The Nitration of 3,5- and 2,6-Diphenyl-4-pyrone

Alan R. Katritzky* and Hassan Faid-Allah

Department of Chemistry, University of Florida,
Gainesville, Florida 32611

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3,5-Diphenyl-4-pyrone is nitrated in the phenyl groups under different conditions *ortho* and/or *para* to yield the 2',2''-di-, the 4',4''-di-, and the 2',2'',4',4''-tetranitro derivatives. 2,6-Diphenyl-4-pyrone undergoes *meta* nitration to give the 3',3''-dinitro derivative.

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Little previous work has been reported on the nitration of 4-pyrones: 3-hydroxy-4-pyrones afford the 2-nitro derivatives [1] and 2-hydroxy-6-methyl-4-pyrone yields the 3-nitro analogue [2]. Nitrophenyl-4-pyrones, although known [3], have apparently not previously been prepared by direct nitration.

We found that the nitration of 3,5-diphenyl-4-pyrone **6** gave different products under different conditions. Nitric acid afforded 3,5-di-(2-nitrophenyl)-4-pyrone **7** (58%). The ^{13}C nmr of the crude product (yield 62%) did not give any evidence for the presence of isomers. From the reaction of **6** with nitronium tetrafluoroborate, we obtained 3,5-di-(4-nitrophenyl)-4-pyrone **10** in 60% recrystallized yield. The ^{13}C nmr spectra of the crude product (64%) again indicated the absence of isomers. Mixed acids converted **6** into 3,5-bis-(2,4-dinitrophenyl)-4-pyrone **5** in 55% recrystallized yield. Further nitrations of compounds **7** and **10** each yielded this same tetranitroderivative **5**.

The orientations of compounds **7**, **10** and **5** were proved spectrally and also by oxidation to give respectively 2-nitro- **12**, 4-nitro- **11** and 2,4-dinitrobenzoic acid **9**.

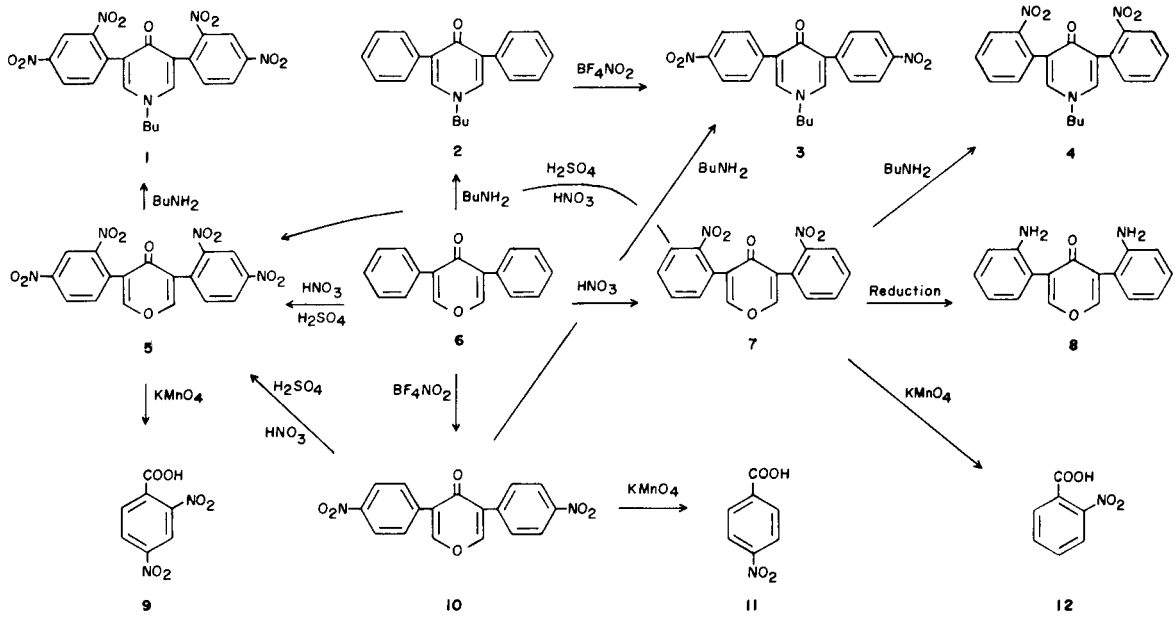
On treatment with *N*-butylamine, compounds **7**, **10** and **5** each gave the corresponding 3,5-diaryl-1-butyl-4-pyridone **4**, **3** and **1**, respectively. Nitration of **2** with nitronium tetrafluoroborate afforded 3,5-di-(4-nitrophenyl)-1-butyl-4-pyridone **3**, whereas nitric acid with **2** gave only a resin. Reduction converted the bis-*ortho*-nitro derivative **7** into the corresponding diamino compound **8**.

Nitration of 2,6-diphenyl-4-pyrone **13** gave 2,6-di-(3-nitrophenyl)-4-pyrone **14**.

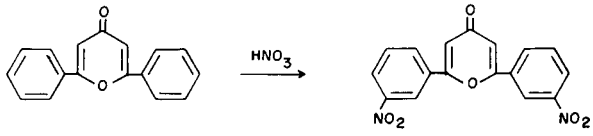
^{13}C NMR Spectra.

The ^{13}C nmr spectra of the foregoing pyrones and pyridones are recorded in (Table I). Spectra of the *o*-nitrophenyl isomers as well as the 2,4-dinitrophenyl, and the *m*-nitrophenyl derivatives each exhibited eight signals for the aromatic and pyrone or pyridone carbons together with a carbonyl carbon signal. These patterns confirm the unsymmetrical nature of the substitution in the phenyl rings. By contrast, the ^{13}C spectra of the *p*-nitrophenyl isomers **3** and **10** showed only the expected seven signals: one for the carbonyl carbon and six for the aromatic and pyrone or pyridone carbons.

^{1}H NMR Spectra.



The structures of the nitropyrones and pyridones were further confirmed by the proton nmr spectra (Table II). The spectra of the *ortho* isomers **4** and **7** exhibit two double doublets each of two proton intensity for H_b and H_e and two triplets each of two proton intensity for H_e and H_d. The spectra showed also a singlet of two proton intensity for H_f. On the other hand the *para*-isomers **3** and **10** showed two double doublets each of four proton intensity for $H_{a,e}$ and $H_{b,d}$ as well as a singlet of two proton intensity for H_f. The *meta*-isomers **14** exhibited two doublets of triplets each of two proton intensity for H_a and H_c; a triplet of two proton intensity for H_b and a split singlet of two proton intensity for H_e. The spectrum showed also the singlet of H_f. The spectra of the 2,4-dinitro derivatives **1** and **5** each exhibited a split singlet of two proton intensity for H_b; a double doublet of two proton intensity for H_d; a doublet of two proton intensity for H_e and a singlet of two proton intensity for H_f.



13 14

EXPERIMENTAL

The ^1H nmr spectra were recorded with a Varian EM 360L spectrometer or on a Nicolet NT-300 spectrometer, operating at a field of 7 tesla in each case tetramethylsilane is used as internal standard. The ^{13}C nmr spectra were recorded on a Joel JNM-FX100 NMR Spectrometer. The ir spectra were obtained using sodium chloride plates on a Perkin-Elmer 297 spectrometer as solutions in bromoform. Mass spectra were recorded on a Kratos MS 30. Melting points were recorded on a Kofler hot stage apparatus and are uncorrected.

The following compounds were prepared using literature methods: **6** (65%) (mp. 188°, Lit [4], 186-187°); **2** (50%) (mp 160°, Lit [5] 159°); **13** (55%) (mp. 140°; Lit [6] 140°).

3,5-Di-(2-nitrophenyl)-4-pyrone (**7**).

3,5-Diphenyl-4-pyrone (2.5 g, 0.01 mole) in acetic acid (15 ml) was refluxed with fuming nitric acid (5 ml, d 1.5) for 2 hours. The reaction mixture was then cooled, poured into ice-cold water, filtered, washed with water, and crystallized from acetic acid (2.0 g, 58%) in needles, mp 234°; ir (bromoform)): 1670 (cm^{-1}) (C=O); ms: m/e (relative abundance) M^+ 338 (1), 293 (18), 292 (100), 264 (2), 247 (4), 246 (1), 237 (2), 236 (12), 219 (4), 218 (37), 208 (9), 206 (11), 190 (18), 184 (41), 187 (13), 180 (18), 179 (4), 176 (6), 164 (6), 152 (6), 134 (9), 104 (31).

Anal. Calcd. for $C_{17}H_{10}N_2O_6$: C, 60.3; H, 3.0; N, 8.3. Found: C, 60.2; H, 3.0; N, 8.1.

3,5-Di-(4-nitrophenyl)-4-pyrone (**10**).

3,5-Diphenyl-4-pyrone (2.5 g, 0.01 mole) in acetic acid (8 ml) was refluxed with nitronium tetrafluoroborate (2.8 g, 0.022 mole) for 5 hours. The reaction mixture was then poured into ice-cold water, the solid which

Table I

^{13}C NMR Spectra [a] of Pyrones and Pyridones

Compound No.	C=O	pyrone C		Aromatic C
		C_2	C_3	
6 [b]	175.3	128.5	131.2	128.3, 128.8, 130.0, 152.2
7	172.3	124.0	125.4	127.1, 130.0, 132.2, 133.6, 148.9, 153.9
10	173.1	123.3	127.0	129.8, 138.2, 147.1, 155.1
5	172.1	117.9	124.6	126.1, 129.7, 132.3, 146.2, 147.4, 153.5
4 [c]	169.7	122.1	125.4	127.0, 128.0, 130.5, 131.2, 136.9, 148.0
3 [d]	170.4	120.9	124.5	128.1, 138.3, 140.4, 144.1
1 [e]	170.2	117.4	125.4	123.6, 132.0, 133.5, 138.6, 145.1, 147.4
8	175.2	128.4	117.1	115.2, 115.9, 129.0, 131.1, 147.3, 154.9
13 [b]	179.8	126.6	131.1	111.1, 125.6, 128.9, 163.0
14	178.8	126.0	132.4	109.5, 112.9, 121.8, 131.0, 148.6, 169.9

[a] Solutions in dimethyl sulfoxide-d_6, δ in ppm. [b] Solutions in deuteriochloroform. [c] Bu^{n}C: 55.0, 31.1, 17.6, 12.0. [d] Bu^{n}C: 54.3, 30.4, 17.1, 11.5. [e] Bu^{n}C: 55.1, 30.7, 17.3, 11.8.

Table II

^1H NMR Spectra [a] of Pyrones

Compound No.	Pyrone H	Chemical Shift of Aromatic H					Coupling Constant J (Hz)							
	2,6 or 3,5	2'	3'	4'	5'	6'	2'3'	2'4'	2'6'	3'4'	3'5'	4'5'	4'6'	5'6'
6	7.85	7.23	7.65	7.29	7.65	7.23	8,8	2,2	2,2	8,8	2,2	8,8	2,2	8,8
7	8.68	NO_2	8.07	7.69	7.84	7.56	—	—	—	8,8	2,2	8,8	2,2	8,8
10	8.60	7.90	8.30	NO_2	8.30	7.90	8,8	—	2,2	—	2,2	—	—	8,8
5	8.71	NO_2	8.78	NO_2	8.62	7.88	—	—	—	—	2,2	—	—	8,8
14	7.28	8.45	7.90	8.50	NO_2	8.79	8,8	2,2	2,2	8,8	—	—	2,2	—

[a] Solutions in DMSO-d_6, δ in ppm.

separated out was filtered and crystallized from ethanol-acetic acid (2.05 g, 60%) in needles mp 225°; ir (bromoform): 1669 (cm^{-1}) (C=O).

Anal. Calcd. for $C_{17}H_{10}N_2O_6$: C, 60.3; H, 3.0; N, 8.3. Found: C, 60.4; H, 3.1; N, 8.6.

3,5-Di-(2,4-dinitrophenyl)-4-pyrone (**5**).

3,5-Diphenyl-4-pyrone (2.5 g, 0.01 mole) in acetic acid (15 ml) was refluxed with a nitrating mixture of concentrated nitric acid and concentrated sulfuric acid (1:1, 20 ml) for 12 hours. The reaction mixture was then left at room temperature for 3 hours, then poured into ice-cold water. The solid which separated out filtered, washed with water and crystallized form acetic acid (2.4 g, 55%) in needles, mp 258°; ir (bromoform) 1665 (cm^{-1}) (C=O).

Anal. Calcd. for $C_{17}H_8N_4O_{10}$: C, 47.7; H, 1.9; N, 13.0. Found: C, 47.9; H, 1.9; N, 12.9.

The tetranitropyrone **5** was also prepared (56-60%) when the nitropyrones **7** and **10** were refluxed with a mixture of nitric acid and sulfuric acid (1:1) for 4 hours.

1-Butyl-3,5-di-(4-nitrophenyl)-4-pyridone (**3**).

1-Butyl-3,5-diphenyl-4-pyridone (0.3 g, 0.001 mole) in acetic acid (8 ml) was refluxed with nitronium tetrafluoroborate (0.28 g, 0.0022 mole) for 4 hours. The reaction mixture was then poured into water, the precipitate which separated out filtered, washed with water and crystallized from ethanol-benzene (0.23 g, 58%) in yellow needles, mp 265°; ir (bromoform): 1645 (cm^{-1}) (C=O); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 0.85 (t, 3H, CH_3, J = 2 Hz), 1.25 (m, 2H, CH_2), 1.60 (m, 2H, CH_2), 3.90 (t, 2H, CH_2, J = 2 Hz), 8.05 (m, 10H, Ar and pyridone protons).

Anal. Calcd. for $C_{21}H_{19}N_3O_5$: C, 64.1; H, 4.8; N, 10.6. Found: C, 64.3; H, 4.8; N, 10.4.

The same compound **3** was also prepared (66%) when a solution of **10** in acetic acid was refluxed with butylamine for 5 hours.

1-Butyl-3,5-di-(2-nitrophenyl)-4-pyridone (**4**).

3,5-Di(-2-nitrophenyl)-4-pyrone (3.3 g, 0.01 mole) in acetic acid (10 ml) was refluxed with butylamine (1.1 ml, 0.012 mole) for 5 hours. The reaction mixture was then poured into water, filtered and crystallized from benzene (2.5 g, 65%) in yellow needles, mp 182°; ir (bromoform): 1645 (cm^{-1}) (C=O); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.25 (t, 3H, CH_3, J = 2 Hz), 1.50 (m, 2H, CH_2), 1.90 (m, 2H, CH_2), 4.15 (t, 2H, CH_2, J = 2 Hz); 8.1 (m, 10H, Ar and pyridone protons).

Anal. Calcd. for $C_{21}H_{19}N_3O_5$: C, 64.1; H, 4.8; N, 10.6. Found: C, 63.8; H, 4.8; N, 10.4.

1-Butyl-3,5-di-(2,4-dinitrophenyl)-4-pyridone (**1**).

3,5-Di-(2,4-dinitrophenyl)-4-pyrone (2.2 g, 0.05 mole) in acetic acid (10 ml) was refluxed with butylamine (0.55 ml, 0.0055 mole) for 7 hours. The reaction mixture was then poured into water, filtered and crystallized from benzene-methanol (1.6 g, 67%) in yellow needles, mp 210°; ir (bromoform): 1655 (cm^{-1}) (C=O); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 0.99 (t, 3H, CH_3, J = 2 Hz), 1.45 (m, 2H, CH_2, 1.80 (m, 2H, CH_2), 4.25 (t, 2H, CH_2, J = 2 Hz), 8.4 (m, 8H, Ar and pyridone protons).

Anal. Calcd. for $C_{21}H_{17}N_5O_9$: C, 52.1; H, 3.5; N, 14.4. Found: C, 52.0; H, 3.5; N, 14.4.

3,5-Di-(2-aminophenyl)-4-pyrone (**8**).

3,5-Di-(2-nitrophenyl)-4-pyrone (1.65 g, 0.005 mole) in ethanol (10 ml) was refluxed with tin (5 g) and concentrated hydrochloric acid (10 ml) for 0.5 hours. The reaction mixture was then poured into water treated with sodium carbonate and extracted with ether. The ethereal solution after washing with water, drying (sodium sulphate) and evaporation afforded **8** which crystallized from methanol (0.78 g, 55%) in yellowish needles, mp 215°; ir (bromoform): 1635 (cm^{-1}) (C=O), 3410, 3340 (NH_2); ^{1}H nmr (dimethylsulfoxide-d_6): δ 4.8 (s, 4H, NH_2), 6.90 (m, 8H, Ar protons), 8.25 (s, 2H, pyrone protons); ms: m/e (relative abundance) M^+ 278 (3), 261 (22), 260 (94), 259 (74), 232 (19), 231 (15), 204 (8), 161 (14), 145 (10), 144 (100), 118 (15), 117 (93), 116 (25), 104 (14), 90 (22), 77 (11).

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.4; H, 5.1; N, 10.0. Found: C, 73.0; H, 5.1; N, 9.8.

2,6-Di-(3-nitrophenyl)-4-pyrone (**14**).

2,6-Diphenyl-4-pyrone (2.5 g, 0.01 mole) in acetic acid (15 ml) was refluxed with fuming nitric acid (5 ml, d, 1.5) for 12 hours. The reaction mixture was then poured into ice-cold water and the solid which separated out was filtered, washed with water and crystallized from acetic acid (1.9 g, 55%) in needles, mp 238°; ir (bromoform): 1662 (cm^{-1}) (C=O).

Anal. Calcd. for $C_{17}H_{10}N_2O_6$: C, 60.3; H, 3.0; N, 8.3. Found: C, 60.0; H, 2.9; N, 8.1.

Oxidation of Nitropyrones.

A mixture of the appropriate nitropyrone (0.005 mole) in acetone (30 ml) was refluxed with sodium carbonate (15 ml, 0.5 *N*). To the boiling mixture, potassium permanganate (0.5 g, 0.0031 mole) in water (20 ml) was added in small portions during 1 hour with vigorous stirring. After the addition was completed, the mixture was boiled for 30 minutes to complete the oxidation. The mixture was then cooled and acidified with 2*N* aqueous hydrochloric acid to give the corresponding nitrobenzoic acid (25-29%); (2-isomer, mp and mixed mp 146°, Lit [7] 145°; 4-isomer, mp and mixed mp 239-241°, Lit [8] 240°; 2,4-dinitro acid, mp and mixed mp 178-179°, Lit [9] 180°).

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