Tetrahedron Letters No. 50, pp 4797 - 4798. 0040-4039/79/1208-4797$02.00/0

PREPARATION OF A 4-MONOKETAL OF JUGLONE METHYL ETHER

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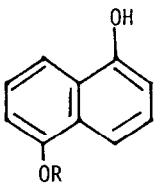
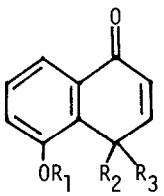
Summary: Oxidation of 5-methoxy-1-naphthol with thallium trinitrate in ethylene glycol/trimethylorthoformate gives the 4-ethylene ketal of juglone methyl ether.

Monoketals of p-quinones, which have been used as important intermediates in several syntheses[1], are made by the selective hydrolysis of the corresponding bisketals (produced by an electrolytic method)[2] or by oxidation of a p-alkoxyphenol.[1,3] McKillop and Taylor[3a] suggested that the monoketal was the last intermediate in the production of p-quinones from phenols by oxidation with thallium trinitrate (TTN).



1a: R=H
1b: R=CH_3



2a: R_1=H; R_2R_3= =O
2b: R_1=CH_3; R_2R_3= =O
2c: R_1=CH_3; R_2=R_3= OCH_3
2d: R_1=CH_3; R_2R_3= -O-CH_2-CH_2-O

We have been studying the oxidation of 1a and 1b to 2a and 2b respectively[4] and now report that monoketals of juglone methyl ether can be obtained by oxidising 1b in a hydroxylic solvent and trimethylorthoformate with TTN at -40°. Originally we worked with methanol which led to the ketal 2c; however ethylene glycol gives better results and leads to the ketal 2d mp 152-154° (petroleum ether/ethyl acetate; 27% yield). This is the first time a monoketal of a quinone has been formed directly from the oxidation of a phenol with a free para position. The isolation of 2d supports the mechanistic ideas proposed by McKillop and Taylor.[3a]

The structure of the ketal follows from its analytical and spectral data and from its conversion on hydrolysis to 2b. The ketal is always accompanied by the quinone 2b; the best method of separating 2b and 2d is by addition of sodium bisulphite which removes the quinone. The ketal is being used in the regioselective preparation of analogues of adriamycinone.[5]

Acknowledgements: This research was assisted by a grant from the David Fund administered by the University of Nebraska Research Council and by a NIH Biomedical Sciences Support Grant 5S07RR07055-12/13. DMSW thanks Dr. Michael Cava for helpful comments.

References

1. G. Buchi and C. P. Mak, J. Am. Chem. Soc., 99, 8073 (1977); D. J. Hart, P. A. Cain and D. A. Evans, ibid., 100, 1548 (1978).
2. D. R. Henton, B. C. Chenard and J. R. Swenton, J. Chem. Soc., Chem. Commun., 326 (1979); M. G. Dolson, D. K. Jackson and J. W. Swenton, ibid., 327 (1979) and earlier references given in these papers.
3. (a) A. McKillop, D. H. Perry, M. Edwards, S. Antus, L. Farkas, M. Nogradi and E. C. Taylor, J. Org. Chem., 41, 282 (1976); (b) G. Buchi, P. S. Chu, A. Hoppamann, C. P. Mak, and A. Pearce, J. Org. Chem., 43, 3983 (1978).
4. D. J. Crouse, S. K. Basu, M. Goemann, D. M. S. Wheeler and M. M. Wheeler, unpublished work.
5. D. M. S. Wheeler, Cancer Chemotherapy Reports, 59 (Part I) 258 (1975); R. S. Grosserode, P. S. Tobin, and D. M. S. Wheeler, Synthetic Communications, 377 (1976); D. J. Crouse, S. L. Hurlbut and D. M. S. Wheeler, Synthetic Communications, in press, 1979.

(Received in USA 13 August 1979)