International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN: 0974-4290
Vol.9, No.04 pp 437-445, 2016

The Behavior of Some Unsymmetrical *o*-Quinones towards Cyclic Secondary Amines. Structural Confirmation Based on X-ray Crystallography.

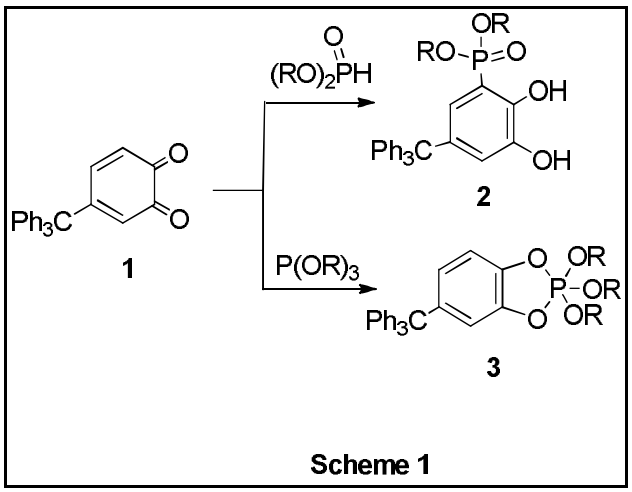
Fatma A. El-Samahy* and Fayez H. Osman

Department of Green Chemistry, National Research Centre, 33 El-Bohouth St., Dokki, Giza, Egypt. P.O.: 12622

Abstract : The reaction of 4-triphenylmethyl-1,2-benzoquinone with morpholine in acetonitrile gave 2-morpholino-4-tritylphenol, 2,6-dimorpholino-4-tritylphenol and 3-morpholino-5-tritylbenzene-1,2-diol, respectively. By the same manner, it was reacted with piperidine, N-methylpiperazine and pyrrolidine to yield the corresponding adducts. 3,5-Di-*tert*-*o*-benzoquinone with morpholine in acetonitrile led to the formation of 2,4-di-tert-butyl-6-morpholinophenol and 2,4-di-tert-butyl-6-(morpholin-3-ylidene)cyclohexa-2,4-dienone. Simillarly, it reacted with piperidine to yield 2,4-Di-tert-butyl-6-(piperidin-1-yl)phenol and 2,4-Di-tert-butyl-6-(piperidin-2-ylidene)cyclohexa-2,4-dienone. All new compounds were identified by spectroscopic tools.

Keywords: 4-triphenylmethyl-1,2-benzoquinone, 3,5-Di-*tert*-*o*-benzoquinone, morpholine, piperidine, pyrrolidine, Structural confirmation, x-ray crystallography.

Introduction

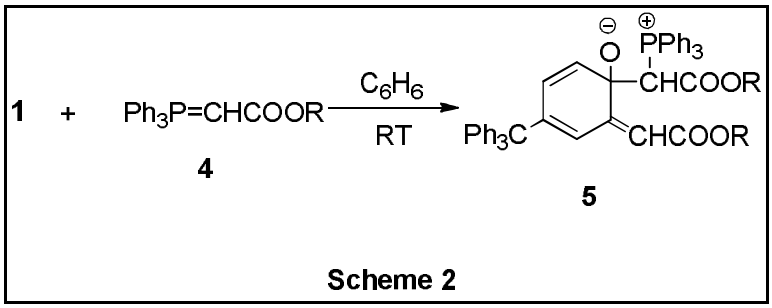


Scheme 1

The morpholine and piperidine skeleton containing species important in the synthesis of organic compounds,[1-3] including pharmaceuticals,[4-11] have selective enzyme inhibition, antimicrobial and antifungal activities.[12-18] The chemistry of *o*-quinones is wide and interesting, for example, they can form chelate semiquinone or catecholate complexes with metals.[19] The behavior of 4-triphenylmethyl-1,2-benzoquinone (**1**)

towards alkyl phosphites[20,21] and Wittig reagents[22,23] was reported. Treatment of quinone **1** with dialkyl phosphates and trialkyl phosphites afforded dihydroxyaryl phosphonates (**2**) and the unsaturated cyclic pentaoxyphosphoranes (**3**)[20] (Scheme 1).

On the other hand, the reaction of Wittig reagents **4** with *o*-quinone **1** led to the formation of 2:1 adducts **5**[22] (Scheme 2).



Scheme 2

These results led us to investigate the present work which describes the reaction of some unsymmetrical *o*-quinones with cyclic secondary amines.

Experimental

The reagent grade chemicals were obtained from commercial sources and purified by either distillation or recrystallization before use. Purity of synthesized compound has been checked by thin layer chromatography. Melting points were determined on an electrical digital- melting point apparatus (Stuart/melting point SMP 30) and uncorrected. The ^{1}H NMR spectra were recorded in deuterated chloroform ($CDCl_3$) or in deuterated dimethylsulphoxide (DMSO-d_6) on JOEL 500 AS (at 500 MHz) or on Varian Mercury VX-300 (at 300 MHz) Spectrometer using tetramethylsilane (TMS) as an internal reference. ^{13}C NMR spectra were recorded on JOEL 500 AS (at 125 MHz) or on Varian Mercury VX-300 (at 75.46 MHz). Mass spectra (EI-MS) were determined at 70 eV on a Finnigan MAT SSQ 7000 spectrometer.

X-Ray structure determination

The crystal data were measured at T = 298K on a Kappa CCD Enraf Nonius FR 590 diffractometer. The crystal structure was solved and refined using maXus (Bruker Nonius, Delft and MacScience, Japan). Mo-Kα radiation (λ = 0.71073Å) and a graphite monochromator were used for data collection.

Compound 8a. $C_{33}H_{34}N_2O_3$, Mr = 506.646, triclinic, crystallizes in space group P1/c, a=10.2259 (2), b = 10.8528 (2), c = 13.9362 (3) Å, v = 1380.73(5) Å^3, z = 2, Dc = 1.219 cm^{-1}, 2θ range 2.910–27.485°, absorption coefficient μ (Mo-Kα) = 0.08 mm^{-1}, F (000) = 892. The unique reflections measured 4124, of which 343 reflections with threshold expression I>3σ (I) were used in the structural analysis. The final agreement factors were R = 0.074 and wR = 0.076 with a goodness-of-fit of 1.024. Further details of the structure determination (complete bond lengths and angles, H atom coordinates, structure factors, temperature factors) have been deposited at the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 IEZ, United Kingdom. Any request should be accompanied by the full literature citation and the CCDC reference numbers 1444686 (**8a)**.

General procedure for the synthesis of compounds 7, 8 and 9.

To a suspension of compound **1** (1.40 g, 4 mmol) in dry acetonitrile (30 mL), cyclic amines (**6**) (2 mL) was added. The mixture was heated under reflux for about 3 h, or stirred at room temperature for about 10 h. Then, the solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with *n*-hexane and acetone (increasing amounts) as eluent to give three fractions **7, 8** and **9**.

2-Morpholino-4-tritylphenol (7a)

The first fraction (80–75% *n*-hexane) afforded a colourless crystalline product, recrystallized from ethyl acetate to yield 0.28 g (17 %) **7a**. M.p.: 245–247 °C; (Found C, 82.65; H, 6.49; N, 3.30. $C_{29}H_{27}NO_2$ requires C,

82.63; H, 6.46; N, 3.32%); IR (KBr): $\overline{\nu}$ = 3401 (OH), 3057 (CH), 1588 (C=C) cm^{-1}; ^1H NMR (300 MHz, DMSO-*d*6) δ = 2.90 (m, 4H, $-CH_2NCH_2-$), 3.66 [m, 4H, $-CH_2OCH_2-$), 6.45, 6.72 (2d, *J* = 7.2 Hz, 2ArH), 6.61 (s, 1H, ArH), 7.10-7.26 (m, 15H, ArH), 8.99 (s, 1H, OH) ppm; ^{13}C NMR: δ = 54.9 (C2, C6 of mopholine ring), 66.19 (CPh_3), 67.25 (C3, C5 of of mopholine ring), 114.15, 116.11, 122.17, 125.02, 126.22, 128.32, 130.19, 139.16, 145.73, 146.23 (aromatic carbons) ppm; MS (70 eV): *m*/*z* = 421 (M^+, 100%), 344 (93), 286(10), 257 (7), 228 (11), 181 (8), 165 (70), 152 (15), 115 (16), 91 (17), 77 (62) and 51 (15).

2,6-Dimorpholino-4-tritylphenol (8a)

The second fraction (75–70% *n*-hexane) gave a colorless crystals, recrystallized from acetone to yield 0.71 g (35% yield) **8a**. M.p.: 190–192 °C; (Found C, 78.20; H, 6.78; N, 5.51. $C_{33}H_{34}N_2O_3$. requires C, 78.23; H, 6.76; N, 5.53%); IR (KBr): $\overline{\nu}$ = 3239 (OH), 3054, 3025(=CH, CH_2), 1598 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 2.83 (m, 8H, 2 $-CH_2NCH_2-$), 3.81 (m, 8H, 2 $-CH_2OCH_2-$), 6.66 (s, 1H, OH), 7.17 - 7.28 (m, 17H, ArH) ppm; ^{13}C NMR: δ = 53.4 (C2, C6 of mopholine rings), 64.09 (CPh_3), 66.05 (C3, C5 of of mopholine rings), 104.15, 123.09, 126.2, 129.2, 131.9, 141.16, 146.3, 147.9 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 506 (M^+, 85%), 475 (35), 459 (13), 433 (7), 391 (8), 339 (9), 313 (10), 254 (10), 243 (37), 235 (11), 178 (8), 165 (100), 152 (15), 115 (16), 91 (27), 77 (37) and 51 (15).

3-Morpholino-5-tritylbenzene-1,2-diol (9a)

The third fraction (70–65% *n*-hexane) yielded colorless crystals, recrystallized from acetone/*n*-hexane to form 0.21 g (12%) **9a**. M.p.: mp 295-297 °C. (Found C, 79.65; H, 6.20; N, 3.23. $C_{29}H_{27}NO_3$ requires C, 79.61; H, 6.22; N, 3.20%); IR (KBr): $\overline{\nu}$ = 3455 (OH), 3052 (=CH, CH_2), 1613 (C=C) cm^{-1}; ^1H NMR (300 MHz, DMSO-*d*6) δ = 2.68 (m, 4H, $-CH_2NCH_2$), 3.21 (m, 4H, $-CH_2OCH_2-$), 6.67, 6.70 (2d, *J* = 2.7 Hz, 2H, ArH), 7.10 - 7.37 (m, 15H, ArH), 8.80 (s, 2H, 2OH) ppm; ^{13}C NMR: δ = 56.41 (C2, C6 of mopholine ring), 63.24 (CPh_3), 67.54 (C3, C5 of of mopholine ring), 106.53,116.71, 121.34, 124.64, 127.26, 129.79, 130.39,139.54, 142.16, 145.37, 148.19 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 437 (M^+, 40%), 408 (5), 380(3), 165 (15), 154 (8), 115 (16), 105 (13), 91 (35), and 77 (100).

2-(Piperidin-1-yl)-4-tritylphenol (7b)

The first fraction (85–80% *n*-hexane) afforded colorless crystals, recrystallized from ethyl acetate/*n*-hexane to form 0.30 g (18%) **7b.** M.p.: 233-235 °C; (Found C, 85.93; H, 7.06; N, 3.39. $C_{30}H_{29}NO$. requires : C, 85.88; H, 6.97; N, 3.34%); IR (KBr): $\overline{\nu}$ = 3411 (OH), 3055 (CH), 1580 (C=C) cm^{-1}; ^1H NMR (300 MHz, DMSO-*d*6) δ = 1.66 (m, 6H, CH_2 at 4 position and 2 CH_2 at 3, 5 positions of piperidine ring), 3.51 (m, 4H, 2 CH_2 at 2, 6 positions of piperidine ring), 6.40, 6.61 (2d, *J* = 7.2 Hz, 2ArH), 6.71 (s, 1H, ArH), 7.08 – 7.33 (m, 15H, ArH), 8.87 (s, 1H, OH) ppm; ^{13}C NMR: 25.31 (CH_2), 26.11 (CH_2), 55.21 (- CH_2NCH_2 -), 62.84 (CPh_3), 106.33,117.41, 122.44, 123.61, 126.46, 129.44, 130.19,138.24, 142.66, 145.57, 147.49 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 419 (M^+, 100%), 342 (63), 284(20), 255 (27), 226 (17), 179 (28), 165 (40), 152 (35), 115 (26), 91 (14), 77 (52) and 51 (25).

2,6-Di(piperidin-1-yl)-4-tritylphenol (8b)

The second fraction (80–75% *n*-hexane) gave colorless crystals, recrystallized from ethylacetate to form 0.66 g (33 %) **8b**. M.p.: 162–164 °C; (Found C, 83.66; H, 7.60; N, 5.54. $C_{35}H_{38}N_2O$. requires C, 83.63; H, 7.62; N, 5.57%); IR (KBr): $\overline{\nu}$ = 3363 (OH), 3058, 3025(=CH, CH_2), 1602 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 1.50 (m, 4H, $2CH_2$, piperidine rings protons) 1.65 (m, 8H, 4 $-CH_2-$, piperidine rings protons), 2.73 (m, 8H, 2 $-CH_2NCH_2-$), 6.59 (s, 1H, OH), 7.14 - 7.24 (m, 17ArH) ppm; ^{13}C NMR: 24.39 (CH_2), 26.45 (CH_2), 56.24 (- CH_2NCH_2 -), 61.94 (CPh_3), 107.23,116.42, 119.56, 122.40, 123.69, 126.16, 129.74, 130.49,138.94, 142.86,143.91, 145.57, 147.49, 148.12 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 502 (M^+, 100%), 433 (15), 342 (9), 251(20), 243 (17), 165 (20), and 84 (15).

3-(Piperidin-1-yl)-5-tritylbenzene-1,2-diol (9b)

The third fraction (65–60% *n*-hexane) yielded colorless crystals, recrystallized from acetone/*n*-hexane to give 0.21 g (12 %) **9b**. M.p.: 230-232 °C; (Found C, 82.79; H, 6.77; N, 3.28. $C_{30}H_{29}NO_2$ requires C, 82.73; H, 6.71; N, 3.22%); IR (KBr): $\overline{\nu}$ = 3425 (OH), 3049 (=CH, CH_2), 1610 (C=C) cm^{-1}; ^1H NMR (500 MHz, DMSO-*d*6)) δ = 1.72 (m, 6H, CH_2 at 4 position and 2 CH_2 at 3, 5 positions of piperidine ring), 3.22 (m, 4H, 2

CH_2 at 2, 6 positions of piperidine ring), 6.55, 6.65 (2d, J = 2.8 Hz, 2H, ArH), 7.23 - 7.43 (m, 15H, ArH), 8.95 (s, 2H, 2OH) ppm; ^{13}C NMR: 24.21 (CH_2), 26.19 (CH_2), 57.25 (- CH_2NCH_2 -), 64.83 (CPh_3), 107.53,116.61, 121.74, 123.67, 126.06, 129.14, 130.39,139.54, 143.56, 145.17, 147.79 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 435 (M^+, 60%), 406 (15), 378 (43), 165 (18), 154 (28), 115 (15), 105 (27), 91 (35), and 77 (100).

2-(4-Methylpiperazin-1-yl)-4-tritylphenol (7c)

The first fraction (90–85% *n*-hexane) afforded a colourless crystal, recrystallized from ethanol to give 0.35 g (33%) **7c**. M.p.: 238-240 °C; (Found C, 82.97; H, 6.99; N, 6.49. $C_{30}H_{30}N_2O$. requires : C, 82.91; H, 6.96; N, 6.45%); IR (KBr): $\bar{\nu}$ = 3440 (OH), 3057 (CH), 1588 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-*d*6) δ = 2.73, 2.89 (m, 8H, 2 -CH_2NCH_2-, piperazine ring), 3.33 (s, 3H, -NCH_3), 6.36 (dd, J = 7.2, 2.4 Hz, ArH), 6.53 (d, 1H, J = 2.4 Hz, ArH), 6.63 (d, J = 7.2 Hz, 1H, ArH), 7.11- 7.32 (m, ArH), 7.95 (s, 1H, OH) ppm ; ^{13}C NMR: 41.91 (NMe), 54.09, 56.15 (- CH_2NCH_2 -), 66.43 (CPh_3), 106.33,116.41, 121.34, 122.67, 127.16, 129.54, 130.19,138.94, 143.16, 146.27, 148.71 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 434 (M^+, 54%), 352 (100), 334 (13), 275(55), 257 (17), 228 (11), 197 (8), 165 (7), 149 (15), 115 (16), 77 (62) and 51 (15).

2,6-bis(4-methylpiperazin-1-yl)-4-tritylphenol (8c)

The second fraction (85–80% *n*-hexane) gave colorless crystals, recrystallized from echloroform/*n*-hexane to yield 0.63 g (30% yield) **8c**. M.p.: 172–174°C. (Found C, 78.96; H, 7.64; N, 10.58. $C_{35}H_{40}N_4O$. requires C, 78.91; H, 7.57; N, 10.52%); IR (KBr): $\bar{\nu}$ = 3423 (OH), 3050, 3025 (=CH, CH_2), 1612 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 2.89, 3.14 (m, 16H, 4 -CH_2NCH_2-, piperazine rings), 3.33, 3.39 [2s, 6H, 2 -NCH_3), 6.26 (d, J = 2.4 Hz, ArH), 6.43 (d, 1H, J = 2.4 Hz, ArH), 7.15- 7.39 (m, ArH), 7.85 (s, 1H, OH) ppm; ^{13}C NMR: 43.11, 44.51 (NMe), 54.69, 56.05 (- CH_2NCH_2 -), 65.49 (CPh_3), 106.13, 116.81, 122.24, 122.77, 126.76, 129.84, 130.29,139.91, 143.36, 147.17, 149.61 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 532 (M^+, 34%), 352 (10), 334 (33), 275 (25), 257 (15), 228 (31), 197 (18), 165 (23), 149 (18), 115 (36), 77 (100) and 51 (15).

3-(4-Methylpiperazin-1-yl)-5-tritylbenzene-1,2-diol (9c)

The third fraction (80–70% *n*-hexane) yielded colorless crystals, recrystallized from ethyl acetate/*n*-hexane to give 0.20 g (11% yield) **9c**. M.p.: 222–224 °C; (Found C, 80.04; H, 6.79; N, 6.28. $C_{30}H_{30}N_2O_2$ requires C, 79.97; H, 6.71; N, 6.22%); IR (KBr): $\bar{\nu}$ = 3417 (OH) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 2.88, 3.38 (2 m, 2 -CH_2NCH_2-, piperazine ring), 3.16 (s, 3H, -NCH_3), 6.77, 6.90 (2d, J = 2.8 Hz, 2H, ArH), 7.10 - 7.37 (m, 15H, ArH), 8.63 (s, 2H, 2OH) ppm; ^{13}C NMR: 43.56 (NMe), 55.39, 56.45 (- CH_2NCH_2 -), 64.93 (CPh_3), 106.73,116.81, 122.04, 123.63, 126.56, 128.94, 130.09,137.94, 143.66, 147.57, 147.71 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 450 (M^+, 35%), 366 (100), 348(53), 165 (15), 153 (28), 115 (16), 105 (13), 91 (35), and 77 (30).

2,6-Di(pyrrolidin-1-yl)-4-tritylphenol (13)

To a suspension of compound **1** (1.40 g, 4 mmol) in dry acetonitrile (30 mL), pyrolidine (**12**) (6 mmol) was added. The mixture was stirred at room temperature for about 3 h. Then, the solid was collected and recrystallized from acetonitrile to give 1.23 g (65%) **13.** M.p.: 160-162°C; (Found C, 83.57; H, 7.26; N, 5.96. $C_{33}H_{34}N_2O$ requires C, 83.51; H, 7.22; N, 5.90%); IR (KBr): $\bar{\nu}$ = 3428 (OH) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.58, 1.74 (2 m, 8H, 2 -CH_2CH_2-, pyrrolidine ring); 2.60, 2.71 (2 m, 8H, 2 -CH_2NCH_2-, pyrrolidine ring); 6.36 (s, 1H, OH); 6.49, 7.31 (m, 17H, ArH) ppm; ^{13}C NMR: 24.67 (CH_2), 54.39, 55.45 (- CH_2NCH_2 -), 65.63 (CPh_3), 106.34, 116.81, 121.74, 123.33, 126.22, 126.57, 128.84, 130.79,136.84, 143.66, 146.11, 147.17, 147.78 (aromatic carbons) ppm; MS (70 eV): *m*/*z* 474 (M^+, 44%), 403 (100, M^+- pyrrolidine), 351(13), 326 (17), 267 (8), 165 (16), 143 (10), 97 (15), and 70 (12).

General procedure for the synthesis of compounds 15 and 16.

The mixture of 3,5-di-tert-butylcyclohexa-3,5-diene-1,2-dione (**14**) (0.44 g, 2 mmol) and cyclic amines (**6**) (3 mmol) in dry acetonitrile (20 mL), was heated under reflux for about 3-5 h. Then, the solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with petroleum ether 60-80 °C and ethyl acetate (increasing amounts) as eluent to give tow fractions **15** and **16**.

2,4-Di-tert-butyl-6-morpholinophenol (15a)

The first fraction (95-90% petroleum ether 60-80°C) yielded a colorless crystalline product, recrystallized from ethyl acetate/n-hexane to give 0.26 g, (45%) **15a.** M.p.: 143-145 °C (Ref.[25]); (Found C, 74.23; H, 10.08; N, 4.90. $C_{18}H_{29}NO_2$ requires C, 74.18; H, 10.03; N, 4.81%); IR (KBr): $\bar{\nu}$ = 3423 (OH), 1617 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-*d*6) δ = 1.24, 1.36 (2s, 18 H, 2 *t*-Bu), 2.75 (t, *J* = 4.5 Hz, 4H, -CH_2NCH_2-), 3.78 (m, 4H, -CH_2OCH_2-), 7.00, 7.o5 (2d, *J* = 2.4 Hz, 2ArH), 7.94 (s, 1H, OH) ppm. ^{13}C NMR: 29.71, 29.91, 31.53 and 31.60 [2 -$(CH_3)_3$], 53.41 (-CH_2NCH_2-), 68.11 (-CH_2OCH_2-), 115.65, 121.12, 134.65, 138.20, 141.55, 147.92 ppm; MS (70 eV): *m/z* 291 (M^+, 100%), 276 (48), 249(10), 218 (12), 188 (8), 145 (11), 88 (16), 57 (7).

2,4-Di-tert-butyl-6-(morpholin-3-ylidene)cyclohexa-2,4-dienone (16a)

The second fraction (90-85% petroleum ether 60-80°C) gave colorless crystals, recrystallized from chloroform/n-hexane to yield 0.14 g (25%) **16a**. M.p.: 183-185 °C; (Found C, 74.76; H, 9.45; N, 4.89. $C_{18}H_{27}NO_2$ requires C, 74.70; H, 9.40; N, 4.84;%); IR (KBr): $\bar{\nu}$ = 3186 (NH), 1642 (C=O), 1591 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.31, 1.45 (2s, 18 H, 2 *t*-Bu), 3.87 (t, *J* = 4.5 Hz, 2H, H at C5), 4.04 (t, 2H, H at C6), 4.42 (d, J = 3.3 Hz, 2H, H at C2), 6.80 (s, 1H, NH), 7.05, 7.32 (2d, *J* = 2.7 Hz, 2ArH) ppm. ^{13}C NMR: 29.82, 29.95, 31.62, 34.62 and 35.57 [2 -$(CH_3)_3$], 50.31 (-NCH_2-), 64.07, 68.34 (-CH_2OCH_2-), 118.19, 123.49, 131.19, 140.38, 143.48, 147.56, 168.23; MS (70 eV): m/z 289 (M^+, 23%), 260 (18), 232 (10), 196 (22), 176 (18), 144 (15), 115 (26), 57 (100).

2,4-Di-tert-butyl-6-(piperidin-1-yl)phenol (15b)

The first fraction (97-95% petroleum ether 60-80°C) produced a colorless crystals, recrystallized from n-hexane to yield 0.28 g (50%) **15b**. M.p.: 81-83°C (Ref.[25]); (Found C, 78.89; H, 10.85; N, 4.89. $C_{19}H_{31}NO$: requires C, 78.84; H, 10.79; N, 4.84%); IR (KBr): $\bar{\nu}$ = 3427 (OH), 1611 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-*d*6) δ = 1.23, 1.36 (2s, 18 H, 2 *t*-Bu), 1.51, 1.69 (2 m, 6H, CH_2 at 4 position and 2 CH_2 at 3, 5 positions of piperidine ring), 2.70 (m, 4H, 2 CH_2 at 2, 6 positions of piperidine ring), 6.98, 7.04 (2d, *J* = 2.4 Hz, 2ArH), 6.89 (s, 1H, OH) ppm; ^{13}C NMR: 24.41 (CH_2), 27.31 (CH_2), 29.53, 31.60, 34.72 and 34.98 [2 - $(CH_3)_3$], 54.41 (-CH_2NCH_2 -), 115.69, 120.42, 133.95, 139.88, 140.95, 147.82 ppm; MS (70 eV): *m/z* 289 (M^+, 63%), 274 (58), 246 (15), 232 (28), 190 (14), 136 (13), 130 (25), 97 (18), 87 (46), 69 (38) 57 (100).

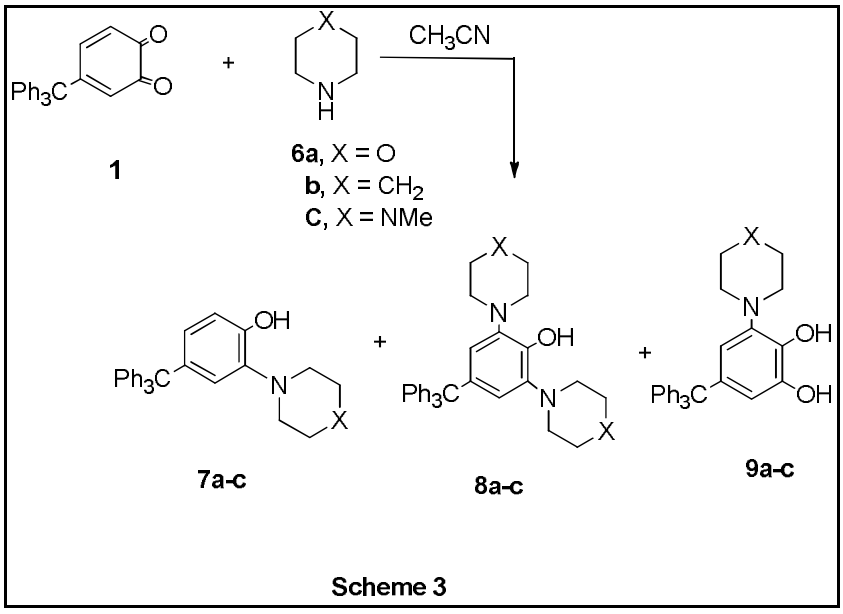
2,4-Di-tert-butyl-6-(piperidin-2-ylidene)cyclohexa-2,4-dienone (16b)

The second fraction (95-90% petroleum ether 60-80°C) gave colorless crystals, recrystallized from dichloromethane/*n*-hexane to form 0.11 g (20%) **16b**. M.p.: 134-136 °C; (Found: C, 79.44; H, 10.23; N, 4.93. $C_{19}H_{29}NO$ requires C, 79.39; H, 10.17; N, 4.87%); IR (KBr): $\bar{\nu}$ = 3226 (NH), 1640 (C=O), 1601 (C=C) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.27, 1.44 (2s, 18 H, 2 *t*-Bu), 1.97 (m, 4H, 2 CH_2), 2.65 (m, 2 H, CH_2) 3.75 (m, 2 H, CH_2), 6.90 (s, 1H, NH), 7.02, 7.36 (2d, *J* = 2.7 Hz, 2ArH) ppm. ^{13}C NMR: 20.69, 21.95, 29.33, 29.60, 29.81, 31.44, 34.35 and 35.40 [2 - $(CH_3)_3$], 51.31 (- NCH_2 -), 117.39, 118.82, 122.69, 135.59, 139.75, 142.86, 146.91, 171.44 ppm; MS (70 eV): m/z**:** 287 (M^+, 33%), 258 (15), 230 (20), 196 (52), 176 (14), 144 (25), 115 (16), 57 (100).

Results and Discussions

The reaction of 4-triphenylmethyl-1,2-benzoquinone (**1**) with morpholine (**6a**) in acetonitrile at room temperature for 7 h or with reflux for 3h led to the formation of a mixture of products **7**, **8** and **9** (Scheme 3). These products were separated on silica gel by column chromatography. The compounds **7**, **8** and **9** were confirmed by analytical and spectral data (see experimental for details). The IR spectra of **7a** showed intense band in the region of 3400 cm^{-1} of the (OH) stretch. The ^{1}H NMR spectrum showed two triplets at 2.90 and 3.66 ppm due to (8H of morphyl group). The H-5 is split into doublet of doublets with J = 8.7 Hz and 2.4 Hz and the resonance of H-3 shows a *meta* doublet with coupling constant J = 2.4 Hz. The H-6 appears as *ortho* doublet with coupling constant J = 8.7 Hz. These coupling constants are in agreement with the expected vales for 1,2,4-trisubstituted benzene.[24] The OH proton appears as a singlet at chemical shift 8.99 ppm. Compounds **8a** and **9a** were supported by elemental analyses, molecular weight determinations (MS), IR and ^{1}H NMR spectra which were compatible with the assigned structures. The IR spectra of **8a** and **9a** showed two bands at 3239 and 3455

cm^{-1} corresponding to the OH group. The ^1H NMR spectrum of **8a** showed two triplets at δ 2.83 and 3.81 ppm for the morphyl groups and a singlet at δ = 6.66 ppm (OH). The aromatic protons appeared as a multiplet in the region δ = 7.17-7.28 ppm. The ^{13}C NMR spectrum of compound **8a** displayed the carbon atoms of morpholine rings at δ 53.4 and 66.05 ppm, respectively. Furthermore, it also shows quaternary carbons at δ = 64.09 ($\underline{C}Ph_3$). The mass spectrum of **8a** recorded a highest ion peak at *m/e* 506 (Scheme 3). Moreover, X-ray diffraction analysis of **8a** confirms the established configuration. ^1H NMR spectrum of **9a** showed tow multiplets at δ = 1.40 and 2.22 ppm attributable to 4H, ($-CH_2OCH_2$), while the protons $-CH_2NCH_2-$ appeared as tow multiplets at δ = 2.68 and 3.21 ppm. The resonance of phenyl protons at C-4 and C-6 are split into two doublets at δ = 6.67 and 6.70 ppm with *meta* coupling constant 2.7 Hz. These data are in agreement with the values of 1,2,3,5-tetrasubstituted benzenes.[24] The phenyl protons (15 ArH) appeared as a multiplets at 7.10 - 7.37 ppm, while the OH appeared as a singlet at δ = 8.80 ppm.



Scheme 3

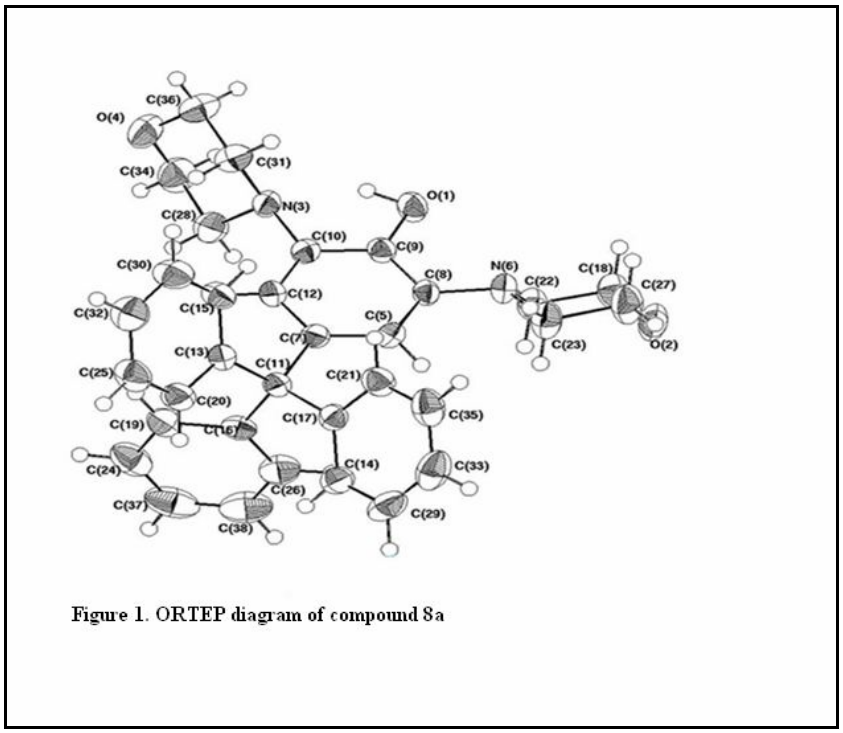
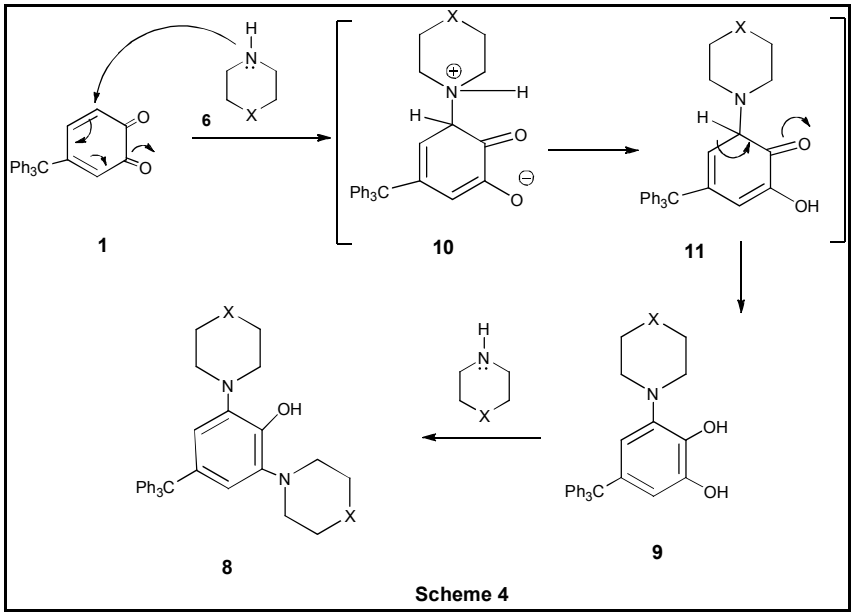


Figure 1. ORTEP diagram of compound 8a

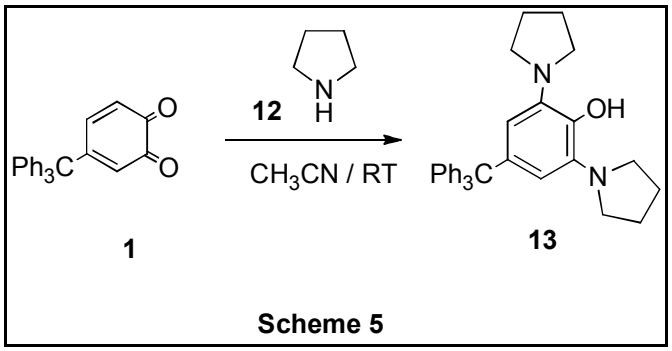
A mechanism proposed for the formation of compounds **8**, **9** is shown in Scheme 4, which based upon the above chemical and spectroscopic results. It is reasonable, therefore, to assign structures **8, 9** for the cyclic amine–quinone adducts. The reaction, which can be rationalized in terms of carbon attack (carbophilic),

presumable, due to the initiated by nucleophilic addition of cyclic amine to the carbon atom at position 6 (Scheme 4). Subsequent rearrangement of **10** to the intermediate **11** is followed by proton transfer to give the products **9** which added another molecule of amines and eliminate a molecule of water to give compounds **8.**



Scheme 4

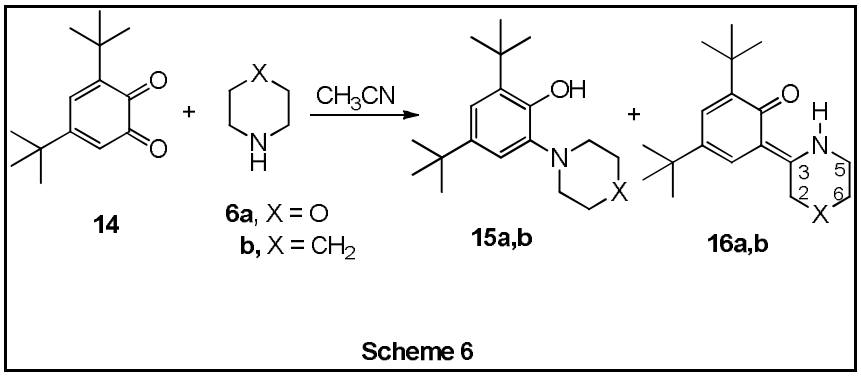
Upon treatment of *o*-quinone **1** with pyrrolidine (**12**) in acetonitrile at room temperature led to the formation of only 1:2 adduct **13** as colourless crystals in 65% yield (Scheme 5). Mass spectroscopy and elemental analysis proved the molecular formula of **13** as $C_{33}H_{34}N_2O$. The IR spectrum of **13** revealed absorption bands at 3428 (OH) cm^{-1}. The OH proton resonated in the ^1H NMR spectrum at δ 6.36, whereas the protons of pyrrolidine rings appeared as a multiplitets at δ 1.58, 1.74 (2 -CH_2CH_2-) and 2.60, 2.71 (2 -CH_2NCH_2-).



Scheme 5

The reaction of 3,5-di-*tert*-butyl-*o*-benzoquinone (**14**) with morpholine and piperidine **6a,b** in boiling acetonitrile afforded the mixture of compounds **15,**[25] and **16** (Scheme 6). The compounds **15** and **16** were separated on silica gel by column chromatography and their structures were elucidated by spectral data and elemental analysis. Mass spectrometry and elemental analysis showed the molecular formula of **15a** as an example as $C_{18}H_{29}NO_2$. The IR spectrum of **15** did not reveal absorptions assigned for carbonyl group, whereas the OH group appeared as a strong absorption band at ν = 3423 cm^{-1}. The ^1H NMR spectrum of **15** showed two singlets at δ 1.24 and 1.36 in addition to two triplets at δ 2.75 and 3.78 ppm (J = 4.5 Hz) corresponding (-CH_2NCH_2-) and (-CH_2OCH_2-) of the morphoyl-protons, respectively. The phenyl ring protons exhibits two doublets at δ 7.00 and 7.05 ppm with singlet at δ 7.94 ppm for OH group. The mass spectrum of the second fraction **16a** displayed the molecular ion (M^++1) peak at m/z 290, which was consistent with the product's structure. The ^1H NMR spectrum of **16a** exhibited two singlets at δ 1.31, 1.45 for 2 *t*-Bu group. The morpholine protons appeared as two triplets at δ 3.87 and 4.04 and doublet at δ 4.42 ppm for protons at C5, C6 and C2 respectively. The spectral data of **16a** displayed a broad singlet (D_2O exchangeable) at δ 6.80 ppm due to NH protons and two douplets at δ 7.05 and 7.32 ppm indicated to H–3 and H-5 protons of phenyl moiety. The ^{13}C

NMR spectrum of **16a** showed 15 distinct resonances, in agreement with the proposed structure. The absorption bands of amino and carbonyl groups appeared at 3186 and 1642 cm^{-1} respectively, in the IR spectrum.



Scheme 6

Conclusion from the present study the reaction of *o*-quinone (**1**) with cyclic secandry amines give a novel type of compounds **7, 8, 9** and **13** not previously observed with other o-quinones. The reaction provides a pathway for the preparation of the reported compounds. When the same reaction carried out with 3,5-di-*tert*-butyl-*o*-benzoquinone (**14**) gave the compounds **15** and **16**.

Acknowledgments

The authors thank the National Research Centre for the financial support (Project No: 10070405).

References

1. Takahata, H.; Banba, Y.; Ouchi, H.; Nemoto, H.; Kato, A.; Adachi, I.; Asymmetric Synthesis of the Four Possible Fagomine Isomers; J. Org. Chem. 2003, 68, 3603-3607.
2. Ouchi, H.; Mihara, Y.; Takahata, H.; A New Route to Diverse 1-Azasugars from *N*- Boc-5-hydroxy-3-piperidene as a Common Building Block J. Org. Chem. 2005, 70, 5207-5214.
3. Hurley, P.B.; Dake, G.R., Synthetic Studies toward Halichlorine: Complex Azaspirocycle Formation with Use of an NBS-Promoted Semipinacol Reaction; J. Org. Chem. 2008, 73, 4131-4138.
4. Misra, V.S.; Singh, S.; Agarwal, R.; Chaudhary, K.C., 2-Bromo-N'-[(E)-4-hydroxybenzylidene]-5-methoxybenzohydrazide. J. Chemical Soc., Pak. 1981, 3, 209-213.
5. Agarwal, R.; Chandhary, K. C.; Misra, V. S.; Synthesis of 1-(4-morpholinophenyl)-4-(3,4-disubstituted benzylidine) imidazolidin-5-ones as CNS active. Indian J Chem B. 1983, 22, 308–10.
6. Agarwal, R.; Agarwal, C.; Singh, C.; Misra, V. S.; Synthesis of 1-(2-arylindol-3-yl)-2[3-(p-morpholinophenyl)-6,8-disubstituted-quinazolin-4(3H)-ones. J Chem Soc Pak. 1984, 6, 84–94.
7. Varma, M. G.; Sharma, V. R.; Saxena, A. K.; Bhalla, T. N.; Sinha, J. N.; Bhargava, K. P.; Antiinflammatory activity of amino acylbenzoates. Pharmacol Res Comm. 1984; 16, 9–20.
8. Varma, R.S.; Prakash, R.; Khan, M.M.; Ali, A. Synthesis of 1-(4-anilino)-morpholines/piperidine and related compounds potential biodynamic agents Indian Drugs 1986, 23, 345-349.
9. Varma, R.S.; Prakash, R.; Prasad, C.R., Synthesis of 1-(4-anilino)-morpholines/piperidine and related compondsas CNS active agents. J Chem Soc Pak. J. Chem. Soc., Pak. 1986, 8, 117-123.
10. Moellering, R.C., Linezolid: The First Oxazolidinone Antimicrobial, Ann. Intern. Med. 2003, 138, 135-143.
11. Flagothier, C.; Piérard-Franchimont, C.; Piérard, G.E., New insights into the effect of amorolfine nail lacquer Mycoses 2005, 48, 91-94.
12. Deshmukh, M.D.; Doshi, A.G., Synthesis of new Schiff bases and their antimicrobial activity. Orient. J. Chem. 1995, 11, 85-86.
13. Indreen, M.; Siddique, M.; Patil, S.D.; Doshi, A.G.; Raut, A.W., Synthesis of Schiff bases of thiophene-2-carboxaldehyde and its antimicrobial activity. Orient. J. Chem. 2001, 17, 131-133.
14. Sridhar, S.K.; Saravanan, M.; Ramesh, A., Synthesis and antibacterial screening of hydrazones Shiff and Mannich bases of isatin derivatives. Eur. J. Med. Chem. 2001, 36, 615-625.

15. Panneerselvam, P.; Nair, R.R.; Vijayalakshmi, G.; Subramanian, E.H.; Sridhar, S.K., Synthesis of Schiff bases of 4-(4-aminophenyl)-morpholine as potential antimicrobial agents. Eur. J. Med. Chem. 2005, 40, 225-229.
16. Alexander, R.; Balasundaram, A.; Batchelor, M.; Brookings, D.; Crépy, K.; Crabbe, T.; Deltent, M.-F.; Driessens, F.; Gill, A.; Harris, S.; Hutchinson, G.; Kulisa, C.; Merriman, M.; Mistry, P.; Parton, T.; Turner, J.; Whitcombe, I.; Wright, S., 4-(1,3-Thiazol-2-yl)morpholine derivatives as inhibitors of phosphoinositide 3-kinase Bioorg. Med. Chem. Lett. 2008, 18, 4316-4320.
17. Hahn, V.; Mikolasch, A.; Wende, K.; Bartrow, H.; Lindequist, U.; Schauer, F., Synthesis of model morpholine derivatives with biological activities by laccase-catalysed reactions. Biotechnol. Appl. Biochem. 2009, 54, 187-195.
18. Yoda, H., Recent Advances in the Synthesis of Naturally Occurring Polyhydroxylated Alkaloids. Curr. Org. Chem. 2002, 6, 223-243.
19. Pierpont, C. G.; Buchanan, R. M., Transition metal complexes of *o*-benzoquinone, *o*-semiquinone, and catecholate ligands. Coord. Chem. Rev. 1981, 38, 45-87.
20. Sidky, M.M.; Osman, F.H., Organophosphorus Compounds. XVIII. The Reaction of Alkyl Phosphites with 4-Triphenylmethyl-1,2-benzoquinone. Tetrahedron, 1973, 29, 1725-1730.
21. Osman, F.H., El-Kateb, A. A.; Sidky, M.M., A Simple Preparation of 3-Hydroxy-4-methoxytetraphenylmethane. Egypt. J. Chem., 1985, 28, 231-234.
22. Osman, F.H.; Abd El-Rahman, N.M.; El-Samahy, F.A., Reaction of Phosphonium Ylides with 4-Triphenylmethyl-1,2-benzoquinone. Tetrahedron, 1993, 49, 8691-8704.
23. Osman, F.H.; El-Samahy, F.A., The Behavior of 4-Triphenylmethyl-1,2-benzoquinone Towards Alkoxycarbonyl methylene(triphenyl)phosphoranes and Triphenylphosphine in Acetic Anhydride. Phosphorus, Sulfer, and Silicon, 1996, 108, 21-30.
24. Zanger, M., The determination of aromatic substitution patterns by nuclear magnetic resonance. Organic Magnetic Resonance, 1972, 4, 1-25.
25. Cherkasov, V.; Druzhkov, N.; Kocherova, T.; Fukin, G.; Shavyrin, A., Interaction of 3,5-di-*tert*-butyl-*o*-benzoquinone with secondary amines a pathway to new sterically hindered N,N-disubstituted *o*-aminophenols. Tetrahedron, 2011, 67, 80-84.

*****