-3), 142.0 (C-4), 148.0 (C-2), 152.3 (C=O), 155.1 (C-6); ms: *m/z* 211 (M^+, 39 %), 165 (31), 139 (58), 137 (45), 135 (18), 121 (16), 119 (16), 93 (76), 84 (97), 49 (100); HRMS (EI) calcd for $C_8H_9N_3O_4$, 211.05930; observed 211.05900.

5-Nitropyridine-2-carbonyl azide (**17**).

A solution of **16** (0.3 g, 1.78 mmol) in DMF (2.5 ml) was added Et_3N (0.25 ml, 1.8 mmol) followed by the addition of diphenylphosphoryl azide (DPPA, 0.4 ml, 1.9 mmol) in DMF (0.5 ml) over 10 min. by stirring and cooling. The solution was stirred for 2 hrs. at 35 °C, poured over ice/CH_2Cl_2 and extracted with CH_2Cl_2. The combined organic extracts were washed with a solution of $NaHCO_3$ followed by water and dried. White solid (0.3 g, 87 %) was obtained after careful evaporation of the solvent. ir (KBr) 3097w, 3070w, 2327m, 2200m, 2141s, 1703s, 1599s, 1528s, 1355s, 1295s, 1247s, 1184s, 1131m, 1014s, 850s, 724s, 670s cm^{-1}; ^1H nmr (400 MHz, DMSO-d_6): δ 8.32 (d, J 8.6, 1H, H-3), 8.79 (dd, J 8.6, 2.6, 1H, H-4), 9.47 (d, J 2.6, 1H, H-6); ^{13}C nmr (75 MHz, DMSO-d_6): δ 125.3, 133.5, 144.9, 146.4, 151.2, 170.3; ms: *m/z* 193 (M^+, 2 %), 165 (43), 152 (7), 151 (100), 135 (5), 124 (6), 123 (31), 119 (14), 107 (11), 92 (9), 91 (13).

5-Nitro-2-pyridyl isocyanate (**18**).

This compound was prepared from 5-nitropyridine-2-carbonyl azide (**17**) as described above for the preparation of isocyanate (**9**) from azide (**8**); ir (film) 3234w, 2388w, 2280s, 1618w, 1453w, 1330m, 1162w, 812s cm^{-1}; ^1H nmr (400 MHz, d_6-benzene): δ 5.78 (d, J 8.9, 1H, H-3), 7.34 (dd, J 8.9, 2.8, 1H, H-4), 8.63 (d, J 2.8, 1H, H-6); ms: *m/z* 165 (M^+, 26 %), 139 (60), 123 (100), 119 (11), 109 (11), 100 (13), 94 (43). HRMS: calcd for $C_6H_3N_3O_3$, 165.01744; observed 165.01746.

Ethyl 5-nitropyridyl-2-carbamate (**19**).

This compound was prepared from 5-nitro-2-pyridyl isocyanate (**18**) as described above for the preparation of ethyl carbamate **13**. Crystalline white product, pure by ^1H nmr, (87 % from azide **17**) was obtained after recrystallization of the crude product; mp 212-213 °C (acetone/pentane), ir (KBr) 3197m, 3140w, 2995br, 1730s, 1594s, 1561w, 1515s, 1401m, 1348s, 1278s, 1227s, 1115m, 1062m, 1010m, 863m, 824w, 769s cm^{-1}; ^1H nmr (300 MHz, d_6-DMSO): δ 1.26 (t, J 7.1, 3H, CH_3), 4.20 (q, J 7.1, 2H, CH_2), 8.06 (d, J 9.4, 1H, H-3), 8.58 (dd, J 9.4, 2.8, 1H, H-4), 9.12 (d, J 2.8, 1H, H-6), 11.02 (s, br, 1H, NH);); ^{13}C nmr (75 MHz, DMSO-d_6): δ 14.3, 61.2, 111.3, 134.1, 139.4, 144.8, 153.3, 156.7; ms: *m/z* 212 (M^++1, 8 %), 211 (M^+, 68), 166 (15), 165 (23), 152 (28), 140 (6), 139 (100), 120 (10), 119 (9), 109 (10); HRMS: calcd for $C_8H_9N_3O_4$, 211.0593; observed 211.0594.

7-Nitro-3-(5-nitro-2-pyridyl)-2*H*-pyrido[1,2-*a*]-1,3,5-triazin-2,4(3*H*)-dione; isocyanate dimer (**20**).

Acyl azide **17** (76.9 mg, 0.388 mmol) in benzene (10 ml) was refluxed under N_2 atmosphere for 3 hrs. The solvent was evaporated and the yellow crude product was recrystallised giving off white crystals (77 %), pure by ^1H nmr; mp 235-237 °C (acetone/pentane), ir (KBr) 3095w, 3050w, 1782m, 1698s, 1652s, 1608m, 1566s, 1529s, 1430m, 1347s, 1301w, 1273m, 1207w, 1132m, 1020w, 927w, 857m, 838m, 777s cm^{-1}; ^1H nmr (300 MHz, DMSO-d_6): δ 7.33 (d, J 9.8, 1H, H-9), 7.86 (d, J 8.7, 1H, H-3'), 8.47 (dd, J 9.8, 2.4, 1H, H-8); 8.89 (dd, J 8.7 2.7, 1 H, H-4'), 9.18 (d, J 2.4, 1 H, H-6), 9.46 (d, J 2.7, 1 H, H-6'); ^{13}C nmr (75 MHz, DMSO-d_6): δ 124.1 (C-9), 124.7 (C-3´), 129.6 (C-8), 135.1 (C-6), 135.2 (C-4´), 136.5 (C-7), 144.7 (C-6´), 145.2 (C-5´), 147.1 (C-10), 151.7 (C-2´), 152.4 (C=O), 154.5 (C=O); ms: *m/z* 221 (2 %), 166 (2), 165 (29), 139 (26), 135 (5), 119 (11). 109 (8), 107 (9).

Anal. Calcd. for $C_{12}H_6N_6O_6$: C, 43.65; H, 1.83; N, 25.45. Found: C, 43.67; H, 1.98; N, 24.27.

2-Amino-5-nitropyridine (**22**).

This compound was prepared from pyridine *via* 3-nitropyridine (**21**) by nitration [5,6] of pyridine followed by amination [8] according to the literature.

Attempt to prepare 5-Nitro-2-pyridyl isocyanate (**18**) from 2-amino-5-nitropyridine (**22**).

Phosgene Reaction.

2-Amino-5-nitropyridine (**22**, 0.10 g, 0.72 mmol) in dry ethyl acetate (7 ml) was slowly added phosgene in toluene (20 % 1.5 ml, 3.3 mmol) at room temperature and refluxed for 4 hrs. The precipitate (108 mg) was collected by filtration, dissolved in HCl (1%, 20 ml) and extracted with CH_2Cl_2 yielding the dimer (**20**) as off white crystals (65 mg, 20 %). The mother liquor was evaporated and dissolved in ethyl acetate. Minor amounts, believed to be the urea product (**25**), pure by ^1H nmr, was obtained as yellow crystals after flash chromatography.

N,*N*´-di(5-nitro-2-pyridyl) urea (**25**).

Compound **25** obtained as described above has the following properties: ir (KBr) 3080w, 2960w, 2930w, 1735m, 1710s, 1605m, 1580m, 1520m, 1495m, 1395m, 1345s, 1300s, 1120m, 855m, 770m cm^{-1}; ^1H nmr (300 MHz, DMSO-d_6): δ 8.08 (d, J 9.3, 2H, H-3), 8.64 (dd, J 9.3 2.7, 2H, H-4), 9.18 (d, J 2.7, 2H, H-6), 10.74 (br, 2H, NH); ^{13}C nmr (75 MHz, DMSO-d_6): δ 111.8, 134.5, 139.6, 144.8, 150.8, 156.0; ms: *m/z* 304 (M^+, 1 %), 166 (14), 165 (83), 139 (100), 135 (9), 119 (29), 109 (15), 107 (14).

Oxalyl Chloride Reaction [7].

Oxalyl chloride (0.40 ml, 4.6 mmol) in dry ethyl acetate (2 mmol) was heated to 60 °C and added 2-amino-5-nitropyridine (**22**, 0.1 g, 0.72 mmol) in dry ethyl acetate (7 ml). The precipitate was collected by filtration after 30 min. affording the piperazinetetrone (**23**, 120 mg, 85 %), pure by ^1H and ^{13}C nmr. Trace amounts of a by-product, believed to be the ethanediamide (**24**), was observed. When the reaction was carried out at room temperature, higher yields of **24** were isolated.

N,*N*'-Di(5-nitro-2-pyridyl)piperazinetetrone (**23**).

Compound **23** obtained as described above has mp 280 °C (decomp. EtOAc); ir (KBr) 3670-3250 br, 3480w, 3100m, 3070m, 2880w, 1725s, 1610m, 1570m, 1535s, 1465m, 1395m, 1360s, 1310s, 1180w, 1120w cm^{-1}; ^1H nmr (300 MHz, d_6-DMSO): δ 7.79 (d, J 8.7, 2H, H-3), 8.91 (dd, J 8.7, 2.8, 2H, H-4), 9.52 (d, J 2.8, 2H, H-6); ^{13}C nmr (75 MHz, DMSO-d_6): δ 124.4, 135.5, 145.0, 145.5, 150.7, 153.5; ms: *m/z* 386 (M^+, 1 %), 359 (2), 358 (18), 261 (1), 193 (1), 167 (1), 166 (12), 165 (100), 149 (3), 139 (4), 135 (1), 119 (40), 107 (26). HRMS: calcd for $C_{14}H_6N_6O_8$, 386.0247; observed 386.0248.

Anal. Calcd. for $C_{14}H_6N_6O_8$: C, 43.55; H, 1.57; N, 21.76. Found: C, 43.60; H, 1.55; N, 21.86.

N,*N*'-di(5-nitro-2-pyridyl)ethanediamide (**24**).

Compound **24** obtained as described above has mp 205 ºC (decomp. acetone/diethyl ether); ir (KBr) 3280m, 1850m, 1775s, 1685m, 1650m, 1610m, 1580m, 1530m, 1470m, 1400m, 1350s, 1295m, 1170m, 1120m, 1020m, 875m, 850m, 765m, 745m, 725m cm^{-1}; ^1H nmr (400 MHz, DMSO-d_6): δ 8.25 (d, J 8.9, 2H, H-3), 8.74 (dd, J 8.9, 2.8, 2H, H-4), 9.28 (d, J 2.8, 2H, H-6), 11.39 (br, 2H, NH); ^{13}C nmr (75 MHz, DMSO-d_6): δ 113.6, 134.6, 140.8, 144.8, 154.7, 161.6; ms: *m/z* 212 (M^+, 1 %), 211 (12), 197 (2), 167 (9), 166 (92), 165 (8), 150 (2), 140 (5), 139 (100), 136 (3), 135 (3), 123 (8), 120 (66), 109 (13).

Pyridine-4-carbonyl azide (**27**).

This compound was prepared from isopicolinic acid (**26**) and DPPA and characterised (mp and ir) according to the literature [12]. Off-white crystals, pure by ^1H and ^{13}C nmr, were obtained in 80 % yield; ^1H nmr (300 MHz, $CDCl_3$): δ 7.72 (dd, J 5.0, 1.3, 2H, H-3,5), 8.71 (dd, J 5.0, 1.3, 2H, H-2,6); ^{13}C nmr (75 MHz, $CDCl_3$): δ 121.9, 137.1, 150.6, 171.2; ms: *m/z* 148 (M^+, 48 %), 120 (50), 106 (100), 92 (8), 78 (39).

1,3,5-Tri-4-pyridinyl-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione; trimer isocyanurate (**28**) [9,10].

This compound was prepared from pyridine-4-carbonyl azide (**27**) as described for the preparation of isocyanates **9** and **18** above. The product was obtained as orange crystals pure by ^1H and ^{13}C nmr; ^1H nmr (300 MHz, DMSO-d_6): δ 7.42 (d, J 6.1, 2H, H-3',5'), 8.36 (d, J 6.1, 2H, H-2',6'); corresponding data in $CDCl_3$: δ 7.02 (dd, J 4.6, 1.5, 2H, H-3',5'), 8.56 (dd, J 4.6, 1.5, 2H, H-2',6'); in d_4-methanol: δ 7.58 (br, d, J 4.2, 2H, H-3',5'), 8.38 (br, 2H, H-2',6'); ^{13}C nmr (75 MHz, DMSO-d_6): δ 113.2, 146.8, 151.1, 154.5; ms: *m/z* 360 (M^+ trimer, 1 %), 120 (M^+ monomer, 100 %), 96 (72), 95 (25), 92 (12).

Methyl 4-pyridylcarbamate (**29**) [13].

The trimer (**28**) was dissolved in methanol by heating. ^1H nmr showed an immediate and complete conversion of the trimer into the methyl carbamate. Flash chromatography afforded quantitative yields of **29**, pure by ^1H and ^{13}C nmr; mp 169-170 °C; ir (KBr) 3246w, 3166w, 3074w, 3028w, 2944w, 1727s, 1622m, 1597s, 1538m, 1405w, 1420m, 1331s, 1307m, 1248m, 1228m, 1210m, 1190m, 1073m, 1000m, 821m, 762m cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 8.48 (d, J 6.4, 2H, H-2,6), 7.35 (d, J 6.4, 2H, H-3,5), 7.04 (br, 1H, NH), 3.83 (s, 3H, OCH_3); ^{13}C nmr (100 MHz, $CDCl_3$): δ 54.1, 113.8, 146.5, 152.0, 154.6; ms: *m/z* 152 (M^+, 100 %), 120 (11), 107 (39), 78 (11). HRMS: calcd for $C_7H_8N_2O_2$, 152.05858; observed 152.05817.

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