ARTICLE

OBC
www.rsc.org/obc

Preparation of nitropyridines by nitration of pyridines with nitric acid†

Alan R. Katritzky,*[a] Eric F. V. Scriven,[a] Suman Majumder,[a] Rena G. Akhmedova,[a] Anatoliy V. Vakulenko,[a] Novruz G. Akhmedov,[a] Ramiah Murugan[b] and Khalil A. Abboud[c]

[a] *Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, FL, USA 32611-7200. E-mail: katritzky@chem.ufl.edu; Fax: 3523929199*

[b] *Reilly Industries Inc, 1500 South Tibbs Avenue, P.O. Box 42912, Indianapolis, Indiana, USA 46242-0912. E-mail: rmurugan@reillyind.com*

[c] *X-ray facility, Department of Chemistry, University of Florida, Gainesville, FL, USA 32611-7200. E-mail: abboud@chem.ufl.edu*

Received 31st August 2004, Accepted 22nd October 2004
First published as an Advance Article on the web 10th January 2005

Nitration of pyridines **1a–o** with nitric acid in trifluoroacetic anhydride, gave the corresponding 3-nitropyridines **6a–n** in yields of 10–83%.

Introduction

Nitration of pyridine and its simple C-alkyl derivatives at a ring carbon atom with nitric acid, nitric acid–sulfuric acid mixtures, or other common nitrating systems, generally results in a very low yield of nitropyridine and is of little synthetic value.[1] Thus, many simple nitropyridines, which are synthetic precursors of potential pharmaceutical and agrochemical importance,[2–7] are not available by conventional direct nitration of the parent pyridine. The lack of reactivity of pyridines in electrophilic substitution has been shown to derive from their protonation. Picolines, lutidines and collidines,[8] essentially exist as completely conjugate acids in the highly acidic conditions usually used for nitration. On the other hand, 2,6-dichloropyridine,[9] which has two inductively electron-withdrawing chlorine atoms, undergoes nitration as the free base to give a reasonable yield of 3-nitro-2,6-dichloropyridine.[10] The relative rates of nitration of pyridine and other heterocycles have been compared with benzenoid compounds.[11] It can be estimated that pyridine itself undergoes nitration at least 10^{22} times slower than benzene.[12] However, pyridine-1-oxide and its simple 2- and/or 3-alkyl derivatives,[13] undergo easy nitration at C-4,[10] and other substituted pyridine-1-oxides[14] can undergo nitration at positions C-2, C-3, or C-4 depending on the nature of the substituents and the reacting species. Other activated pyridines, for instance pyridones,[15–17] and pyridinamines,[18,19] can be nitrated easily.

Bakke and coworkers were the first to report a remarkable reaction of pyridines with dinitrogen pentoxide in sulfur dioxide solution, to give *N*-nitropyridinium ion intermediates which, on treatment with water, gave 3-nitropyridines in good yield.[2,20] They proposed that this reaction proceeds by a [1,5] sigmatropic shift of the nitro group from the 1- to the 3- position in the pyridine ring rather than an electrophilic aromatic substitution. A mixture of 3-nitropyridine and 3,5-dinitropyridine was obtained in low yield by Suzuki and coworkers from the reaction of pyridine with dinitrogen pentoxide generated *in situ* from nitrogen dioxide and ozone.[21,22] A similar attempt was made recently to generate dinitrogen pentoxide, the anhydride of nitric acid, from nitric acid itself using phosphorus pentoxide,[23] for the *in situ* reaction with pyridine. Some 3-nitropyridine was obtained, but in low yield. We were interested in the production of nitropyridines using nitric acid, which is readily available, cheap and overcomes the problem of handling the unstable and difficult-to-obtain reagent, dinitrogen pentoxide. We sought to generate dinitrogen pentoxide easily *in situ*, under conditions in which it would react with pyridines immediately. An equilibrium concentration of dinitrogen pentoxide has been proposed to exist in the nitric acid–acetic anhydride system,[24,25] and for benzoyl nitrate.[25–27] These observations led us to select the nitric acid–TFAA system.

Results and discussion

We wish to report the first direct nitrations of pyridine **1a**, simple mono-(**1a–j, l**) and di-(**1m–o**) substituted pyridines and compound **1k** by treatment with nitric acid in trifluoroacetic anhydride and subsequent addition of sodium metabisulfite. Products were isolated by extraction with dichloromethane and purified by column chromatography. They were characterized by ^{1}H and ^{13}C NMR spectroscopy and by elemental analysis.†

We initially developed a procedure for the direct nitration of pyridine itself. We optimized the relative amounts of the reactants required for the nitration of pyridine (pyridine : concentrated nitric acid : TFAA 1 : 2.5 : 6.0) and the conditions (reaction time after addition of nitric acid 12 h at 0–24 °C and then after the addition to sodium metabisulfite solution 12 h at 24 °C). This standard protocol was then used for the nitration of all the pyridine derivatives described in Table 1. In the case of pyridine nitration, divergence from the standard protocol described above in some cases led to greatly diminished yields of 3-nitropyridine.

Yields of β-nitropyridines obtained using the standard protocol (Method A) were generally higher than those obtained using N_2O_5,[2] and in three cases much higher, for products **6b**, **6c** and **6j** (Table 1). For example, 3-chloropyridine gave 3-chloro-5-nitropyridine in 76% yield using Method A but only a 15% yield was obtained using N_2O_5.[2] One exception was 3-acetylpyridine which was obtained in somewhat lower yield (20%) compared with the yield from N_2O_5 nitration (33%).[2] We obtained no β-nitro product from 2-fluoropyridine by Method A. However, treatment with a mixture of potassium nitrate, TFA and TFAA afforded 2-fluoro-5-nitropyridine (**6i**) in 10% yield. In contrast to the picolines, 2,4- and 3,4-lutidines both gave lower yields of β-nitro products (Table 2) using Method A compared to N_2O_5 nitration.[2] Treatment of 2,5-lutidine by Method A gave a surprising result, 5-methyl-2-trinitromethylpyridine (**6o′**) was obtained

† Electronic supplementary information (ESI) available: experimental procedures and NMR spectra. See http://www.rsc.org/suppdata/ob/b4/b413285h/

DOI: 10.1039/b413285h

Table 1 Products obtained by nitration of mono-substituted pyridines **1a**–**1l**

				Literature			
Product	R	Mp/°C	Yield (%)[a]	Yield (%)	Mp/°C	Method	Reference
6a	H	40.5	83	18	38–40	[b]	29
				68	35–36.5	[c]	30
				77	[d]	[c]	2
6b	2-CH_3	106.5	68	17	106–108	[b]	29
				19	103–106	[c]	30
					106–108	[c]	31
				42	[d]	[c]	2
6c	3-CH_3	102.3	62	Trace	95–96	[b]	29
				37	[d]	[c]	2
6d	4-CH_3	Oil	86	24	Oil	[c]	30
				70	[d]	[c]	2
6e	3-C_2H_5	Oil	64	41	Oil	[b]	29
6f	4-C_2H_5	Oil	25	—	[d]		Novel
6g	3-($COCH_3$)	82.5	20	33	[d]	[c]	32
				19	[d]	[c]	2
6h	4-($COCH_3$)	Oil	83	50	35–36.5	[c]	30
				75	[d]	[c]	2
6i	2-F	Oil	10[e]	[d]	[d]	[b]	33
				[d]	[d]	[b]	34
6j	3-Cl	72.5	76	15	[d]	[c]	32
				15	[d]	[c]	2
6k	3,4-Benzo	58.0	37	29	54–55	[c]	31
				42	[d]	[c]	33
6l	4-$N(CH_3)_2$–pyridine	49.5	32	81	49–50	[b]	18

[a] Method A. [b] Previously prepared indirectly. [c] Previously reported as prepared by Bakke. [d] Data not available. [e] Method B.

Table 2 Products obtained by nitration of di-substituted pyridines **1m**–**1o**

				Literature			
Product	R	Mp/°C	Yield (%)	Yield (%)	Mp/°C	Method	Reference
6m	2,4-Di-CH_3	Oil	52[a]	66	[b]	[c]	32
				66	[b]	[c]	2
6n	3,4-Di-CH_3	45.7	30[a]	58	[b]	[c]	32
				58	[b]	[c]	2
6o	2,5-Di-CH_3		0[a]	<3	[b]	[c]	32
				<3	[b]	[c]	2
6o′		66.5	10[a,d]				Novel

[a] Method A. [b] Data not available. [c] Previously reported as prepared by Bakke. [d] Substitution of three protons at the 2-methyl group by nitro groups.

in 10% yield. The structure of 5-methyl-2-trinitromethylpyridine (**6o′**) was confirmed by X-ray analysis (Fig. 1).‡

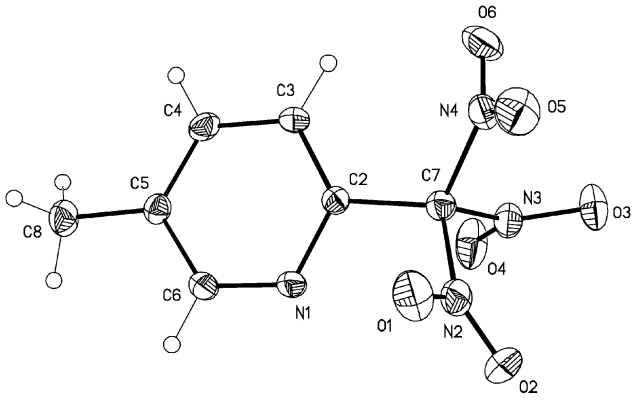
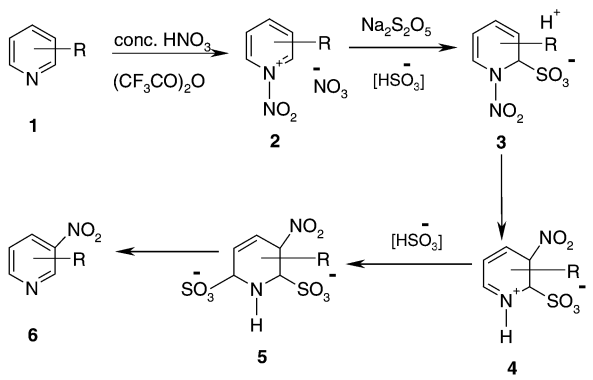


Fig. 1 Perspective view of the X-ray structure of **6o′**.

This product was not obtained by Bakke using the N_2O_5 method,[2] although he obtained 2,5-dimethyl-3-nitropyridine (**6o**) in low yield (<3%).

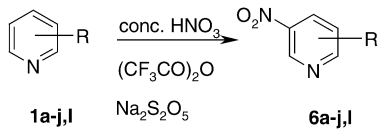
‡ CCDC reference number 249216. See http://www.rsc.org/suppdata/ob/b4/b413285h/ for crystallographic data in .cif format.

The yields of β-nitro products from the nitration of pyridine, the picolines and lutidines using our method are comparable in most cases with those of Bakke who used isolated dinitrogen pentoxide. Therefore, the mechanism of nitration in our case probably follows the pathway for which Bakke has adduced evidence,[28] (Schemes 1–5).

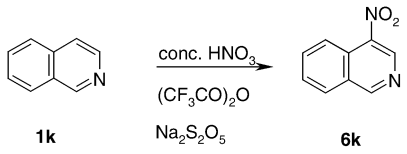


Scheme 1

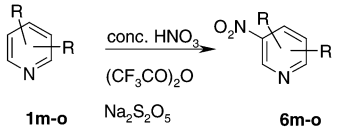
Nitration of isoquinoline (**1k**) by Method A gave a yield of 3-nitroisoquinoline (37%) comparable to that observed by Bakke



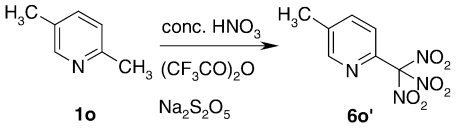
Scheme 2



Scheme 3



Scheme 4



Scheme 5

when he used N_2O_5 as the nitrating agent in SO_2–CH_3NO_2 (42%).[2]

Conclusion

A new general high yield reaction for the preparation of nitropyridines is reported that employs cheap and readily available nitric acid. In fourteen cases of alkyl, halo and acetylpyridines, preparatively useful yields of the corresponding β-nitro compound are obtained. Three nitro groups have been introduced into the α-methyl substituent of 2,5-lutidine under our nitration conditions.

Experimental

Melting points are uncorrected. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ (with TMS for ^{1}H and chloroform-*d* for ^{13}C as the internal reference) unless specified otherwise. X-ray data were collected at 173 K on a Siemens SMART PLATFORM equipped with a CCD area detector and a graphite monochromator utilizing Mo Kα radiation ($\lambda = 0.71073$ Å). Cell parameters were refined using up to 8192 reflections. A full sphere of data (1850 frames) was collected using the ω-scan method (0.3° frame width). The first 50 frames were re-measured at the end of data collection to monitor instrument and crystal stability (maximum correction on I was < 1%). Absorption corrections by integration were applied based on measured indexed crystal faces. The X-ray structure was solved by the Direct Methods in SHELXTL6,[35] and refined using full-matrix least squares. The non-H atoms were treated anisotropically, whereas the hydrogen atoms were calculated in ideal positions and were riding on their respective carbon atoms. A total of 155 parameters were refined in the final cycle of refinement using 1656 reflections with $I > 2\sigma(I)$ to yield R_1 and wR_2 of 3.58% and 10.20%, respectively. Refinement was done using F^2.†

Crystal data for 6o′

$C_7H_6N_4O_6$, $M = 242.16$, monoclinic, $a = 8.0407(8)$ Å, $b = 11.7673(11)$ Å, $c = 11.2852(10)$ Å, $V = 1012.74(16)$ Å^3, $T = 173(2)$ K, $P21/c$, $Z = 4$, μ(Mo Kα) = 0.141 mm^{-1}, 6137 reflections measured, 2287 ($R_{int} = 0.0374$). The final $wR(F^2)$ was 0.1020 (1656).

General method of preparation of nitropyridines

Method A. Trifluoroacetic anhydride [10 ml, 42 mmol] was chilled in an ice bath and the pyridine or substituted pyridines [17 mmol] were slowly added and stirred at chilled conditions for 2 h followed by the dropwise addition of concentrated nitric acid [1.9 ml, 36 mmol]. After stirring for 9–10 h, the solution was dripped slowly into a chilled aqueous solution of sodium metabisulfite [3.2 g, 17 mmol in 25 ml of water]. After 24 h, the solution was brought to pH 6–7 from pH 2–3 by addition of 25% NaOH solution, extracted with methylene chloride and the extract was dried over anhydrous sodium sulfate; the solvent was evaporated to give the nitropyridines which were further purified by column chromatography using hexane : ethyl acetate (1 : 1).

Method B. Potassium nitrate (20 mmol) was taken in a flask, evacuated of air and purged with nitrogen gas. TFA (20 mmol) was then added to potassium nitrate. After stirring for 10 min, TFAA (10 mmol) was added to the mixture, which was stirred for a further 15 min. Pyridine (10 mmol) was added very slowly dropwise with a syringe. After stirring for 6 h, sodium metabisufite solution [2.0 g in 15 ml of water] was added slowly under cooling to the mixture, which was stirred for 12 h. The pH was then brought to 6–7 with conc. NaOH under cooling and extracted with chloroform. The chloroform layer was dried with anhydrous magnesium sulfate and the solvent removed to give the nitropyridines which were further purified by column chromatography using hexane : ethyl acetate (1 : 1).

3-Nitropyridine (6a). Yellow prisms (83%);^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 7.60 (dd, $J = 8.4$, 4.8 Hz, 1H), 8.53 (ddd, $J = 8.4$, 2.6, 1.5 Hz, 1H), 8.96 (dd, $J = 4.8$, 1.5 Hz, 1H), 9.46 (d, $J = 2.6$ Hz, 1H); ^{13}C NMR: δ_C 123.7, 130.9, 144.1, 144.9, 154.7.

Anal. (Found: C, 48.44; H, 3.10; N, 22.14. Calcd. for $C_5H_4N_2O_2$: C, 48.39; H, 3.25; N, 22.57%).

2-Methyl-5-nitropyridine (6b). White prisms (68%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.71 (s, 3H), 7.36 (d, $J =$ 8.5 Hz, 1H), 8.37 (dd, $J = 8.5$, 2.6 Hz, 1H), 9.33 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR: δ_C 24.8, 123.3, 131.2, 142.4, 144.6, 165.4. Anal. (Found: C, 52.38; H, 4.28; N, 20.05. Calcd. for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28%).

3-Methyl-5-nitropyridine (6c). Yellow prisms (62%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.51 (s, 3H), 8.30 (br s, 1H), 8.75 (br s, 1H), 9.27 (d, $J = 2.3$ Hz, 1H); ^{13}C NMR: δ_C 18.1, 131.0, 134.4, 142.2, 144.0, 155.4. Anal. (Found: C, 52.24; H, 4.26; N, 20.03. Calcd. for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28%)

4-Methyl-3-nitropyridine (6d). Yellow oil (86%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.67 (s, 3H), 7.36 (d, $J = 4.9$ Hz, 1H), 8.67 (d, $J = 5.0$ Hz, 1H), 9.15 (s, 1H); ^{13}C NMR: δ_C 19.9, 127.0, 142.9, 145.8, 147.0, 152.9. Anal. (Found: C, 51.80; H, 4.28; N, 19.98. Calcd. for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28%).

3-Ethyl-5-nitropyridine (6e). Yellow oil (64%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.37 (t, $J = 7.6$ Hz, 3H), 2.87 (q, $J =$ 7.6 Hz, 2H), 8.34 (br s, 1H), 8.79 (br s, 1H), 9.25 (d, $J = 2.3$ Hz, 1H); ^{13}C NMR: δ_C 14.5, 25.4, 129.6, 140.2, 142.1, 144.0, 154.5. Anal. (Found: C, 55.24; H, 5.20; N, 18.72. Calcd. for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41%).

4-Ethyl-5-nitropyridine 6f. Yellow oil (25%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.34 (t, $J = 7.6$ Hz, 3H), 2.99 (q, $J =$ 7.6 Hz, 2H), 7.40 (d, $J = 5.1$ Hz, 1H), 8.71 (d, $J = 5.1$ Hz, 1H), 9.09 (s, 1H); ^{13}C NMR: δ_C 13.4, 25.2, 124.9, 145.4, 145.5, 147.6, 152.9. Anal. (Found: C, 55.37; H, 5.18; N, 18.20. Calcd. for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41%).

3-Acetyl-5-nitropyridine (6g). White prisms (20%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.76 (s, 3H), 8.97 (t, J = 2.4 Hz, 1H), 9.44 (d, J = 2.4 Hz, 1H), 9.60 (d, J = 2.4 Hz, 1H); ^{13}C NMR: δ_C 27.0, 130.3, 132.4, 144.3, 148.1, 154.2, 194.3. Anal. (Found: C, 50.67; H, 3.53; N, 16.84. Calc for $C_7H_6N_2O_3$: C, 50.61; H, 3.64; N, 16.87%).

4-Acetyl-5-nitropyridine (6h). Yellow oil (83%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.60 (s, 3H), 7.36 (dd, J = 4.9, 0.7 Hz, 1H), 8.97 (dd, J = 4.9, 0.7 Hz, 1H), 9.37 (s, 1H); ^{13}C NMR: δ_C 29.9, 120.6, 144.7, 145.7, 150.9, 155.1, 197.8. Anal. (Found: C, 50.67; H, 3.52; N, 16.74. Calcd. for $C_7H_6N_2O_3$: C, 50.61; H, 3.64; N, 16.87%).

2-Fluoro-5-nitropyridine (6i). Yellow oil (10%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 7.14 (ddd, J = 8.9, 3.2, 0.6 Hz, 1H), 8.62 (ddd, J = 8.9, 6.4, 2.9 Hz, 1H), 9.15 (ddd, J = 2.9, 1.1, 0.6 Hz, 1H); ^{13}C NMR: δ_C 110.5 (J_{CF} = 16.6 Hz), 136.8 (J_{CF} = 10.6 Hz), 142.6, 144.8 (J_{CF} = 17.4 Hz), 165.7 (J_{CF} = 249.7 Hz).

3-Chloro-5-nitropyridine (6j). White prisms (76%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 8.50 (t, J = 1.7 Hz, 1H), 8.89 (d, J = 1.7 Hz, 1H), 9.34 (d, J = 1.7 Hz, 1H); ^{13}C NMR: δ_C 130.8, 132.5, 142.7, 144.2, 154.0. Anal. (Found: C, 38.33; H, 1.87; N, 17.39. Calcd. for $C_5H_3ClN_2O_2$: C, 37.89; H, 1.91; N, 17.68%).

4-Nitroisoquinoline (6k). Orange needles (37%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 7.79 (ddd, J = 8.1, 7.8, 1.0 Hz, 1H), 7.96 (ddd, J = 8.1, 8.1, 1.4 Hz, 1H), 8.13 (dddd, J = 8.1, 1.4, 0.7, 0.5 Hz, 1H), 8.62 (ddd, J = 8.7, 1.0, 0.7 Hz, 1H), 9.26 (s, 1H), 9.43 (d, J = 0.8 Hz, 1H); ^{13}C NMR: δ_C 122.5, 127.8, 128.4, 128.9, 129.0, 134.0, 141.1, 158.0. Anal. (Found: C, 62.03; H, 3.41; N, 15.96. Calcd. for $C_9H_6N_2O_2$: C, 62.05; H, 3.47; N, 16.08%).

3-Nitro-4-(*N*,*N*-dimethylamino)pyridine (6l). Yellow microcrystals (32%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 3.00 (s, 6H), 6.79 (d, J = 6.2 Hz, 1H), 8.27 (d, J = 6.2 Hz, 1H), 8.77 (s, 1H). ^{13}C NMR: δ_C 41.5, 110.6, 148.0, 149.1, 151.3, 153.0. Anal. (Found: C, 50.25; H, 5.40; N, 24.95. Calcd. for $C_7H_9N_3O_2$: C, 50.28; H, 5.43; N, 25.14%).

2,4-Dimethyl-5-nitropyridine (6m). Yellow oil (52%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.61 (s, 3H), 2.63 (s, 3H), 7.26 (br s, 1H), 9.10 (s, 1H); ^{13}C NMR: δ_C 20.2, 24.3, 126.6, 143.2, 143.8, 145.7, 163.3. Anal. (Found: C, 55.46; H, 5.35; N, 18.24. Calcd. for $C_7H_8N_2O_2$: C, 55.24; H, 5.30; N, 18.41%).

3,4-Dimethyl-5-nitropyridine (6n). Yellow prisms (30%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.39 (s, 3H), 2.47 (s, 3H), 8.54 (s, 1H), 8.87 (s, 1H); ^{13}C NMR: δ_C 15.0, 17.0, 134.2, 140.2, 143.1, 153.1, 166.7. Anal. (Found C, 55.54; H, 5.34; N, 18.29. Calcd. for $C_7H_8N_2O_2$: C, 55.24; H, 5.30; N, 18.41%).

5-Methyl-2-(trinitromethyl)pyridine (6o′). White prisms (10%); ^{1}H NMR: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.50 (s, 3H), 7.78 (dd, J = 8.2, 1.4 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 8.59 (br s, 1H); ^{13}C NMR: δ_C 18.6, 124.5, 127.8, 138.0, 139.1, 139.8, 150.8. The structure of **6o′** was determined by X-ray analysis.‡

References

1 F. Friedl, *Chem. Ber.*, 1912, **45**, 428.
2 J. M. Bakke, *Pure Appl. Chem.*, 2003, **75**, 1403.
3 J. M. Bakke, H. S. H. Gautun, C. Rømming and I. Sletvold, *ARKIVOC*, 2001, **x**, 26.
4 J. Chen, G. Ling and S. Lu, *Tetrahedron*, 2003, **59**, 8251.
5 D. L. Romero, R. A. Morge, C. Biles, N. Berrios-Peña, P. D. May, J. R. Palmer, P. D. Johnson, H. W. Smith, M. Busso, C.-K. Tan, R. L. Voorman, F. Reusser, I. W. Althaus, K. M. Downey, A. G. So, L. Resnick, W. G. Tarpley and P. A. Aristoff, *J. Med. Chem.*, 1994, **37**, 999.
6 R. W. Millar, R. P. Claridge, J. P. B. Sandall and C. Thompson, *ARKIVOC*, 2002, **iii**, 19.
7 S. Youssif, *ARKIVOC*, 2001, **i**, 242.
8 A. R. Katritzky and B. J. Ridgewell, *J. Chem. Soc.*, 1963, 3882.
9 C. D. Johnson, A. R. Katritzky, B. J. Ridgewell and M. Viney, *J. Chem. Soc. B*, 1967, 1204.
10 C. D. Johnson, A. R. Katritzky, N. Shakir and M. Viney, *J. Chem. Soc. B*, 1967, 1213.
11 A. R. Katritzky, B. Terem and E. V. Scriven, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1600.
12 A. R. Katritzky and W.-Q. Fan, *Heterocycles*, 1992, **34**, 2179.
13 A. R. Katritzky and C. D. Johnson, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 608.
14 A. R. Katritzky and M. Kingsland, *J. Chem. Soc. B*, 1968, 862.
15 P. J. Brignell, A. R. Katritzky and H. O. Tarhan, *J. Chem. Soc. B*, 1968, 1477.
16 A. R. Katritzky, H. O. Tarhan and S. Tarhan, *J. Chem. Soc. B*, 1970, 114.
17 A. G. Burton, P. J. Halls and A. R. Katritzky, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1953.
18 A. G. Burton, R. D. Frampton, C. D. Johnson and A. R. Katritzky, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1940.
19 G. Bianchi, A. G. Burton, C. D. Johnson and A. R. Katritzky, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1950.
20 J. M. Bakke, I. Hegbom, E. Øvereeide and K. Aaby, *Acta Chem. Scand.*, 1994, **48**, 1001.
21 T. Mori and H. Suzuki, *Synlett*, 1995, 383.
22 H. Suzuki, M. Iwaya and T. Mori, *Tetrahedron Lett.*, 1997, **38**, 5647.
23 R. Murugan, E. F. V. Scriven, G. F. Hillstrom and P. K. Ghoshal, Int. Patent WO 2002090328, 2002; R. Murugan, E. F. V. Scriven, G. F. Hillstrom and P. K. Ghoshal, *Chem. Abstr.*, 2002, **137**, 352895.
24 Y. Ito, Y. Hamada and M. Hirota, *Chem. Pharm. Bull.*, 1972, **20**, 2678.
25 M. E. Kurz, L. T. A. Yang, E. P. Zahora and R. C. Adams, *J. Org. Chem.*, 1973, **38**, 2271.
26 V. Gold, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 1950, 2467.
27 F. Francis, *Chem. Ber.*, 1906, **39**, 3798.
28 J. M. Bakke and J. Riha, *Acta. Chem. Scand.*, 1999, **53**, 356.
29 Y. Tohda, M. Eiraku, T. Nakagawa, Y. Usami, M. Ariga, T. Kawashima, K. Tani, H. Watanabe and Y. Mori, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 2820.
30 J. M. Bakke and E. Ranes, *Synthesis*, 1997, 281.
31 M.-C. Liu, T.-S. Lin and A. C. Sartorelli, *Synth. Commun.*, 1990, **20**, 2965.
32 J. M. Bakke, E. Ranes, J. Riha and H. Svensen, *Acta Chem. Scand.*, 1999, **53**, 141.
33 Y. Uchibori, M. Umeno and H. Yoshioka, *Heterocycles*, 1992, **34**, 1507.
34 J. H. Clark and D. J. Macquarrie, *Tetrahedron Lett.*, 1987, **28**, 111.
35 SHELXTL6, Bruker-AXS, Madison, Wisconsin, USA, 2000.