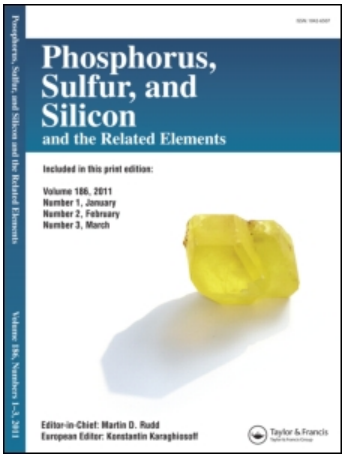


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SOME SULFUR AND NITROGEN SUBSTITUTED XYLOQUINONES

B. Wladislaw[a]; L. Marzorati[a]; S. Lima Netto[a]
[a] Instituto de Química, Universidade de São Paulo, São Paulo, Brazil

To cite this Article Wladislaw, B. , Marzorati, L. and Netto, S. Lima(1987) 'SOME SULFUR AND NITROGEN SUBSTITUTED XYLOQUINONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 33: 3, 173 — 177
To link to this Article: DOI: 10.1080/03086648708074298
URL: http://dx.doi.org/10.1080/03086648708074298

Phosphorus and Sulfur, 1987, Vol. 33, pp. 173–177
Photocopying permitted by license only

SOME SULFUR AND NITROGEN SUBSTITUTED XYLOQUINONES†

B. WLADISLAW*, L. MARZORATI and S. LIMA NETTO
Instituto de Química, Universidade de São Paulo, Caixa Postal 20.780, São Paulo, Brazil

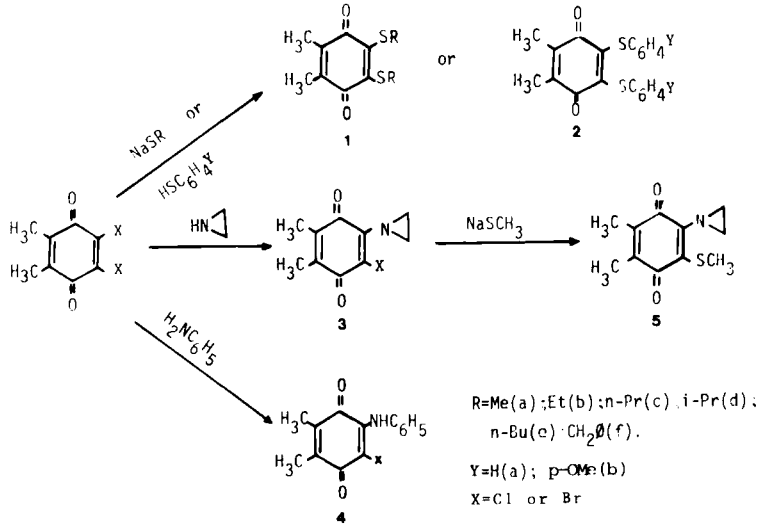
(Received November 8, 1986; in final form February 23, 1987)

This paper reports reactions of dihalogeno-xyloquinone with sulfur and nitrogen nucleophiles, leading to the di- and mono-substituted derivatives, respectively. The mixed nitrogen-sulfur and carbon-nitrogen derivatives were also synthesized. New reactions, oxidation of dimethylthioxyloquinone to yield a mono-sulfinyl derivative and treatment of the latter with thionyl chloride, are described.

Although dihalogeno-xyloquinones are known compounds[2a,b] their reactions with sulfur and nitrogen nucleophiles have not been reported. These reactions seemed to be of interest in view of potential biological activity of the expected thio- and amino-substituted xyloquinones, in comparison with the naphthoquinone and benzoquinone analogues.[3]

RESULTS AND DISCUSSION

The reaction of dichloroxyloquinone with sodium alkyl mercaptides and aromatic thiols afforded, respectively, dialkylthio- (**1**) and diarylthio-xyloquinones (**2**) (Scheme 1).



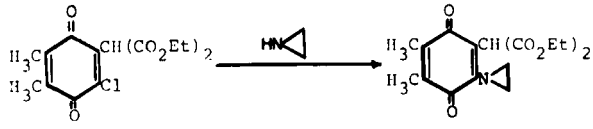
Scheme 1

However, the reactions with aziridine and aniline lead to the corresponding mono-amino-substituted derivatives (**3**) and (**4**). It is noteworthy that all attempts

† Author to whom all correspondence should be addressed.

to substitute the halogen atom by a nitrogen nucleophile in these compounds failed. However, the chlorine atom in (**3**) could be substituted by the methylthio group to give compound (**5**) (Scheme 1).

Another mixed 2,3-disubstituted xyloquinone was obtained starting from a mono-malonyl ester derivative[2b] (**6**), in which the chlorine atom could be substituted by aziridine to afford compound (**7**) (Scheme 2).

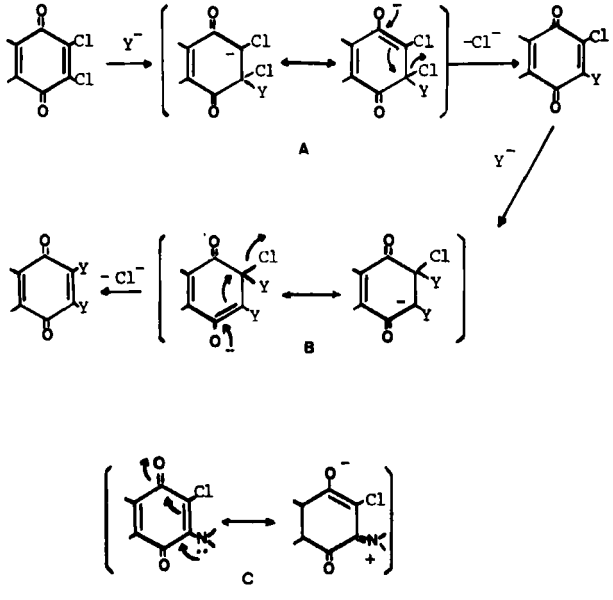


6 7

Scheme 2

It should be mentioned that the lack of reactivity of the 2-halo-3-aminoxyloquinones (**3**) and (**4**) toward nitrogen nucleophiles is in accord with that observed in the naphthoquinone series,[4] and in chloranil;[5] in the latter case being attributed to the mesomeric effect of the amino group. In fact, this effect has been eliminated by acetylation.

However, in view of our experimental results, some additional mechanistic observations can be added. It has been suggested[6,7] that substitution of chlorine atoms by nucleophiles in the enedionic system involves addition + elimination through the anionic intermediates (**A**) and (**B**) (See Scheme 3). It seems reasonable to suggest that the reactivity toward a second substitution should depend on the relative stabilities of the monosubstituted quinone and of the intermediate (**B**).



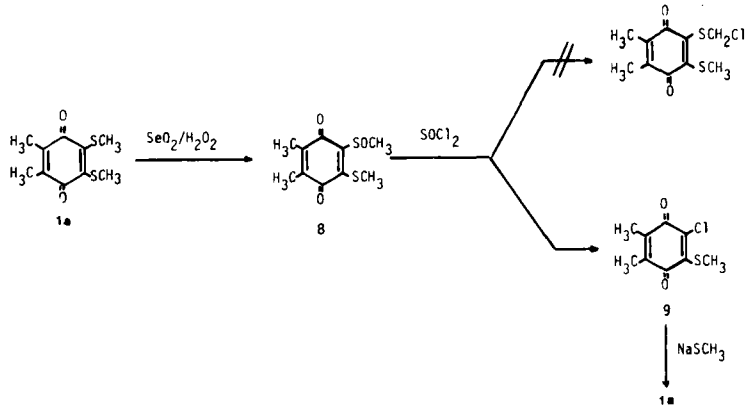
Scheme 3

Thus, the lack of reactivity of the mono-amino-substituted quinones toward weak nucleophiles, such as aniline and aziridine, is due to its increased stabilization (Scheme 3, structure **C**).

The increased reactivity of the dichloroxyloquinone toward sulfur nucleophiles, in comparison with the nitrogen nucleophiles, can be explained, in part, by the decrease of stabilization of the mono-alkylthioxyloquinone due to the decrease of the resonance donor properties of the sulfur atom.[8,9] Furthermore, it seems reasonable to suggest that the intermediate anion **B** (Scheme 3) could be stabilized by expansion of sulfur *d* orbitals.

As for the carbon monosubstituted quinone (**6**) (Scheme 2), the lack of any additional stabilization can be responsible for substitution of chlorine by aziridine.

The reaction of dimethylthioxyloquinone (**1a**) with reagents, such as hydrogen peroxide, 3-chloroperoxybenzoic acid, sodium periodate and perselenic acid, was also investigated. However, only the last one, generated "in situ" from SeO_2 and H_2O_2,[6] proved to be effective, leading to the mono-sulfinyl derivative (**8**) (Scheme 4). The attempts to oxidize the second sulfur atom or the sulfinyl to the sulfonyl group failed. As analogous results were obtained in this laboratory[7] when 2,3-dimethylthionaphthoquinone and 2,3-dimethylthiobenzoquinone-cyclopentadiene adduct[5] were treated with the same reagent, it is now reasonable to suggest that the formation of mono-sulfoxide is characteristic for the 2,3-dialkylthio-enedionic system.



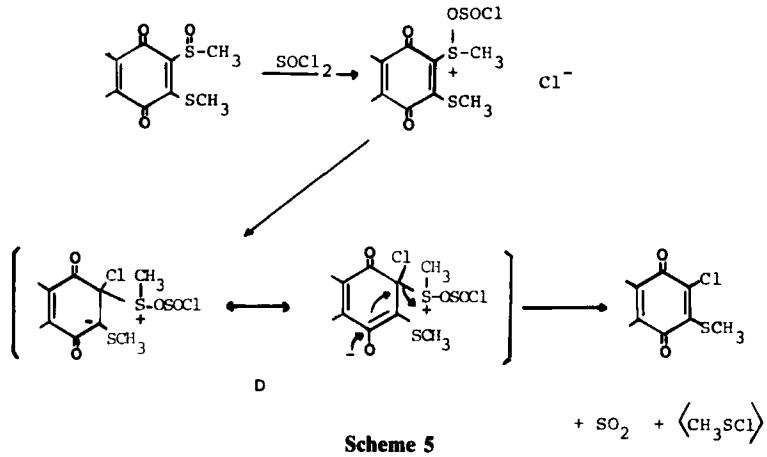
Scheme 4

When sulfoxide (**8**) (Scheme 4) is treated with thionyl chloride, no Pummerer-type reaction takes place but, instead, the substitution of sulfinyl group by chlorine occurs. The resulting 2-chloro-3-methylthioxyloquinone (**9**) was easily transformed, by reaction with sodium methyl mercaptide, into the 2,3-dimethylthioxyloquinone (**1a**).

The unexpected result in the reaction with thionyl chloride is indicative of an addition-elimination mechanism (Scheme 5), following the general mechanism for reactions of halogeno-enedione systems with nucleophiles.

It also seems reasonable to suggest that in this case the stabilization of the

intermediate anion (**D**) by sulfur *d* orbitals could be responsible for the substitution of the sulfinyl group by chlorine.



Scheme 5

EXPERIMENTAL

General Data. The ^{1}H NMR spectra, reported in parts per million (δ), were obtained with a Varian T-60 spectrometer, using TMS as an internal standard. IR spectra were obtained with a Perkin–Elmer Model 283 spectrometer. Column Chromatography and T.L.C. were performed on Merck Kieselgel 60 (70-230 ASTM) and 60G, respectively. All thiols used were commercial products.

2,3-*Dialkylthioxyloquinones* (**1**). *General procedure.* To a suspension of 2,3-dihalogeno-xyloquinone (5 mmol) in dry methanol, was added a methanolic solution (10 mmol) of sodium alkyl mercaptide. After stirring for 15 min., the reaction mixture was poured into acidified water. If solid was formed, it was filtered and recrystallized from methanol. In the case of oily crude product, it was purified by column chromatography.

2,3-*Dimethylthioxyloquinone* (**1a**). Yield 65%. Anal.Calcd. for $C_{10}H_{12}O_2S_2$C 52.7; H 5.26. Found C 52.3; H 5.10. ^{1}H NMR (CCl_4). Signals at 1.98 (6H, s); 2.57 (6H, s). I.R. (CCl_4). Band at 1645 (C=0).

2,3-*Diethylthioxyloquinone* (**1b**). Yield 44% Anal. Calcd. for $C_{12}H_{16}O_2S_2$ C 56.2; H 6.25. Found C 56.6; H 6.20. ^{1}H NMR (CCl_4). Signals at 1.31 (6H, t); 1.99 (6H, s); 3.22 (4H, s). I.R. (CCl_4). Band at 1640 (C=O).

2,3-*Di-n-propylthioxyloquinone* (**1c**). Yield 42%. Anal. Calcd. for $C_{14}H_{20}O_2S_2$ C 59.1; H 7.04. Found C 59.3; H 6.87. ^{1}H NMR (CCl_4). Signals at 1.10 (6H, t); 1.44 (4H, m); 1.99 (6H, s); 3.12 (4H, t). I.R. (CCl_4). Band at 1650 (C=O).

2,3-*Di-i-propylthioxyloquinone* (**1d**). Yield 40%. Anal. Calcd. for $C_{14}H_{20}O_2S_2$ C 59.1; H 7.04. Found C 59.4; H 7.12. ^{1}H NMR (CCl_4). Signals at 1.31 (12H, d); 1.99 (6H, s); 4.12 (2H, m). I.R. (CCl_4). Band at 1640 (C=O).

2,3-*Di-n-butylthioxyloquinone* (**1e**). Yield 30%. Anal. Calcd. for $C_{16}H_{24}O_2S_2$ C 61.5; H 7.69. Found C 61.3; H 7.69. Found C 61.3; H 7.78. ^{1}H NMR (CCl_4). Signals at 0.98 (6H, m); 1.53 (8H, m); 1.99 (6H, s); 3.12 (4H, m). I.R. (CCl_4). Band at 1650 (C=O).

2,3-*Dibenzylthioxyloquinone* (**1f**). Yield 45%. Anal. Calcd. for $C_{22}H_{20}O_2S_2$ C 69.5; H 5.26. Found C 69.5; H 5.33. ^{1}H NMR (CCl_4) 1.95 (6H, s); 4.35 (4H, s); 7.35 (10H, s). I.R. (CCl_4). Band at 1675 (C=O).

2,3-*Diarylthioxyloquinones* (**2**). *General Procedure.* To a suspension of 2,3-dihalogeno-xyloquinone (5 mmol) in 95% ethanol, the aromatic thiol (10 mmol) was added dropwise. After refluxing for 1 hour, the reaction mixture was allowed to cool to room temperature, and, then, poured into acidified water. If necessary, after filtration, the solid was recrystallized from ethanol.

2,3-*Diphenylthioxyloquinone* (**2a**). Yield 47%. Anal. Calcd. for $C_{20}H_{16}O_2S_2$ C 68.2; H 4.54. Found C 68.3; H 4.57. ^{1}H NMR (CCl_4). Signals at 1.96(6H, s); 7.27(10H, s). I.R. ($CHCl_3$). Band at 1650(C=O).

2,3-*Di-p-methoxyphenylthioxyloquinone* (**2b**). Yield 35%. Anal. Calcd. for $C_{22}H_{20}O_4S_2$ C 64.1; H 4.85. Found C 63.8; H 4.97. ^{1}H NMR (CCl_4). Signals at 1.94 (6H, s); 3.78(6H, s); 7.04(8H, m). I.R.(CCl_4). Band at 1655 (C=O).

2-*Aziridinyl*-3-*Chloroxyloquinone* (**3**). To a solution of 2,3-dichloroxyloquinone (5 mmol) in 30 ml of diethyl ether, aziridine was added(10 mmol). The reaction mixture was kept at 0°C, with stirring, for

20 min. The resulting solid was filtered and recrystallized from ethanol (0.80 g; 85%). m.p. 92–4°C. Anal. Calcd. for $C_{10}H_{10}NO_2Cl$ C 56.6; H 4.71; N 6.60. Found C 56.2; H 5.01; N 5.98. ^1H NMR(CCl_4). Signals at 1.98 (6H, s); 2.36(4H, s). I.R.(CCl_4). Band at 1645 (C=O).

2-Anilino-3-bromoxyloquinone (**4**). This compound was obtained by reaction of 2,3-dibromoxyloquinone (3.4 mmol) in 30 ml of diethyl ether with aniline (6.8 mmol) at 40°C. The resulting solid was purified by column chromatography using chloroform as eluent. Anal. Calcd. for $C_{14}H_{12}NO_2Br$ C 54.9; H 3.92; N 4.58. Found C 55.0 H 3.89 N 4.88. ^1H NMR (CCl_4). Signals at 2.08(d, 6H); 6.81–7.43(m, 5H).

2-Aziridinyl-3-methylthioxyloquinone (**5**). To a suspension of 2-aziridinyl-3-chloroxyloquinone (**3**) (1.3 mmol), in 30 ml of dry methanol, was added, dropwise, a solution of sodium methyl mercaptide (1.7 mmol). The reaction mixture was poured into cold water, extracted with 3 portions of 20 ml of dichloromethane and dried. After removal of solvent, the solid residue was recrystallized from methanol, yielding 0.11 g (33%) of dark red crystals m.p. 99–100°C. Anal. Calcd. for $C_{11}H_{13}NO_2S$ C 59.2; H 5.83; N 6.28. Found C 59.2; H 6.09; N 6.13. ^1H NMR (CCl_4). Signals at 1.98(6H, s); 2.26(3H, s); 2.39(4H, s). I.R. (film). Band at 1645 (C=O).

2-Chloro-3-malonylxyloquinone (**6**). This compound was prepared according to the literature procedure.[2b]

2-Aziridinyl-3-malonylxyloquinone (**7**). To a solution of 2-chloro-3-malonylxyloquinone (1.2 mmol) in 10 ml of dry chloroform, aziridine (1.2 mmol) was added. After stirring for 5 min at r.t., the solvent was removed. The orange solid residue was purified by T.L.C., using chloroform as eluent. Anal. Calcd. for $C_{17}H_{21}O_6N$ C 60.90; H 6.27 N 4.18. Found C 60.88 H 6.27 N 4.02. ^1H NMR. Signals at 1.31(6H, t); 2.04(6H, s); 2.36 (4H, s); 4.37(4H, q); 4.81(1H, s).

2-Methylsulfinyl-3-methylthioxyloquinone (**8**). To a solution of 2,3-dimethylthioxyloquinone (**1a**) (3.9 mmol) in 8 ml of methanol, was added a solution (8.1 mmol) of selenium dioxide in 1.0 ml of hydrogen peroxide (29%) and 2 ml of water. After stirring for 5 min. at r.t., the reaction mixture was poured into water, extracted with dichloromethane and dried. After removal of solvent, the dark red residue was treated with cold carbon tetrachloride, yielding a crystalline orange solid (0.34 g; 35%). m.p. 130–1°C. Anal. Calcd. for $C_{10}H_{12}O_3S_2$ C 49.2; H 4.91. Found C 48.7; H 4.96. ^1H NMR ($CDCl_3$). Signals at 2.04 (6H, s); 2.69(3H, s); 2.95(3H, s). IR ($CHCl_3$). Bands at 1660 (C=O) and 1090 (S=O).

Reaction of 2-methylsulfinyl-3-methylthioxyloquinone with thionyl chloride. To a solution of 2-methylsulfinyl-3-methylthioxyloquinone (0.80 mmol) in 5 ml of dry dichloromethane, was added 1.0 ml of thionyl chloride. The reaction mixture was stirred at r.t. for 40 min. The removal of solvent and excess of thionyl chloride left an oil which was purified by column chromatography, using a mixture of hexane/ethyl acetate (6:4) as eluent. ^1H NMR (CCl_4). Signals at 1.98 (6H, s); 2.28(3H, s). IR (CCl_4). Band at 1700 (C=O). The pure product (**9**) reacted with a methanolic solution of sodium methyl mercaptide, affording (**1a**).

ACKNOWLEDGMENT

We thank the "Fundação de Amparo ã Pesquisa do Estado de São Paulo" (FAPESP) for a Scholarship (to S.L.N) and for financial support. We acknowledge also grants (to B.W. and L.M.) from the "Conselho Nacional de Pesquisa-CNPq"

REFERENCES

1. A preliminary report of this work was presented at the 11th International Symposium on the Organic Chemistry of Sulfur, Lindau, Federal Republic of Germany, 1984.
2. (a) K. Fickentscher, *Chem. Ber.*, **102,** 1739 (1969); (b) L. I. Smith and F. L. Austin, *J. Am. Chem. Soc.*, **64,** 528 (1942).
3. S. Petersen, W. Gauss and E. Urbschat, *Angew. Chem.*, **67,** 217 (1955).
4. N. P. Buu-Hoi, *Bull. Soc. Chim. Fr.*, **11,** 578 (1944).
5. A. Marxer, *Helv. Chim. Acta.*, **40**(62), 502 (1957).
6. B. Wladislaw, L. Marzorati and C. Di Vitta, *Phosphorus and Sulfur,* **25,** 147 (1985).
7. M. F. Aldersley, F. M. Dean and R. N. Nazhir, *J. Chem. Soc. Perkin Trans I,* 1753 (1983).
8. D. Smith and P. J. Taylor, *Spectrochim. Acta,* **32A,** 1503 (1976).
9. R. Bedford and P. J. Taylor, *Org. Magn. Reson.*, **9,** 49 (1977).
10. S. Wolfe and L. A. LaJohn, *Tet. Lett.* **24**(35), 3789 (1983).