Tetrahedron Letters, Vol. 33, No. 34, pp. 4983-4984, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

SYNTHESIS OF ISOTOPICALLY LABELLED UBIQUINONES

Andrzej A. Duralski and Anthony Watts

Department of Biochemistry, University of Oxford,

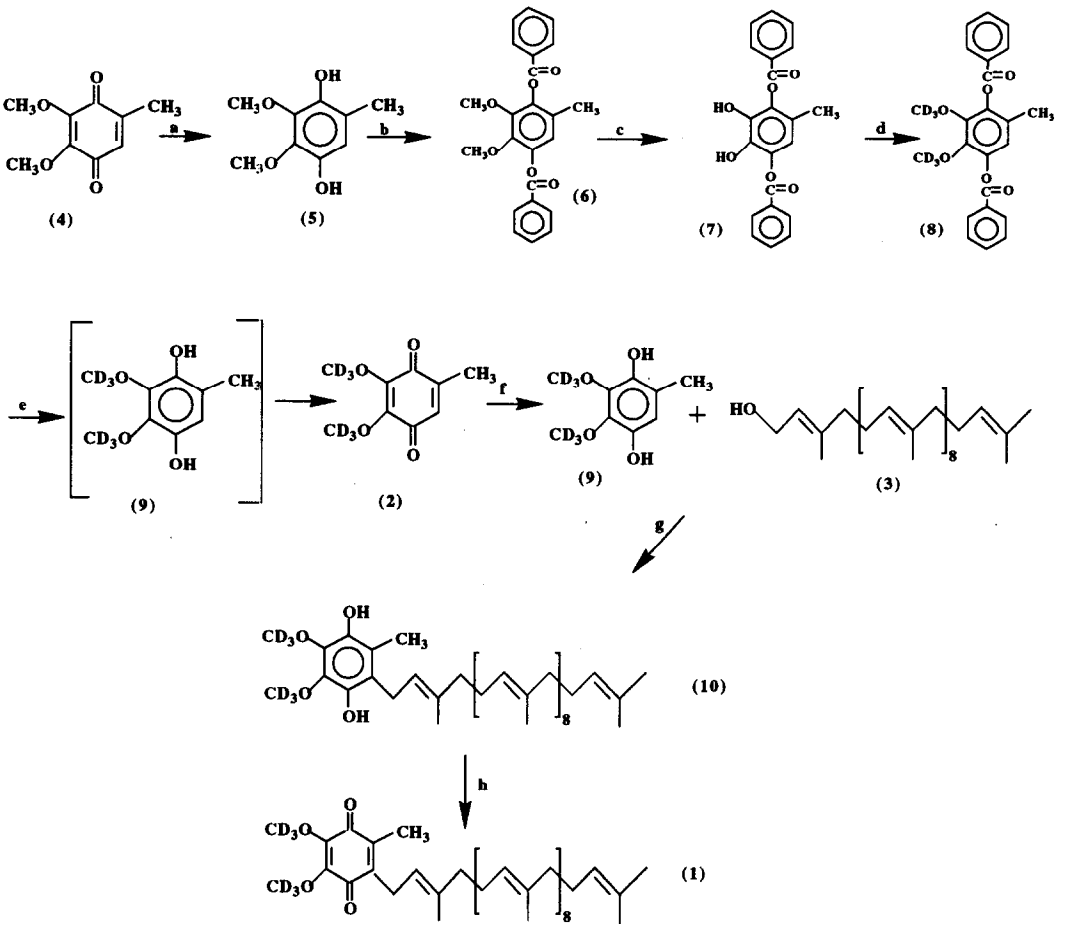
South Parks Road, Oxford, OX1 3QU.

Abstract; Ubiquinones (1) of various chain lengths have been synthesized. The key step involves the condensation of a long chain polyunsaturated alcohol onto an aromatic intermediate. The synthetic methodology allows for the incorporation of isotopic labels in the methoxy groups attached to the ring portion of the molecule.

We wish to report herein a simple, efficient procedure for the synthesis of ubiquinones (1) labelled with deuterium at the methoxy groups in the ring portion of the molecule. Ubiquinone (1) is one of a group of lipidic compounds that are essential electron carriers in the inner mitochondrial membrane and other energy producing membranes of living cells. However, the detail of the molecular function of ubiquinone (1) in electron transport and proton translocation are still unclear[1,2]. Biophysical studies using deuterium NMR spectroscopy could lead to a greater understanding of these processes. Thus it is necessary to have access to the specifically labelled lipid. It has been possible to introduce deuterium biosynthetically into the ubiquinone (1) but this proceeds in a non-specific manner and in low yield[3]. Chemical exchange of the two methoxy groups on the benzoquinone ring of ubiquinone (1) for deuterated methoxyls has also been described. The drawbacks in this procedure, however, are the low yields and side reactions due to drastic reaction conditions[4]. Previous synthetic procedures[5-7] have not been adapted for specific deuterium labelling.

The synthesis involves the condensation of a deuterium labelled benzoquinone (2) to an isoprenoid (3) chain. The labelled benzoquinone (2) is derived from the non-labelled analogue (4). Using this procedure ubiquinones (1) containing two, three and ten isoprene units have been synthesized. This method can be readily adapted for labelling ubiquinone with ^{13}C. All reactions in the synthetic procedure summarised below occur in reasonable yield and only two of the intermediate compounds together with the target compound require purification.

ACKNOWLEDGEMENTS
Funding was provided from the EC contract no. SC1000115 and from the Research and Equipment committee of the University of Oxford and from the EP Abraham Cephalosphorin Research Fund.



(a) aq. Sodium hydrosulphite/ether 2 minutes. (b) Benzoyl chloride (6 molar equivalents), pyridine, room temperature, nitrogen, 24 hours. (c) Sodium iodide (1.25 molar equivalents), trimethylsilyl chloride (1.25 molar equivalents), acetonitrile, nitrogen, 50°C. (d) CD_3I (9 molar equivalents), potassium carbonate (3.6 molar equivalents), acetone, nitrogen, 50°C, 4 hours. (e) Chloroform/methanol/10% aq. KOH (2:7:1 v/v/v). (f) aq. Sodium hydrosulphite/ether, 2 minutes. (g) Boron trifluoride etherate, 1,4-dioxane, nitrogen, room temperature. (h) aq. $FeCl_3$/ether, 2 minutes.

REFERENCES

1. B.L. Trumpower, *J. Bioenerget. Biomembr.*, **1981**, *13*, 1.
2. B.L. Trumpower (Ed), Functions of Quinones in Energy Conserving Systems, Academic Press, New York (1982).
3. W. Lubitz, E.C. Abresch, R.J. Debus, R.A. Isaacson, M.Y. Okamura and G. Feher, *Biochim. Biophys. Acta*, **1985**, *808*, 464.
4. B.A. Cornell, M.A. Keniry, A. Post, R.N. Robertson, L.E. Weir and P.W. Westerman, *Biochemistry*, **1987**, *26*, 7702.
5. K. Suta, S. Inoue and R. Yamaguchi, *J. Org. Chem.*, **1972**, *37*, 1889.
6. Y. Masaki, K. Hashimoto and K. Kaji, *Chem. Pharm. Bull.*, **1984**, *32*, 3959.
7. I Tabushi, H. Kuroda and H. Karakuba, *Tett Letts.*, **1978**, 2086.

(Received in UK 18 June 1992)