Addition of 3(5)-methylpyrazole to *p*-benzoquinone

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Abstract

Four derivatives have been isolated and identified in the reaction between 3(5)-methylpyrazole and *p*-benzoquinone. ^{1}H and ^{13}C NMR, including ^{13}C CPMAS NMR have been used to characterize these 1-pyrazolyl derivatives of 1.4-dihydroxybenzene. A discussion of their structure and *meso*/*d,l* isomerism is provided.

Keywords: 3(5)-Methylpyrazole, *p*-benzoquinone, *meso/d,l* isomerism

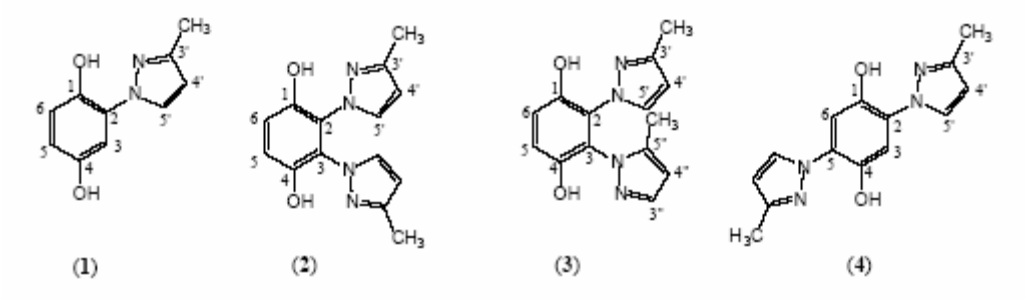
Introduction

We[1-3] and others[4-7] have studied the addition of *N*-unsubstituted azoles to *p*-benzoquinone. In the case of pyrazolyl derivatives, the resulting hydroquinones (1,4-dihydroxybenzenes) have been extensively used as ligands in coordination chemistry,[8-11] and some biochemical studies of the reactivity of imidazole towards benzoquinone have been reported.[12]

With the double purpose of studying the reactivity of *p*-benzoquinone towards an unsymmetrical pyrazole and to prepare new ligands we report in this paper the reaction between 3(5)-methylpyrazole and *p*-benzoquinone.

Results and Discussion

The reaction of 3(5)-methylpyrazole and *p*-benzoquinone afforded four compounds (**1**)-(**4**) in an overall yield of about 47% (calculated on disubstituted derivatives). The relative proportions are (**1**) 29%, (**2**) 16%, (**3**) 38% and (**4**) 17%. As we have discussed elsewhere, the formation of bis-pyrazolyl hydroquinones implies the oxidation of the mono adducts by *p*-benzoquinone.[2]



(1) (2) (3) (4)

^{1}H and ^{13}C NMR spectroscopies

The assignment of proton signals is reported in Table 1. In the case of the pyrazole signals of compound **3**, it is based on the fact that $J_{45} > J_{34}$ ($J_{4'5'} > J_{3''4''}$).[13] To distinguish between 2,3- and 2,5-disubstituted derivatives, we have used the criteria, previously established, that the pyrazole protons are shielded in the 2,3-bis derivative and slightly deshielded in the 2,5- one.[2]

The chemical shifts of the OH groups deserve some attention. In $CDCl_3$ when the pyrazolyl substituent is coplanar with the benzene ring (compounds **1** and **4**), the OH is strongly deshielded by the intramolecular hydrogen bond (IMHB) O-H···N and appears at 11 ppm. If there is no adjacent pyrazole ring (compound **1**, 4-OH) or if the ring is almost perpendicular due to the steric requirement of another pyrazole (compounds **2** and **3**), then the OH appears at 5-7 ppm. In DMSO, the IMHB disappear to be replaced by intermolecular O-H···DMSO hydrogen bonds and all the OH signals appear about 9-10 ppm.

The results concerning the ^{13}C NMR spectra are reported in Tables 2 and 3. Assignments are based on previous studies on pyrazoles[14-16] and azolylhydroquinones.[1-3]

In the solid state, using the CPMAS technique, we have recorded the ^{13}C NMR spectra of these compounds (Tables 2 and 3), all of them being very well resolved. Compound **1** does not present any anomaly; the splitting of C-5' should correspond to some amount of disorder in the conformation of the pyrazole ring. Although there is a 1-O-H···N IMHB present in this compound, some degree of freedom would remain. Compound **4**, with its two IMHB's, should be planar and rigid: the CPMAS spectrum is very similar to that obtained in DMSO solution.

Table 1. ^{1}H NMR spectra (δ, ppm, J, Hz) of compounds (**1**)-(**4**).

Comp.	H-3	H-5	H-6	H-4'	H-5'	H-3"	H-4"	1-OH	4-OH	CH_3
1	6.85	6.63	6.94	6.25	7.79	----	----	11.17	4.95	2.37
	J_{35}=2.7	J_{56}=8.8		$J_{4'5'}$=2.4						
1[b]	7.09	6.53	6.81	6.27	8.26	----	----	9.95	9.03	2.25
	J_{35}=2.9	J_{56}=8.7		$J_{4'5'}$=2.4						

2[a] ---- 6.98 6.98 6.11 6.76 ---- ---- 7.56 7.56 2.38
$J_{4'5'}$=2.5
2[b] ---- 6.92 6.92 6.04 7.17 ---- ---- 9.55 9.55 2.12
$J_{4'5'}$=2.3
3[a] ---- 7.10 6.97 6.04 6.42 7.77 6.16 9.97 6.45 2.34
J_{56}=9.0 $J_{4'5'}$=2.5 $J_{3"4"}$=1.8 1.66
3[b] ---- 7.00 6.92 5.96 7.01 7.29 5.99 9.57 9.48 2.07
J_{56}=9.0 $J_{4'5'}$=2.4 $J_{3"4"}$=1.6 1.07
4[a] 7.10 ---- 7.10 6.27 7.84 ---- ---- 11.30 11.30 2.36
$J_{4'5'}$=2.5
4[b] 7.40 ---- 7.40 6.29 8.30 ---- ---- 10.21 10.21 2.27
$J_{4'5'}$=2.3

[a] $CDCl_3$; [b] DMSO-d_6.

Compounds **2** and **3**, having the pyrazolyl residues nearly orthogonal to the benzene plane, can exist in two conformations: the *meso* and the *d,l*:

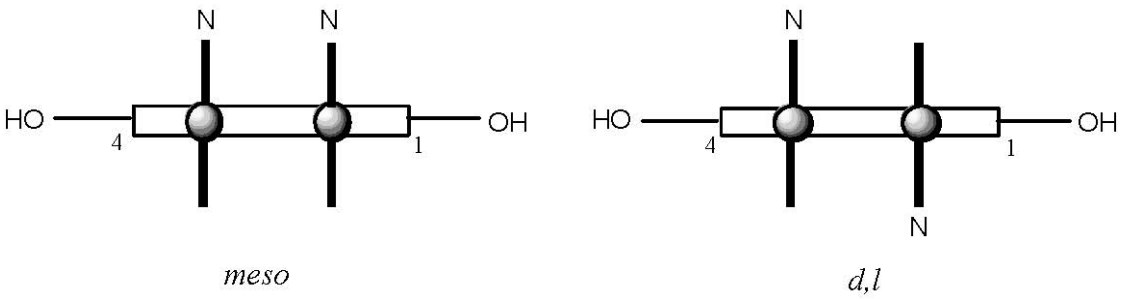


Table 2. ^{13}C NMR spectra (δ, ppm, J, Hz) of compounds (1) and (4).

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	C-3'	C-4'	C-5'	CH_3
1[a]	142.5	124.8	104.7	148.9	114.1	119.2	148.5	106.8	123.7	13.4
	^1J=157.3	^1J=161.6	^1J=157.3	^1J=177.1	^1J=157.3	^1J=128.0				
	^3J=5.2									
1[b]	139.2	122.9	101.6	150.3	114.8	117.9	147.4	106.5	125.2	13.3
	124.5									
4[c]	140.5	124.3	109.7	140.5	124.3	109.7	147.9	106.3	130.8	13.2
	^1J=161.2	^3J=8.1	^1J=175.6	^1J=190.7	^1J=127.3					
	^3J=4.4 (OH)	^2J=8.2	^2J=9.8							
	^3J=3.7 (Me)									
4[b]	140.5	121.2	105.5	140.5	121.2	105.5	147.0	105.5	127.1	12.8

[a] $CDCl_3$; [b] CPMAS; [c] DMSO-d_6.

In solution, the rotational barrier being low,[2] both conformations are in rapid equilibrium at room temperature and only average signals are observed. In the solid state, depending on the crystallization, one of them or both can be present. In the case of **2**, the simplicity of the CPMAS spectrum (Table 3) points out to a single conformation (probably the *d,l* which seems more usual).[1,2] The pyrazole rings have different chemical shifts (the lower values have been tentatively assigned to the substituent at position 2) but only one methyl signal. Probably the torsion angles at C-2 and C-3 are different (and different from 90°).

Compound **3** has no symmetry at all, therefore if *meso* and *d,l* isomers are present in the crystal up to four signals are expected for some carbons in the ^{13}C CPMAS NMR spectrum. Four signals were observed for C-3' and three for C-4", thus, it is reasonable to assume that both conformations have crystallized together.

Concerning the relative amounts of the four compounds, the 3-methyl derivatives **1**, **2** and **4** clearly dominate (they account for 62% of the total), but the presence of 38% of the mixed derivative **3** indicates that probably small amounts of pure 5-methyl derivatives have been lost.

Table 3. ^{13}C NMR spectra (δ, ppm, J, Hz) of compounds (2) and (3).

Comp. C-1 C-2 C-3 C-4 C-5 C-6 C-3' C-4'

2[a] 145.3 124.0 124.0 145.3 116.8 116.8 148.0 105.8
^{1}J=162.2 ^{1}J=175.4
^{2}J=8.2
^{3}J=3.2 (Me)
2[b] 143,4 ~122 124 143.4 117.8 117.8 147.8 106.9
3[a] 144.6 122.4 125.9 146.7 118.1 116.1 147.7 105.4
^{3}J=8.5 ^{3}J=7.2 ^{3}J=5.7 ^{3}J=9.2 ^{1}J=161.6 ^{3}J=162.2 ^{1}J=175.3
^{2}J=8.3
^{3}J=3.0 (Me)
3[b] 143.0 123.5 123.5 143.0 118.6 118.6 147.6 108.0
149.0 105.6
151.0 104.4
151.5

Comp. C-5' C-3" C-4" C-5" 3'-CH_3 5"-CH_3

1[a] 133.0 148.0 105.8 133.0 13.3 ----
^{1}J=189.0 ^{1}J=127.0
^{3}J=9.5
1[b] 130.6 150.0 107.7 132.3 13.4
3[a] 132.1 139.2 104.5 140.6 13.2 10.6
^{1}J=188.9 ^{1}J=183.3 ^{1}J=174.4 ^{2}J=6.0 ^{1}J=127.0 ^{1}J=128.8
^{2}J=9.6 ^{2}J=5.9 ^{2}J=10.4
^{3}J=3.2 (Me)
3[b] 130.4 137.6 108.0 143.0 12.4 10.3
134.1 139.3 105.6 9.3
104.4

[a] DMSO-d_6 ; [b] CPMAS.

Experimental Section

General Procedures. Melting points were determined in a microscope hot stage apparatus and are uncorrected. Column chromatography was performed on silicagel Merck 60 (70-230 mesh) using the appropriate eluent. The R_f values were measured on tlc aluminium sheets of silica gel 60 F254 (layer thickness 0.2 mm) with the solvent indicated in each case. Mass spectra were

obtained with a Shimadzu QP-5000 spectrometer at 60 eV using the EI mode. ^{1}H NMR (400.13 MHz) and ^{13}C NMR (100.62 MHz) spectra in solution were obtained using a Bruker DRX-400 instrument. Chemical shifts (δ) in ppm are referred to Me_4Si. Solid state ^{13}C CPMAS NMR spectra were recorded using a Bruker AC-200 instrument (50.32 MHz) and standard CP pulse sequences were employed. All spectra were recorded at 300 K. 1,4-Benzoquinone and 3(5)-methylpyrazole are commercial products.

Addition of 3(5)-methylpyrazole to *p*-benzoquinone. To a solution of 2 g (18.5 mmol) of 1,4-benzoquinone in 20 mL of dioxane were added with stirring, 1.51 g (18.5 mmol) of 3(5)-methylpyrazole. The mixture was heated under reflux for 15 h. A precipitate separated which was filtered off (**4**). The solution was evaporated under reduced pressure to yield a mixture of **1**, **2** and **3**. The three components, as white solids, were separated by column chromatography (eluent: CH_2Cl_2/EtOH 99:1).

2-(3-Methyl-1-pyrazolyl)-1,4-dihydroxybenzene (1). Relative amount 29%, mp. 150-1 °C (CH_2Cl_2/hexane). R_f = 0.42 (CH_2Cl_2/EtOH 99:1). IR (KBr, ν cm^{-1}) 3350, 3160, 1620, 1515, 1475, 1425, 1370, 1320, 1300, 1260, 1245, 1215, 1190, 1120, 1075, 1040, 980, 965, 880, 830, 780, 770, 745, 690, 630. MS (m/z, %) 191 (M+·+1, 10), 190 (M+·, 100), 161 (85), 135 (14), 133 (25), 120 (12), 108 (15), 107 (10), 95 (13), 94 (13), 93 (10), 81 (14), 80 (12), 79 (10), 68 (20), 67 (20), 66 (16), 65 (13), 55 (22), 54 (22), 53 (41), 52 (35), 51 (23), 50 (10). Anal. Calc. for $C_{10}H_{10}N_2O_2$: C 63.14, H 5.29, N 14.72. Found C 62.82, H 5.21, N 14.76 %.

2,3-Bis(3-methyl-1-pyrazolyl)-1,4-dihydroxybenzene (2). Relative amount 16%, mp. 142-3 °C (CH_2Cl_2/hexane). R_f = 0.39 (CH_2Cl_2/EtOH 99:1). IR (KBr, ν cm^{-1}) 3600-2600, 1615, 1600, 1525, 1500, 1490, 1460, 1410, 1360, 1285, 1235, 1220, 1195, 1135, 1120, 1100, 1050, 1025, 1010, 890, 850, 820, 810, 760, 720, 655, 640. MS (m/z, %) 271 (M+·+1, 17), 270 (M+·, 100), 214 (10), 200 (10), 189 (12), 188 (56), 187 (16), 160 (21), 159 (11), 134 (15), 132 (25), 131 (13), 119 (11), 94 (15), 93 (17), 83 (25), 82 (13), 81 (11), 79 (16), 78 (12), 68 (20), 67 (16), 66 (19), 65 (13), 64 (11), 55 (16), 54 (34), 53 (31), 52 (32), 51 (15). Anal. Calc. for $C_{14}H_{14}N_4O_2.H_2O$: C 58.33, H 5.59, N 19.43. Found C 58.15, H 5.41, N 19.31 %.

2-(3-Methyl-1-pyrazolyl)-3-(5-methyl-1-pyrazolyl)-1,4-dihydroxybenzene (3). Relative amount 38%, mp. 166-7 °C (CH_2Cl_2/hexane). R_f = 0.29 (CH_2Cl_2/EtOH 99:1). IR (KBr, ν cm^{-1}) 3140, 2920, 1515, 1480, 1465, 1410, 1370, 1360, 1330, 1290, 1240, 1210, 1200, 1135, 1125, 1080, 1065, 990, 935, 905, 855, 815, 775, 725, 665, 630. MS (m/z, %) 271 (M+·+1, 17), 270 (M+·, 100), 189 (13), 188 (58), 187 (17), 160 (16), 159 (11), 134 (16), 132 (23), 131 (10), 94 (14), 93 (16), 83 (28), 82 (12), 81 (11), 79 (13), 78 (11), 68 (27), 67 (17), 66 (20), 65 (12), 55 (16), 54 (35), 53 (30), 52 (27), 51 (14). Anal. Calc. for $C_{14}H_{14}N_4O_2$: C 62.21, H 5.22, N 20.72. Found C 62.21, H 5.16, N 21.13 %.

2,5-Bis(3-methyl-1-pyrazolyl)-1,4-dihydroxybenzene (4). Relative amount 4%, mp. 280-2 °C (CH_2Cl_2). R_f = 0.85 (CH_2Cl_2/EtOH 99:1). IR (KBr, ν cm^{-1}) 3140, 2920, 1530, 1465, 1405, 1365 1355, 1260, 1225, 1200, 1090, 1055, 1030, 960, 860, 810, 770, 650, 605. MS (m/z, %) 271 (M+·+1, 17), 270 (M+·, 100), 160 (10), 159 (13), 135 (53), 108 (37), 107 (21), 83 (11), 68 (14),

67 (17), 66 (11), 53 (29), 52 (14). Anal. Calc. for $C_{14}H_{14}N_4O_2$: C 62.21, H 5.22, N 20.72. Found C 61.98, H 5.34, N 20.68 %.

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References and Notes

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