HETEROCYCLES, Vol. 60, No. 10, 2003, pp. 2343 - 2348
Received, 17th July, 2003, Accepted, 28th August, 2003, Published online, 1st September, 2003

EPOXIDATION OF QUINONES WITH UREA HYDROGEN PEROXIDE

Jaime A. Valderrama,* M. Florencia González, and Cristián Torres
Facultad de Química, Pontificia Universidad Católica de Chile. Casilla 306, Santiago-22, Chile. jvalderr@puc.cl

Abstract – Quinones reacted with urea-hydrogen peroxide complex in the presence of a base at room temperature, to give the corresponding quinone epoxides in 22-92% yields. The advantages of this new quinone epoxidation procedure are the requirement of organic solvent media, a easily handled solid reagent and a simple workup procedure.

INTRODUCTION

The hydrogen bonded urea-hydrogen peroxide complex (UHP),[1] a commercially available solid reagent, has been reported as oxidizing agent for a variety of oxidative transformations.[2-6] However, to our knowledge, there is no published work about the application of UHP to the preparation of quinone epoxides. Quinone epoxides are valuable starting products for the synthesis of a broad variety of quinone derivatives. For example, they have been used in the synthesis of the 2,5-dihydroxy-1,4-benzoquinone,[7] a commercially available building block, the (±)-terreic acid[8] and the antiprotozoal active parvaquone.[9]
Here, we report on the epoxidation of 1,4-naphthoquinones by urea-hydrogen peroxide adduct under basic and non-aqueous conditions. This constitutes a practical method to prepare quinone epoxides using a safe and easily handled reagent.

RESULTS AND DISCUSSION

Preliminary experiments have been carried out using UHP and1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane at room temperature (Table 1, Method A). Under these conditions, the epoxidation reaction afforded moderate yields with quinones (**1**) and (**2**) (Entries 1 and 2); it provided poor yields with quinones (**4**) and (**6**) (Entries 4 and 6), and failed to give the sensitive quinone epoxide (**11**)[8] (Entry 3). The halogenated naphthoquinones (**7**) and(**8**) were inert to these treatments.

When the treatment of the starting quinones (**1**-**6**) was carried with UHP and K_2CO_3 in methanol at room temperature (Table 1, Method B), the corresponding epoxides (**9-14**) were isolated in 38-76% yields (Entries 1-5).

It is worth mentioning that treatment of halogenated quinones (**7**) and (**8**) by using method B, afforded the corresponding methoxy-substituted quinones (**15**) and (**16**) (Entries 7 and 8) which were inert to subsequent epoxidation reactions. Formation of compounds (**15**) and (**16**) from halogenated quinones (**7**) and (**8**) can be explained by substitution reactions with methanol, promoted by the base. We verify this assumption by reacting (**7**) and (**8**) with methanol in the presence of K_2CO_3, that afforded products (**15**) and (**16**) in 62 and 74% yields, respectively.

The epoxidation of quinones (**1**-**4**) and (**6**) was examined using UHP and K_2CO_3 in dichloromethane at room temperature (Table 1, Method C). Under these conditions yields of the corresponding quinone epoxides (**9**) and (**14**) were improved in relation to methods A and B, however, the oxidation required long reaction times (Entries 1 and 6). Quinone (**2**) was inert to this treatment and extensive decomposition was observed with quinone **3**.

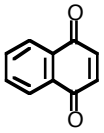
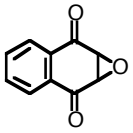
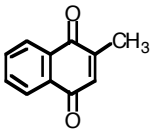
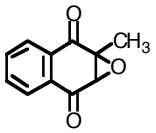
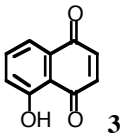
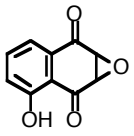
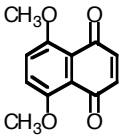
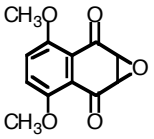
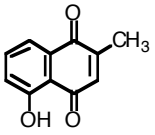
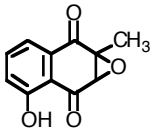
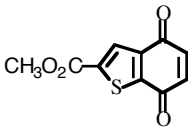
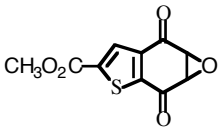
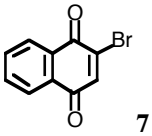
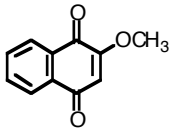
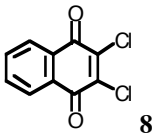
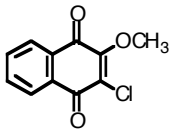
The results summarized in Table 1 show the efficiency of UHP when K_2CO_3 is used as base instead of DBU. It is also significant that epoxidation is, in general, more favorable in methanol than in dichloromethane. This suggest that solubility of the oxidant complex[10] is an essential factor for the oxidative process and explains the lack of reactivity of the less electrophilic quinone (**3**) to epoxidation with UHP-K_2CO_3 in dichloromethane.

In conclusion, we have demonstrated that urea-hydrogen peroxide complex is an efficient reagent for the epoxidation of 1,4-quinones under mild reaction conditions. The potential advantages of this methodology are the use of inexpensive and easily handled reagents and non-aqueous conditions.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR spectra were measured on Bruker AM-200 in $CDCl_3$. Chemical shifts are expressed in ppm downfield relative to TMS (scale) and the coupling constants (*J*) are reported in Hz. The ^{1}H NMR and ^{13}C NMR spectra were acquired in deuteriochloroform at 200 and 50 MHz respectively on a Bruker AM-200 spectrometer. The elemental analysis was performed in the Analytical Laboratory of our Faculty. Analytical thin layer chromatography was performed on Merck DC-Alufolien GF_{254} The UHP and starting quinones (**1**-**3**, **7**), and (**8**) are commercially available. Quinones (**4**) and (**6**) were prepared according to reported methods .[11,12]

Table 1. Reaction products from the reaction of quinones with the UHP complex in basic media

Entry	Quinone	Product	Time (h)	Yield(%)[a]	Method
1	 **1**	 **9**	0.7 0.5 120	65 54 92	A B C
2	 **2**	 **10**	0.5 0.7 -	50 76 -[b]	A B C
3	 **3**	 **11**	- 0.12 -	-[c] 50 -[c]	A B C
4	 **4**	 **12**	1,7 0.5 144	38 71 48	A B C
5	 **5**	 **13**	10	58	B
6	 **6**	 **14**	0.4 0.5 12	22 38 63	A B C
7	 **7**	 **15**	0.5	44	B
8	 **8**	 **16**	- 1 -	-[b] 25 -[b]	A B C

a) Isolated yields. b) No reaction, c) Decomposition products (TLC)

General procedure:

Method A: A suspension of the quinone (0.50 mmol), urea-hydrogen peroxide (0.056 g, 0.60 mmol), DBU (0.0912 g, 0.60 mmol) in dichloromethane (15 mL) was stirred at rt until a TLC showed that the starting quinone had disappeared (Table 1). Removal of the solvent under reduced pressure followed by chromatography of the residue on silica gel, using dichloromethane as the eluent, gave quinone epoxides (**9**, **10**, **12**) and (**14**).

Method B: A suspension of the quinone (0.50 mmol), urea-hydrogen peroxide (0.056 g, 0.60 mmol), K_2CO_3 (0.083 g, 0.60 mmol) in methanol (15 mL) was stirred at rt until a TLC showed that the starting quinone had disappeared (Table 1). The mixture was partitioned between water (20 mL) and chloroform (20 mL), the organic layer was washed with water (2x10 mL), dried over $MgSO_4$ and evaporated to dryness. Quinone epoxides (**9**-**14**) were purified by chromatography on silica gel.

Method C: The procedure was the same of method B, except that dichloromethane was used as the solvent. Epoxides (**9**, **12**) and (**14)** were purified by column chromatography.

2,3-Epoxy-2,3-dihydro-1,4-naphthoquinone (9): mp: 137-138°C (lit.,[13] mp 134.5-135.5°C), ^{1}H NMR ($CDCl_3$, δ, ppm): 3.99 (s, 2H, 2- and 3-H), 7.70-7.80 (m, 2H, 6- and 7-H) 7.90-8.00 (m, 2H, 5- and 8-H); ^{13}C NMR ($CDCl_3$, δ, ppm): 55.3, 127.1, 131.7, 134.7, 190.7.

2,3-Epoxy-2-methyl-2,3-dihydro-1,4-naphthoquinone (10): mp: 97-99°C (lit.,[14] mp 96-97°C); ^{1}H NMR ($CDCl_3$, δ, ppm): 1.71 (s, 3H, CH_3), 3.84 (s, 1H, 3-H), 7.60-7.80 (m, 2H, 6- and 7-H), 7.80-8.10 (m, 2, 5- and 8-H); ^{13}C NMR ($CDCl_3$, δ, ppm): 14.7, 61.4, 61.5, 126.7, 127.4, 132.0, 132.1, 134.4, 134.6, 191.8, 191.9. . The ^{1}H NMR spectrum was identical with that reported.[14]

2,3-Epoxy-5-hydroxy-2,3-dihydro-1,4-naphthoquinone (11): mp: 146-148°C (lit.,[8] mp 144-145 °C), IR (KBr, δ, cm-1); ^{1}H NMR ($CDCl_3$, δ, ppm): 3.98 (d, 1H, J = 3.70 Hz, 2- or 3-H), 4.01 (d, 1H, J = 3.70 Hz, 3- or 2-H), 7.28 (dd, 1H, J = 8.24, 1.31 Hz, 6-H), 7.50-7.70 (m, 2H, 7- and 8-H), 11.22 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, δ, ppm): 55.1, 55.4, 114.2, 119.6, 124.7, 131.9, 137.4, 161.8, 189.7, 195.8.

5,8-Dimethoxy-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone (12): mp: 195-196 °C (lit.,[11] m.p. 195 °C); ^{1}H NMR ($CDCl_3$, δ, ppm): 3.88 (s, 6H, $2CH_3$), 3.98 /s, 2H, 2- and 3-H), 7.22 (s, 2H, 6- and 7-H ; ^{13}C NMR ($CDCl_3$, δ, ppm): 55.4, 55.6, 119.1, 121.3, 152.3, 191.0.

2-Methyl-5-hydroxy-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone (13): mp: 91-93°C (lit.,[16] mp 95-96°C); ^{1}H NMR ($CDCl_3$, δ, ppm): 1.71 (s, 3H, CH_3), 3.80 (s, 1H, 3-H), 7.45 (dd, 1H, J = 7.8; 1.7 Hz, 8-H), 7.55 (dd, 1H, J = 7.8; 1.7 Hz, 6-H), 7.63 (t, 1H, J = 7.8 Hz, 7-H), 11.17 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, δ, ppm). 14.6, 61.3, 61.4, 114.4, 119.8, 124.2, 132.2, 137.2, 161.4, 190.8, 196.7. These spectral data coincide with those reported.[15,16]

5,6-Epoxy-2-methoxycarbonyl-5,6-dihydro-benzo[*b*]thiophene-4,7-quinone (14): mp: 94-96°C; ^{1}H NMR ($CDCl_3$, δ, ppm): 3.93 (d, 1H, *J* = 3.45 Hz, 5- or 6-H), 3.95 (s, 3H, CH_3), 3.99 (d, 1H, *J* = 3.45 Hz, 6- or 5-H), 8.06 (s, 1H, 3-H); ^{13}C NMR ($CDCl_3$, δ, ppm): 53.2, 55.4, 55.5, 131.0, 140.0, 141.6, 146.1, 160.9, 164.4, 164.9; Anal. Calcd for $C_{10}H_6O_5S$: C, 50.42; H. 2.54; S, 13.46. Found: C. 51.00; H, 2.40; S, 13.27.

2-Methoxy-1,4-naphthoquinone (15): mp 181-183 °C (lit.,[17] mp 184-184 °C); ^{1}H NMR ($CDCl_3$, δ, ppm): 3.91 (s, 3H, CH_3), 6.18 (s, 1H, 3.H), 7.60-7.90 (m, 2H, 6- and 7-H), 8.10-8.20 (m, 2H, 5- and 8-H); ^{13}C NMR ($CDCl_3$, δ, ppm): 56.4, 109.9, 126.2, 126.7, 131.0, 132.0, 133.4, 134.3, 160.4, 180.1, 184.6. The ^{1}H NMR spectrum was identical with that reported.[17]

2-Chloro-3-methoxy-1,4-naphthoquinone (16): mp: 151-153°C (lit.,[18] mp 153°C); ^{1}H NMR ($CDCl_3$, δ, ppm): 4.32 (s, 3H, CH_3), 7.60-7.80 (m, 2H, 6- and 7-H), 8.00-8.20 (m, 2H, 5- and 8-H); ^{13}C NMR ($CDCl_3$, δ, ppm): 61.8, 126.8, 126.9, 130.8, 131.0, 133.9, 134.4, 156.8, 178.6, 179.7.

ACKNOWLEDGEMENTS

We thank the Fondo Nacional de Ciencia y Tecnología (Grant N° 1020885) for financial support of this study. We are grateful to Dr. Alain Fournet from Institut de Recherche pour le Développement (IRD) for the generous gift of plumbagine.

REFERENCES AND NOTES

1. C.-S. Lu, W. Hughes, and P. A. Giguère, *J. Am. Chem. Soc.*, 1941, **63**, 1507.

2. M. S. Cooper, H. Heaney, A. J. Newbold, and W. R. Sanderson, *Synlett*, 1990, 533.

3. H. Heaney, *Aldrichimica Acta*, 1993, **26**, 35.

4. R. S. Varma and K. P. Naicker, *Org. Lett.*, 1999, **1**, 189.

5. J. Legros, B. Crousse, D. Bonnet-Delpon, and J.-P. Bégué, *Eur. J. Org. Chem.*, 2002, 3290.

6. R. J. J. Nel, H. van Rensburg, P. S. van Heerden, J. Cohetes, and D. Ferreira, *Tetrahedron*, 1999, **55**, 9727.

7. R. G. Jones and H. A. Shonle, *J. Am. Chem. Soc.*, 1945, **67**, 1034.

8. A. Rashid and G. Read, *J. Chem. Soc. C*, 1967, 1323.

9. J. P. A. Harrity, W. J. Kerr, D. Middlemiss, and J. S. Scott, *J. Organomet. Chem.*, 1997, **532**, 219.

10. The urea-hydrogen peroxide complex is soluble in methanol and not soluble in dichloromethane.

11. J. F. Garden and R. H. Thomson, *J. Chem. Soc.*, **1957**, 2483.

12. J. A. Valderrama and C. Valderrama, *Synth. Commun.*, 1997, **27**, 2143.

13. L. F. Fieser, W. F. Campbell, E. M. Fry, and M. D. Gates, Jr. *J. Amer. Chem Soc.*, 1939, **61**, 3216.

14. H. Wynberg and B. Marsman, *J. Org. Chem.*, 1980, **45**, 158.

15. M. Higa, N. Noha, H. Yokaryo, K. Ogihara, and S. Yogi, *Chem. Pharm. Bull.*, 2002, **50**, 590.

16. K. Ogihara, R. Yamashiro, M. Higa, and S. Yogi, *Chem. Pharm. Bull.*, 1997, **45**, 437.

17. F. Fariña, E. Fernández, V. Gimeno, and J. A. Valderrama, *An. Quím.*, 1995, **91**, 220.

18. J. A. VanAllan, W. J. Priest, A. S. Marshall, and G. A. Reynolds, *J. Org. Chem.*, 1968, **33**, 1100.