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AN IMPROVED ROUTE TO STEGANONE

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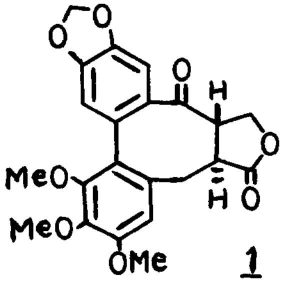
A new route, readily applicable on a large scale, is described to the phenanthrene (8) the key intermediate in the synthesis of steganone (1).

Our efficient synthesis[1] of the bisbenzocyclooctadiene lignan steganone (1) employed the highly substituted phenanthrene (8) as the key intermediate. As the photochemical process we used was not convenient for large scale work we have developed a new high yielding route admirably adapted for scaling up purposes.

The readily available methyl 3,4,5-trimethyoxybenzoate was reduced with lithium aluminium hydride then treated with iodine/silver trifluoroacetate to give the iodo-alcohol[2] (2) m.p. 57-58°. Oxidation with pyridinium dichromate[3] in dichloromethane, followed by condensation with cyclohexylamine gave the iodo-imine (3) m.p. 71-72° in 86% overall yield from the starting ester. Reaction of (3) with a tetrahydrofuran solution of 3,4-methylenedioxyphenylzinc chloride[4] at -20° in the presence of $Ni(PPh_3)_4$[5] followed by hydrolysis with dilute hydrochloric in refluxing dichloromethane gave the biphenyl aldehyde (4) m.p. 89-90° in 80% yield. Condensation of (4) with lithio-2-trimethylsilyl-1,3-dithian[6] in tetrahydrofuran then gave the ketene dithioacetal (5) m.p. 100-101°. Subsequent treatment of (5) with mercuric chloride/hydrochloric acid in refluxing 90% methanol gave the ester (6). Heating (6) with neat pyrrolidine then furnished the amide (7) which, by treatment with phosphorus oxychloride (2 equ.) in refluxing chloroform gave the desired phenanthrene (8) m.p. 133-135° in 63% overall yield from the aldehyde (4).[7]

References and notes

1) D. Becker, L.R. Hughes and R.A. Raphael, J.C.S. Perkin I, 1977, 1674.
2) F.E. Ziegler and J.A. Schwartz, J. Org. Chem., 1978, 43, 985.
3) E.J. Corey and G. Schmidt, Tetrahedron Letters, 1979, 399.
4) Prepared by treatment of 1-bromo-3,4-methylenedioxybenzene with n-butyllithium at -78° followed by reaction with anhydrous zinc chloride (see ref 5)
5) E. Negishi, A.O. King and N. Okukado, J. Org. Chem., 1977, 42, 1821.
6) D. Seebach, M. Kolb and B.-Th. Gröbel, Chem. Ber., 1973, 106, 2277.
7) All structures were fully confirmed by analytical and spectroscopic data.
8) Support from the National Science Foundation (Graduate Fellowship to E.R.L.) and Roche Products Limited is gratefully acknowledged.



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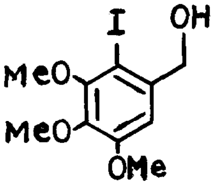

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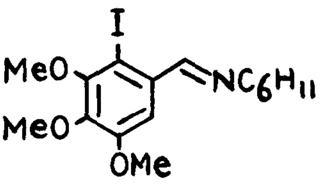

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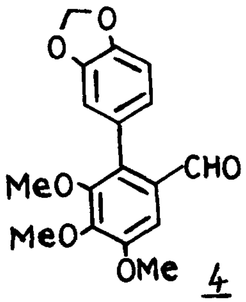

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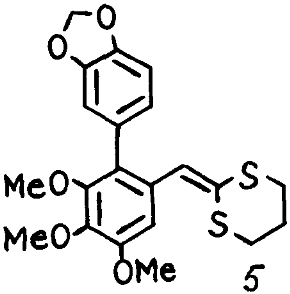

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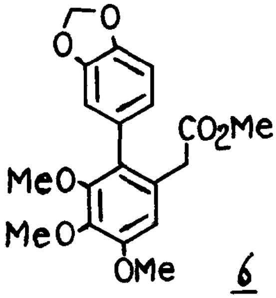

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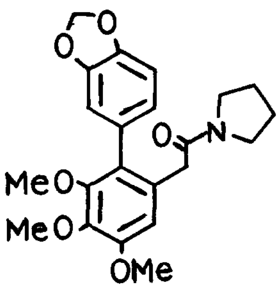

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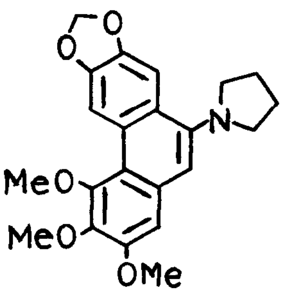

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