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# THE REACTION OF α-CHLORO-α-PHENYLTHIOKETONES WITH PHENOLS: AN ALTERNATIVE SYNTHESIS OF BENZOFURANS

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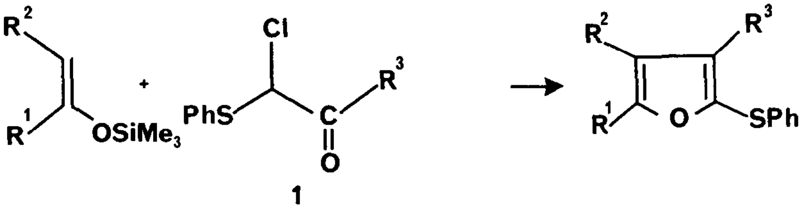
*Summary: A new synthesis of benzofurans has been developed using the Lewis acid catalysed reaction of readily available α-chloro-α-phenylthioketones with phenols.*

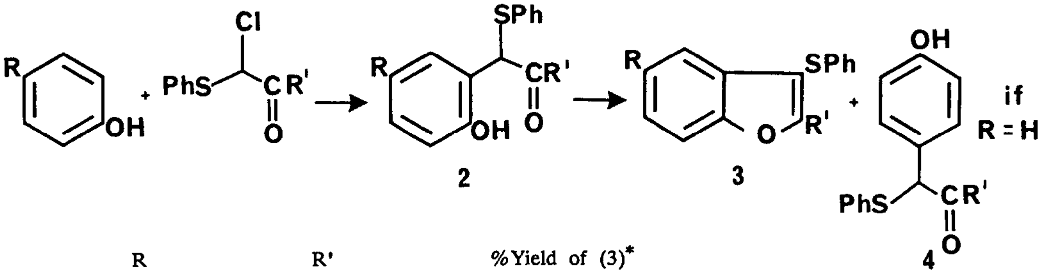
Whilst studying the synthesis of benzofuran analogues of the pharmacologically important indole alkaloids it became apparant that it would be beneficial to develop a convergent one-step synthesis of the benzofuran nucleus. The benefit of such routes is emphasised by a consideration of the structure of such compounds as the anti-tumour agent rocaglamide[1] and the recently elucidated eupomatenoids.[2]

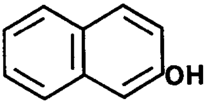
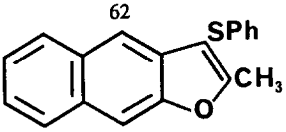
We were drawn to a report of the synthesis of furans by the reaction of an enol ether and the chlorophenylthioketone (1).[3] Combining this observation with our experience of phenylthiolkylation reagents[4] and their known reaction with phenols[5] led us to study the reaction of (1) and its derivatives with simple phenols.



As seen in the TABLE the reaction of (1) with phenol itself gives predominantly reaction at the ortho position to form, presumably, the intermediate ketone (2) which then cyclizes to the benzofuran (3). This is in marked contrast to the reaction of (1) with O-silylated enolates and titanium tetrachloride when initial attack occurs at the carbonyl group[3]. In our reaction one observes about 20% of the para-substituted product (4) which can readily be removed from the benzofuran. The yields of benzofuran are modest which does we believe reflect their instability in the presence of Lewis acids. However the ease with which the benzofuran nucleus can be constructed and the convergent nature of

TABLE



| R | R' | %Yield of (3)* |
|---|---|---|
| H | $CH_3$ | 75 |
| H | $CH_2CH_2Br$ | 61 |
| $CH_3$ | $CH_3$ | 63 |
| $C_2H_5$ | $CH_3$ | 62 |
|  | $CH_3$ | <br>45 |

*based upon the recovered phenol[7]

the procedure are useful advantages which have been of value in our indole alkaloid analogue synthesis since the sulphur group is easily removed under conventional conditions (Ra/Ni-EtOH) so giving ready access to 2-substituted benzofurans.[6]

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## References and Notes

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2. B.A. McKittrick and R. Stevenson, *J. Chem. Soc. Perkin Trans I*, 1983, 475.
3. L. Duhamel and J. Chauvin, *Chemistry Letters*, 1985, 693 and references therein.
4. T.V. Lee and J. Okonkwo, *Tetrahedron Letters*, 1983, 24, 323.
5. I. Fleming and J. Iqbal, *Synthesis*, 1982, 937; K. Suzuki and M. Sekiya, *Chemistry Letters*, 1979, 1241 and M. Kennedy, A.R. Maguire and M.A. McKervey, *Tetrahedron Letters*, 1986, 27, 761.
6. All new compounds gave satisfactory analytical and/or spectral data. X-ray analysis confirmed that initial attack occurs at the phenylthio bearing carbon in contrast to the reaction with sily enol ethers in reference 3.
7. In each case 15-20% of unreacted phenol was recovered.

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