A CONVERGENT MERCURY MEDIATED LIGNAN SYNTHESIS

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Bis(thiophenyl) derivatives of dibenzylbutyrolactones undergo cyclisation elimination and dehydrogenation when treated with mercuric trifluoroacetate. The process is a short, efficient synthesis of certain arylnaphthalene lignans.

The reaction of gem-dithioaryl compounds with a heavy metal salt or an alkylating agent provides access to stabilised cations or their equivalents under non-acidic conditions. On the other hand benzylic alcohols readily yield cations under mild acidic conditions.¹ Thus it is conceivable that in a molecule (1) containing both groups that ring closure could be carried out in a carefully controlled fashion (Scheme) giving ready access to several important classes of lignan.



In order to test the feasibility of the heavy metal initiated ring closure without possible complexities due to the benzylic alcohol group of (1), we initiated a study of compounds (2), readily available as shown in Scheme 2.² We have previously shown that lactones (2) are converted in high yields to dibenzylbutyrolactones (3), which are members of a class of lignan that includes the first lignans to be discovered in mammals.² We hoped that heavy metal treatment of (2) would yield the stabilised cation (4), which would undergo cyclisation to (5) and heavy metal assisted elimination to (6). Compounds (6) should be valuable intermediates as they could be specifically hydrogenated or undergo dehydrogenation to the naphthalene lactones (7) (Scheme 2).



In the event it was found with all reagents tried $(Hg(0_2C.CF_3)_2, HgCl_2/Pr_2^1NEt, CuCl_2/ZnCl_2)$ in a wide variety of conditions, the only cyclised products that were obtained were the aryInaphthalenes (7). Accepting this, we found that optimum conditions for the cyclisation of (2a) involved an excess of $Hg(0_2CCF_3)_2$ and a stream of oxygen through the reaction mixture to give (7a), retro-justicidin B, in 59% isolated yield. In addition two acyclic lactones assigned structures (8a) and (9a) were isolated as well as diphenyldisulphide.



The second dithioketal (2b) gave two arylnaphthalenes formulated as (7b) and (10) in 20% and 34% yield. Compound (7b) was completely characterised but (10) was never obtained absolutely pure and its structure is based on U.V., 1 H n.m.r. and mass spectral data.

Thus although the process could not be stopped at the desired dihydronaphthalene lignans (6), but instead gave the arylnaphthalene lignans (7) it is a short efficient synthesis of the latter compounds and shows that the concept of the metal mediated cyclisation in non-acidic conditions is viable.

* Except where stated all new compounds were completely characterised.4

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References

- F.E. Zeigler and J.A. Schwartz, <u>J.Org.Chem.</u>, 1978, <u>45</u>, 985; A.G. Gonzalez, J.P. Perez and J.M. Truzillo, <u>Tetrahedron</u>, 1978, <u>34</u>, 1011.
- 2. A. Pelter, R.S. Ward and P. Satyanarayana, <u>Tetrahedron Letters</u>, 1981, <u>22</u>, 1549.
- 3. D.C. Ayres in 'Chemistry of Lignans', (Ed. C.B.S. Rao), Andhra University Press, 1978, Chapter 5.
- 4. $(\underline{7a}): m.p. 218-220^{\circ}; M^{\dagger}; 364.0946(C_{21}H_{16}O_6); \delta(CDCl_3)3.86s(3H), 4.05s(3H), 5.22s(2H), 6.08m(2H), 6.7-7.3m(5H), 8.30s(1H). (\underline{7b}): M^{\dagger}; 320.1047(C_{20}H_{16}O_4); \delta(CDCl_3) 3.85s(3H), 3.97s(3H), 5.25s(2H), 6.9-7.8m(7H), 8.40s(1H). (\underline{10}): M^{\dagger}; 320.1048(C_{20}H_{16}O_4); \delta(CDCl_3) 3.87s(3H), 3.99s(3H), 5.24s(2H), 6.7-8.0m(7H), 8.37s(1H).$

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