Direct nitration of five membered heterocycles

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Dedicated to Dr. A.V. Rama Rao on the occasion of his 70th birthday

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Abstract

Direct nitration of a variety of furans, pyrroles, thiophenes, pyrazoles, imidazoles, isoxazoles and thiazoles (17 compounds) with nitric acid/trifluoroacetic anhydride affords mononitro derivatives in average yield of 60 %.

Keywords: Nitration, nitric acid, trifluoroacetic anhydride, nitrofurans, nitropyrroles, nitrothiophenes, nitropyrazoles, nitroimidazoles, nitroisoxazoles, nitrothiazoles

Introduction

Nitro derivatives of five-membered heterocycles are of considerable interest: some are biologically active[1] with anti-inflammatory or vasodilator activity[2] others are useful synthetic intermediates for many biologically active compounds; for instance, nitroimidazoles form the basis of nitro-heterocycles analogous to megazol, an antiparasitic agent[3].

Nitration of five membered ring heterocycles like furans[4], pyrroles[5], thiophenes[6], pyrazoles[7], imidazoles[8], isoxazoles[9] and thiazoles[10] has usually been carried out using either a mixture of concentrated (or fuming) nitric acid and concentrated sulfuric acid, or in some cases with concentrated nitric acid and acetic anhydride (followed by pyridine in case of furans only). The nitration of some of these heterocycles, for example pyrazoles and imidazoles[11], isoxazoles[12, 13] and isothiazoles[12] has been studied kinetically. Previous efforts to find milder nitration conditions for direct nitration have included use of cerium (IV) ammonium nitrate[14], montmorillonite impregnated with bismuth nitrate[15] and nitrations with dinitrogen pentoxide[16, 17].

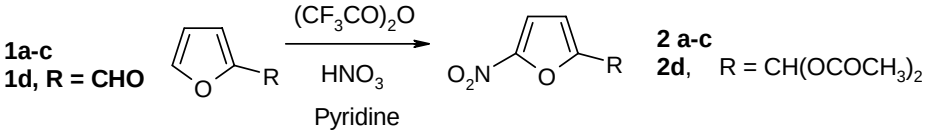
In light of our success in the direct nitration of pyridines and pyridine analogs with concentrated nitric acid in trifluoroacetic anhydride, which we believe involves N_2O_5[18] led us to apply this method to nitration of five-membered heterocycles and we discuss our results here.

While the present work was in progress, Shackelford and coworkers reported[19] the use of tetramethylammonium nitrate in triflic anhydride and included results of nitration of aromatics like furans, thiophenes and isoxazoles. Our work complements and significantly extends that of Shackelford group.

Results and Discussion

Furans

Typically furans have been nitrated using acetyl nitrate to give addition products, which are subsequently converted on treatment with pyridine into 2-nitrofurans[20, 21, 22, 23]. We have now achieved the direct nitration of furan itself and a series of its derivatives with nitric acid in trifluoroacetic anhydride (method A as described in the experimental section) (Scheme 1) (Table 1). Compounds **2a-d** were characterized spectroscopically (see Experimental).



Scheme 1

Table 1. Nitration of furans

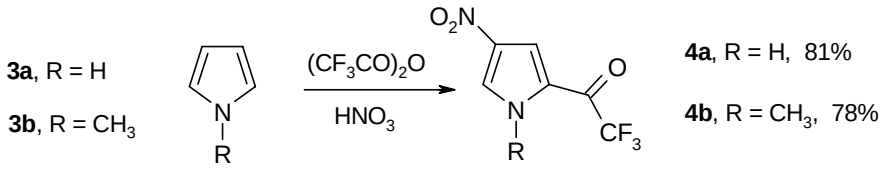
Product	R	Yield %, by method A	Literature methods		
			Overall Yield[b] %	Method[e] / Reagents	Ref.
2a	H	68%	14%	[e] $[NO_2][BF_4]$	21
			[c]	[e] Ac_2O; HNO_3	22
			[c]	[e] Ac_2O; HNO_3	23
			[c]		24
			[c]	[e] $[NO_2][BF_4]$	25
2b	CH_3	65%	[c]	[e] RaI_2; Ac_2O; HNO_3	26
			34%[d]	[f]	27
2c	$C(CH_3)_3$	75%			novel
2d	$CH(OCOCH_3)_2$	58%[a]	40%	[e] Ac_2O; HNO_3	28
			[c]	[e] Ac_2O; HNO_3	29
			[c]	[e] Ac_2O; HNO_3	30
			15%	[e] Ac_2O; HNO_3	31
			43%	[e] Ac_2O; HNO_3	32

Method A is described in the Experimental section; [a]using method A but replacing TFAA by Ac_2O; [b]overall yield is the final yield after multistep conversion to nitrofurans starting with furan; [c]cross reference of the compound without reported yield; [d]overall yield is 34% following the reaction sequence 2-furfuraldehyde –[80%]—2-furfuryl alcohol – [76%]—2-iodomethyl-5-nitrofuran – [56%]—2-methyl-5-nitrofuran; [e]general method of synthesis of nitrofurans from furans in two steps using acetyl nitrate via an addition product which is subsequently converted by pyridine into 2-nitrofurans; [f]indirect method starting from 2-iodomethyl-5-nitrofuran using thiophenolate anion as the reagent.

Inspection of Table 1 clearly shows the advantage of our new method. In most published nitration procedures for furan, nitroacetate intermediates had to be isolated. Our one step nitration procedure produces much higher yields without isolation of any intermediate.

Pyrroles

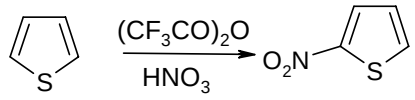
Again acetyl nitrate has been used for the nitration of pyrrole[33], to give mainly the 2-nitro derivatives (55%). Our nitration method B, gave novel compounds **4a-b** from **3a-b** respectively (Scheme 2), structures were confirmed spectroscopically (see Experimental).



Scheme 2

Thiophenes

Thiophenes are easy to nitrate compared to other five membered heterocycles. They react with mild nitrating agents such as copper nitrate[34], usually in the 2-position. Thiophene (**5**), on nitration with our reagent gave a 78% yield of 2-nitroderivative (**6**) by method B (Scheme 3) (Table 2). Shackelford reported the nitration of methyl 2-thiophenecarboxylate to give a mixture of 2- and 4- nitro derivatives (1.6:1) in 91% yield[19].



5 **6**, 78%

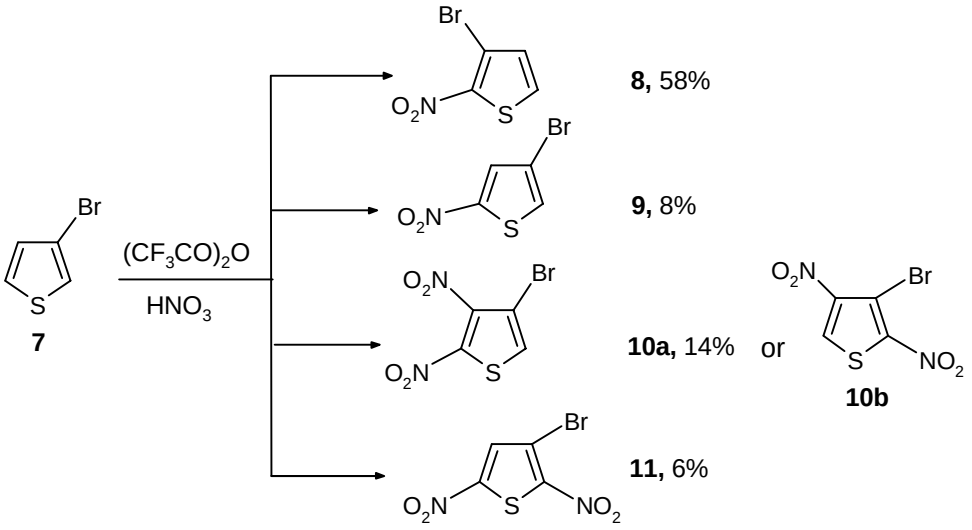
Scheme 3

Table 2. Nitration of thiophenes

Product	Yield %, by method B	Literature methods		
		Overall Yield %	Method / Reagents	Ref.
6 2-nitro	78%	72%[a]	$Cu(NO_3)_2/Ac_2O$	34
		70%[a]	K10 clay; HNO_3	35
		23%[b]	NH_4NO_3/Tf_2O	36
8 3-bromo-2-nitro	58%	56%[c]	HNO_3	37

Method: B as described in the Experimental section; [a]yield from thiophene; [b]yield from thiophene 2-boronic acid; [c]yield from 3-bromothiophene.

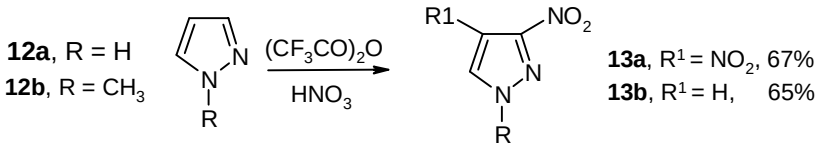
We found that the nitration of 3-bromo-thiophene (**7**) gave a complicated mixture with the main product (**8**) (58%). The other component were found to be **9**, **10a-b**, and **11**. The structure of **10a** was not unambigiously diffretiated from the structure **10b** (Scheme 4).



Scheme 4

Pyrazoles

Acetyl nitrate has been employed to nitrate pyrazoles at one of the nitrogen atoms and subsequent rearrangement at 140 ºC has been observed to give 3- or 5-nitropyrazoles, sometimes as a mixture.[40] Pyrazole (**12**) on treatment with our nitrating system following method B gave a 41% yield of the 3,4-dinitrated derivative (**13**) while *N*-methylpyrazole under the same reaction condition gave a 65% yield of the 3-nitro product (**13**). This orientation was confirmed by nOe experiments (Scheme 5) (Table 3).



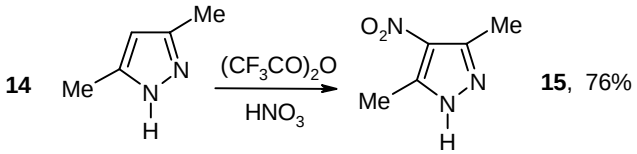
Scheme 5

Table 3. Nitration of pyrazoles

Product	Yield %, by method B	Literature methods		
		Overall Yield[a] %	[f]Method / Reagents	Ref.
13a 3,4-dinitro	41%	68%[b]	[f]conc.HNO_3/conc.H_2SO_4	40
13b 3-nitro-1-methyl	65%	28%[c]	[f]fuming HNO_3 / 80% aq. H_2SO_4;18hrs	41
		3.6%	[f]HNO_3	42
14 3,5-dimethyl-4-nitro	76%	49%[d]	[f]70%HNO_3 in 80% H_2SO_4; 118ºC/5hrs	43
		[e]	[f]HNO_3	44
		27%	[g]	45

Method B as described in the Experimental section; [a]overall yield is the final yield after multistep conversion to nitropyrazole starting with pyrazole as starting material; [b]overall yield is 68% following the reaction sequence as pyrazole –[80%]—3-nitropyrazole – [86%]—3,4-dinitropyrazole; [c]overall yield is 28% following the reaction sequence as pyrazole –[90%]—1-methylpyrazole – [32%]—3,4-dinitropyrazole; [d]overall yield is 53% following the reaction sequence as 3,5-dimethylpyrazole –[94%]—4-bromo-3,5-dimethylpyrazole – [53%]—3,5-dimethyl-4-nitropyrazole; [e]cross reference of the compound without reported yield; [f]direct conversion of pyrazole or its derivatives to nitropyrazole; [g]ring cyclization to pyrazole using dinitromethane as one of the reactants.

3, 5-Dimethylpyrazole (**14**), on the other hand, gives only 3,5-dimethyl-4-nitropyrazole in 76% yield (Scheme 6) (Table 3).

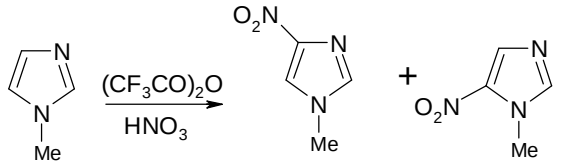


Scheme 6

Imidazoles

Imidazoles unsubstituted at nitrogen are easily nitrated by mixed acid nitration[46,47]. The direct nitration of N-substituted imidazoles is more difficult and most nitro-*N*-methylimidazoles have been prepared by the N-methylation of the corresponding nitroimidazoles.

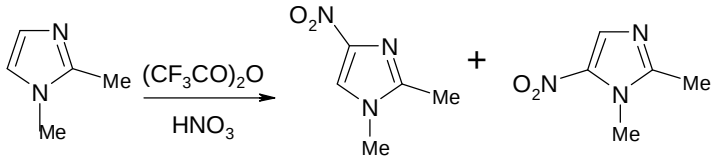
A mixture of 4-nitro- (**17a**) and 5-nitroimidazoles (**17b**) was obtained by the action of concentrated nitric acid on 1-methylimidazole (**16**) in trifluoroacetic anhydride at 0-5°C for 12.0 h according to method B (Scheme 7) (Table 4). Yields quoted for (**17**) and (**19**) are that of pure isomers isolated by column chromatography.



16 **17a**, 61% **17b**, 28%

Scheme 7

Similarly, a mixture of 1,2-dimethyl-4-nitroimidazole (**19a**) and 1,2-dimethyl-5-nitroimidazoles (**19b**) was obtained by the action of concentrated nitric acid on 1,2-dimethylimidazole (**18**) in trifluoroacetic anhydride at 0-5°C for 12.0 h according to method B (Scheme 8).



18 **19a**, 58% **19b**, 35%

Scheme 8

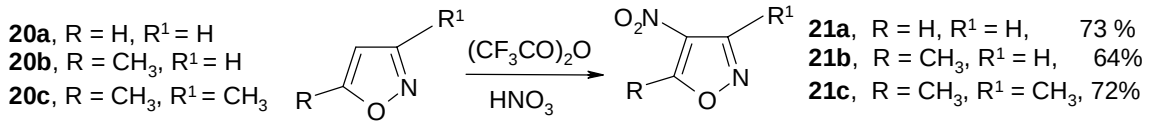
Table 4. Nitration of imidazoles

Product	Yield %, by method B	Literature methods		
		Overall Yield[a] %	[f]Method / Reagent	Ref.
17a 1-methyl-4-nitro	61%	22%[b]	[f]Me_2SO_4/ range of catalyst.	48
		44%[c]	[f]Me_2SO_4	49
17b 1-methyl-5-nitro	28%	34%[d]	[f]Me_2SO_4/ range of catalyst.	48
		57%	[f]Dimethyl carbonate/18-Crown-6 / K_2CO_3	50
		59%	[f]t-BuOK; Reflux in DMF	51
19a 1,2-dimethyl-4-nitro	58%	47%[e]	[f]Dimethyl carbonate/18-Crown-6 / K_2CO_3	50
		25%	[f]Me_2SO_4	52
19b 1,2-dimethyl-4-nitro	35%	80%	[f]Me_2SO_4	53

Method B as described in the Experimental section. [a]overall yield is the final yield after multistep conversion to nitroimidazole starting with imidazole as starting material. [b]overall yield is 22% following the reaction sequence as imidazole –[91%]—4-nitroimidazole – [24%]—1-methyl-4-nitropyrazole. [c]overall yield is 44% following the reaction sequence as imidazole –[91%]—4-nitroimidazole – [48%]—1-methyl-4-nitropyrazole. [d]overall yield is 34% following the reaction sequence as imidazole –[91%]—4-nitroimidazole – [37%]—1-methyl-4-nitropyrazole. [e]overall yield is 47% following the reaction sequence as 2-methylimidazole –[91%]—2-methyl-4-nitroimidazole – [52%]—1,2-dimethyl-4-nitroimidazole. [f]indirect conversion of imidazole to 4-nitro-1-methyl or 4-nitro-1,2-dimethyl imidazole through nitration and subsequent N-methylation of imidazoles.

Isoxazoles

Nitroisoxazoles have been synthesized using various nitrating agents like nitronium fluoroborate[54], ammonium nitrate/TFAA[55] or just nitration with mixed acid[56]. Our nitration method A when applied to nitration of isoxazole (**20a**), 5-methylisoxazole (**20b**) and 3,5-dimethylisoxazole (**20c**); 2-nitroisoxazole (**21a**)**,** 5-methyl-3-nitroisoxazole (**21b**) and 3,5-dimethyl-4-nitroisoxazole (**21c**) were obtained in the yield of 73%, 64%, and 72% respectively. (Scheme 9) (Table 5). Shackelford[19] found that 3,5-dimethylisoxazole was converted to the 4-nitro derivatives in 96% isolated yield using tetramethylammonium nitrate in triflic anhydride.



Scheme 9

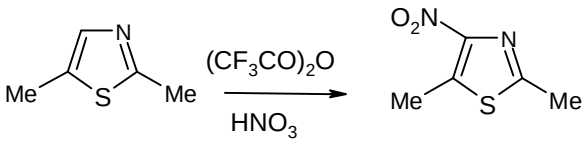
Table 5. Nitration of isoxazoles

Product	Yield %, by method B	Literature methods		
		Overall Yield[a] %	[c]Method / Reagent	Ref.
21a 4-nitro	73%	51%	[c]NH_4NO_3 / TFA	57
		[b]	[c]HNO_3 / H_2SO_4	58
		3.5%	[c]HNO3 / H_2SO_4	56
		35%	[c]NO_2BF_4[z]	54
21b 5-methyl-4-nitro	64%	63%	[c]NH_4NO_3 / TFA	57
		67%	[c]HNO_3 / H_2SO_4	58
		80%	[c]HNO_3 / H_2SO_4	55
		96%	[c]$(CH_3)_4NNO_3/Tf_2O$	19
21c 3,5-dimethyl-4-nitro	72%	86%	[c]HNO3 / H_2SO_4	55
		20%	[d]	59

Method B as described in the Experimental section. [a]overall yield is the final yield of the conversion to nitroisoxazole starting with isoxazole as starting material. [b]cross reference of the compound without reported yield. [c]direct nitration method of isoxazole to nitrooxazole by using different reagents. [d]ring closure method to synthesize nitrooxazole.

Thiazoles

Nitration of thiazoles had not previously been studied extensively.[60] 2,5-Dimethylthiazole (**22**), gave 2,5-dimethyl-4-nitrothiazole (**23**) in 67% yield (Scheme 10), which was characterized spectroscopically (see Experimental). We did not study the nitration of thiazole because it was insoluble in our nitration system.



22 **23**, 67%

Scheme 10

Experimental Section

General Procedures. 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.

General method of preparation of nitro derivatives of five membered heterocycles

Method A. A mixture of trifluoroacetic anhydride (10 mL) and fuming nitric acid (2.4 mL) was chilled at –15ºC and after 1 h a solution of (10 mmol) in trifluoroacetic anhydride (2 mL) was slowly added to the reaction mixture keeping the temperature at -15ºC. The reaction mixture was stirred at -15ºC for 2 h and then the solvents were removed and pyridine (2 mL) was added to the reaction mixture, stirred for 15 min. And then the solvent was again removed and the oily residue was poured in ice and extracted with diethyl ether. The crude product was then purified over a silica gel column to give pure nitro derivatives.

Method B. Trifluoroacetic anhydride [10 mL] was chilled in an ice bath and the substrate heterocycle [17 mmol] was slowly added. After 1 h, concentrated nitric acid [3.0 mL] was added dropwise with cooling. After stirring for 12 h at room temperature, the excess trifluoroacetic acid and nitric acid were removed under vacuum to get the nitro derivatives, which were purified by column chromatography.

Compound characterization

2-Nitrofuran (2a). Yellowish microcrystals (68 %), mp 28.0−29.0 °C (lit.[61] mp 28.8−29.2 °C). ^{1}H NMR: δ 6.68 (dd, *J* = 3.6, 1.8 Hz, 1H), 7.34 (dd, *J* = 3.6, 1.0 Hz, 1H), 7.57 (dd, *J* = 1.8, 1.0 Hz, 1H); ^{13}C NMR: δ 111.43, 113.35, 144.95, 152.71.

2-Methyl-5-nitrofuran (2b). White prisms (65 %), mp 42.5-43.5 ºC (lit.[62] mp 43.5 ºC). ^{1}H NMR: δ 2.46 (dd, *J* = 0.9, 0.5 Hz, 3H), 6.31 (dq, *J* = 3.6, 0.9 Hz, 1H), 7.26 (dq, *J* = 3.6, 0.5 Hz, 1H); ^{13}C NMR: δ 13.98, 110.01, 113.19, 151.26, 156.84.

2-(*tert*-Butyl)-5-nitrofuran (2c). Yellowish prisms (75 %), mp 56.0-57.0 ºC. ^{1}H NMR: δ 1.36 (s, 9H), 6.24 (d, *J* = 3.8 Hz, 1H), 7.23 (d, *J* = 3.8 Hz, 1H); ^{13}C NMR: δ 28.52, 33.45, 106.39, 112.75, 151.19, 168.30. Anal. Calcd for $C_8H_{11}NO_3$ (169.18): C, 56.80; H, 6.55; N, 8.28. Found: C, 56.74; H, 6.75; N, 8.08.

(Acetyloxy)(5-nitro-2-furyl) methyl acetate (2d). White prisms (58 %), mp 88.6-90.0 ºC (lit.[30] mp 91.0-92.0 ºC). ^{1}H NMR: δ 2.18 (s, 6H), 6.74 (d, *J* = 3.7 Hz, 1H), 7.30 (d, *J* = 3.7 Hz, 1H), 7.72 (s, 1H); ^{13}C NMR: δ 20.53, 82.45, 111.45, 112.29, 150.37, 168.05. Anal. Calcd for $C_9H_9NO_7$ (243.17): C, 44.45; H, 3.73; N, 5.76. Found: C, 44.68; H, 3.67; N, 5.68.

2,2,2-Trifluoro-1-(4-nitro-1*H*-pyrrol-2-yl)-1-ethanone (4a). White prisms (81 %), mp 112.0–113.0 ºC. ^{1}H NMR: δ 7.64 (q, *J* = 1.8 Hz, 1H), 8.48 (d, *J* = 1.5 Hz, 1H), 13.86 (br s, 1H); ^{13}C NMR: δ 116.14 (q, $J_{C\text{-}F}$ = 289.7 Hz), 114.68 (q, $J_{C\text{-}F}$ = 3.4 Hz), 124.22, 129.14, 137.76, 170.15 (q, $J_{C\text{-}F}$ =36.1 Hz). Anal. Calcd for $C_6H_3F_3N_2O_3$ (208.10): C, 34.63; H, 1.45; N, 13.46. Found C, 34.71; H, 1.22; N, 13.26.

2,2,2-Trifluoro-1-(1-methyl-4-nitro-1*H*-pyrrol-2-yl)-1-ethanone (4b). White prisms (72 %), mp 63.5-64.5 ºC. ^{1}H NMR: 4.08 (d, *J* = 0.5 Hz, 3H), 7.69 (q, *J* = 1.8 Hz, 1H), 7.84 (dq, *J* = 1.8, 0.6 Hz, 1H); ^{13}C NMR: δ 38.99, 116.11, 117.29, 123.69, 131.28, 136.07, 171.33. Anal. Calcd for $C_7H_5F_3N_2O_3$ (222.12): C, 37.85; H, 2.27; N, 12.61. Found C, 38.01; H, 2.13; N, 12.34.

2-Nitrothiophene (6). White prisms (78 %), mp 42.0–43.0 ºC (lit.[63] mp 45.5 ºC). ^{1}H NMR: δ 7.07 (q, *J* = 4.1, 5.3 Hz, 1H), 7.55 (dd, *J* = 1.6, 5.3 Hz, 1H), 7.93 (dd, *J* =1.6, 4.1Hz, 1H); ^{13}C

NMR: δ 126.97, 128.54, 132.50, 152.58. Anal. Calcd for $C_4H_3NO_2S$ (129.14): C, 37.20; H, 2.34; N, 10.85. Found C, 37.33; H, 2.22; N, 10.70.

3-Bromo-2-nitrothiophene (8). Yellowish prisms (58 %); mp 79.0-80.0 ºC (lit.[37] mp 81.0-83.0 ºC). ^{1}H NMR: δ 7.13 (d, *J* = 5.6 Hz, 1H), 7.54 (d, *J* = 5.6 Hz, 1H); ^{13}C NMR: δ 112.95, 130.97, 132.54, 146.54. Anal. Calcd for $C_4H_2BrNO_2S$ (208.03): C, 23.09; H, 0.97; N, 6.73. Found C, 23.38; H, 0.78; N, 6.53.

3-Bromo-5-nitrothiophene (9). Yellowish prisms (8 %); mp 45.0-46.0 ºC (lit.[64] mp 46-47.0 ºC). ^{1}H NMR: δ 7.47 (d, *J* = 1.9 Hz, 1H), 7.85 (d, *J* = 1.9 Hz, 1H); ^{13}C NMR: δ 109.98, 129.46, 130.55, 152.06.

3-Bromo-4,5-dinitro-thiophene (10a or **10b).** Yellow prisms (4 %); mp 178-180.0ºC, lit.[65] mp 165-166ºC for **10b**; ^{1}H NMR: δ 7.95 (s, 1H); ^{13}C NMR: δ 112.82, 131.26, 133.17, 152.03.

3-Bromo-2,5-dinitro-thiophene (11). Yellow microcrystals prisms (10 %); m.p.: 111-112ºC, lit.[67] m.p. : 112-113ºC; ^{1}H NMR: δ 7.89 (s, 1H); ^{13}C NMR: δ 111.28, 131.46, 148.40, 151.70 .

3,4-Dinitro-1*H*-pyrazole (13a). White prisms (41 %); mp 90-91ºC (lit.[40] mp 87.5-88.5). ^{1}H NMR: δ8.57 (s, 1H); ^{13}C NMR: δ 132.38, 133.58, 135.38.

1-Methyl-3-nitro-1*H*-pyrazole (13b). White prisms (65 %), mp 81.0–82.0 ºC (lit.[41] mp 80.0-84.0 ºC). ^{1}H NMR: δ 4.02 (s, 3H), 6.89 (d, *J* = 2.4 Hz, 1H), 7.44 (dq, *J* = 2.4, 0.3 Hz, 1H). ^{13}C NMR: δ 40.42, 103.14, 132.64, 155.37. Anal. Calcd for $C_4H_5N_3O_2$ (127.10): C, 37.80; H, 3.97; N, 33.06. Found C, 38.16; H, 3.79; N, 32.79.

3,5-Dimethyl-4-nitro-1*H*-pyrazole (15). Brownish needles (76%), mp 122.0–123.0 ºC (lit.[43] mp 126.0–127.0 ºC). ^{1}H NMR: δ 2.46 (s, 6H); ^{13}C NMR: δ 12.69, 130.04, 143.46. Anal. Calcd for $C_5H_7N_3O_2$ (141.13): C, 42.55; H, 5.00; N, 29.77. Found C, 42.67; H, 5.02; N, 29.43.

1-Methyl-4-nitro-1*H*-imidazole (17a). White prisms (39 %), mp 133.0–134.0 ºC (lit.[48] mp 134 ºC). ^{1}H NMR: δ 3.83 (s, 3H), 4.72 (br d, *J* = 1.5 Hz, 1H), 7.78 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR: δ 34.55, 120.19, 136.61, 148.00. Anal. Calcd for $C_4H_5N_3O_2$: C, 37.80; H, 3.97; N, 33.06. Found C, 38.16; H, 3.83; N, 32.86.

1-Methyl-5-nitro-1*H*-imidazole (17b). Orange prisms (22 %), mp 59.0-60.0 ºC (lit.[33] mp 60.0 ºC). ^{1}H NMR: δ 4.02 (d, *J* = 0.6 Hz, 3H), 7.59 (br s, 1H), 7.98 (d, *J* = 1.1 Hz, 1H); ^{13}C NMR: δ 35.02, 132.86, 138.87, 141.52.

1,2-Dimethyl-4-nitro-1*H*-imidazole (19a). White needles (53 %), mp 182.0–184.0 ºC (lit.[50] mp 184 ºC). ^{1}H NMR: δ 2.39 (s, 3H), 2.47 (s, 3H), 8.54 (s, 1H), 8.87 (s, 1H); ^{13}C NMR: δ. 12.85, 33.74, 120.71, 146.10, 145.07.

1,2-Dimethyl-5-nitro-1*H*-imidazole (19b). White prisms (18 %), mp 134.0–135.0 ºC (lit.[66] mp 134.0–135.0 ºC). ^{1}H NMR: δ 2.39 (s, 3H), 2.47 (s, 3H), 8.54 (s, 1H), 8.87 (s, 1H); ^{13}C NMR: δ. 13.70, 32.90, 131.89, 149.98.

4-Nitroisoxazole (21a). Yellow prisms (73 %), mp 45.0–46.0 ºC (lit.[57] mp 46.0–47.0 ºC). ^{1}H NMR: δ 8.85 (s, 1H), 9.32 (s, 1H); ^{13}C NMR: δ 144.44, 157.84. Anal. Calcd for $C_3H_2N_2O_3$ (114.06): C, 31.59; H, 1.77; N, 24.56. Found C, 31.63; H, 1.55; N, 24.31.

5-Methyl-4-nitroisoxazole (21b). Yellow oil (64 %), (lit.[57] bp 88.0–90.0 / 18 Torr). ^{1}H NMR: δ 2.87 (d, *J* = 0.7 Hz, 3H), 8.76 (q, *J* = 0.7 Hz, 1H); ^{13}C NMR: δ 12.97, 131.08, 145.88, 170.66.

Anal. Calcd for $C_4H_4N_2O_3$ (128.09): C, 37.51; H, 3.15; N, 21.87. Found C, 37.68; H, 2.95; N, 21.64.

3,5-Dimethyl-4-nitroisoxazole (21c). Yellowish prisms (72 %), mp 63.0-64.0 ºC (lit.[55] mp 63.0-64.0 ºC). ^{1}H NMR: δ 2.56 (s, 3H), 2.82 (s, 3H); ^{13}C NMR: δ 11.49, 13.81, 130.14, 155.50, 171.89.

2,5-Dimethyl-4-nitro-1,3-thiazole (23). Brownish prisms (67 %), mp 55.5–56.5 ºC (lit.[60] mp 56.5 ºC). ^{1}H NMR: δ 2.71 (s, 3H), 2.79 (s, 3H); ^{13}C NMR: δ 13.10, 19.08, 138.36, 150.84, 161.29. Anal. Calcd for $C_5H_6N_2O_2S$ (158.18): C, 37.97; H, 3.82; N, 17.71. Found C, 38.08; H, 3.74; N, 17.54.

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