An Efficient Furan Ring Transfer Reaction: A Versatile Key Intermediate Leading to the Basic Skeleton of Naturally Occurring Fused Furans

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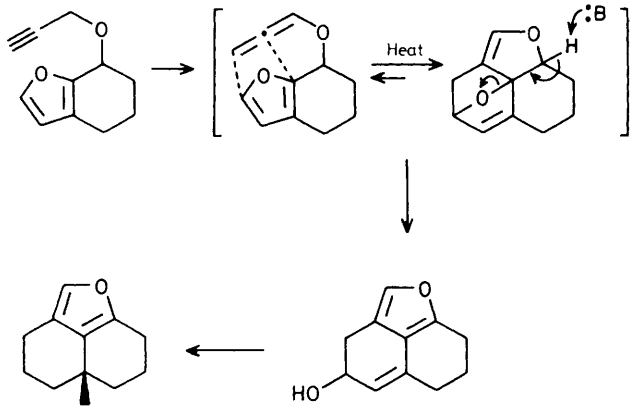
Base-catalysed furan ring transfer reaction of the tetrahydrobenzofuranyl propynyl ether (**2**) followed by Claisen ([3,3]) rearrangement provides a simple route to the tricyclic furan (**8**), a versatile intermediate for the synthesis of viridin and related compounds.

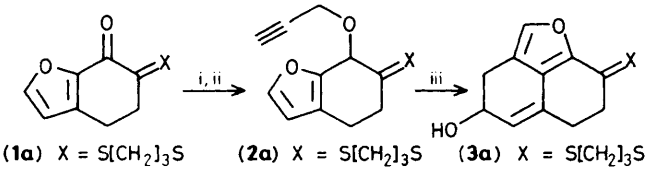
There has been much recent attention on the isolation of steroidal secondary metabolites such as viridin and virone.[1—3] A characteristic of the structures of these metabolites is the fused furo-decalinone system possessing an angular methyl group, which is also present in antifungal marine natural products such as halenaquinone[4] and xestoquinone.[5]

We now describe a new and versatile synthesis of the tricyclic furan (**8**), potentially a key intermediate leading to viridin and related compounds, based on our previously developed furan ring transfer reaction[6] and angular alkylation *via* Claisen rearrangement (Scheme 1).

The ethers (**2a**) and (**2b**) required for the furan ring transfer reaction were prepared in two steps from 7-oxo-4,5,6,7-tetrahydro-1-benzofuran (**1b**)[7] and its dithioacetal derivative (**1a**),† as shown in Scheme 2. Thus, $LiAlH_4$ reduction and propynylation of (**1a**) or (**1b**) gave the corresponding acetylenic compounds (**2a**) or (**2b**)‡ in 60—80% yields. Treatment of (**2a**) or (**2b**) with potassium t-butoxide (10 equiv.) in refluxing t-butyl alcohol (83 °C; 30 min) resulted in a smooth furan ring transfer reaction to give the tricyclic furans (**3a**) or (**3b**)‡ in >90% yields.



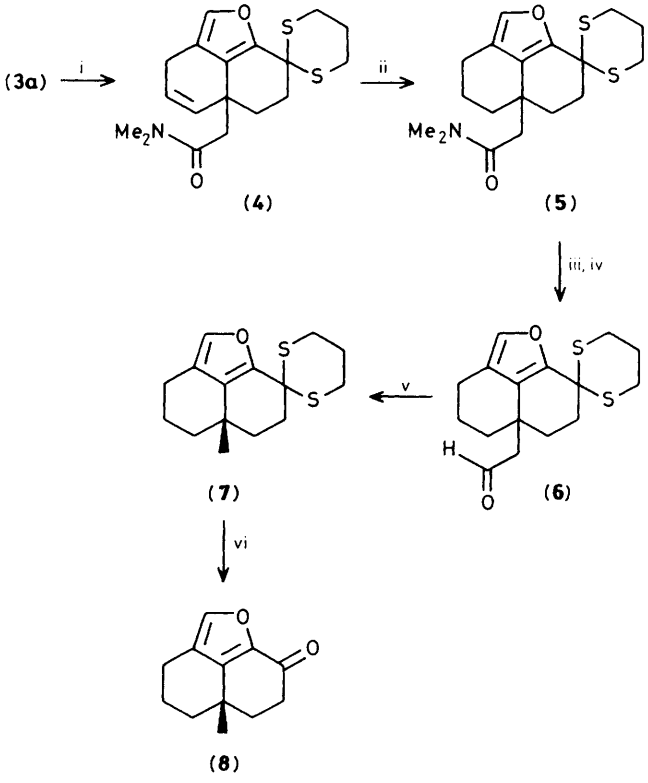
Scheme 1



(**1a**) X = $S[CH_2]_3S$ (**2a**) X = $S[CH_2]_3S$ (**3a**) X = $S[CH_2]_3S$

(**1b**) X = H_2 (**2b**) X = H_2 (**3b**) X = H_2

Scheme 2. *Reagents and conditions:* i, $LiAlH_4$, tetrahydrofuran (THF), room temp., **a** >95%, **b** >90%; ii, Bu^nLi, hexamethylphosphoric triamide (HMPA), THF, then $CH{\equiv}CCH_2Br$, room temp., **a** 82%, **b** 65%; iii, Bu^tOK (10 equiv.), Bu^tOH, 83 °C, 30 min, **a** 92%, **b** 90%.



Scheme 3. *Reagents and conditions:* i, $Me_2NC(OMe)_2Me$, xylene, 140 °C, 30 min, 55—60%; ii, 2,4,6-tri-isopropylphenylsulphonylhydrazine, NEt_3, THF–MeOH, room temp., 100%; iii, $LiEt_3BH$, THF, room temp., 90%; iv, Collins reagent, CH_2Cl_2, 31%; v, $RhCl(PPh_3)_3$, benzene, 80 °C, 92%; vi, $Hg(ClO_4)_2$, THF, 30—40%.

† Compound (**1a**) (m.p. 141—141.5 °C) was easily obtained by treatment of (**1b**) with 1,3-bis(*o*-nitrophenylthio)propane (m.p. 87—89.5 °C) in the presence of NaH in tetrahydrofuran.[8]

‡ All new compounds gave satisfactory analytical and spectral data. (**2a**), m.p. 86.5—87 °C; i.r., $\nu_{max.}$ 3310 and 2120 cm^{-1}; ^1H n.m.r., δ ($CDCl_3$) 7.37 (d, *J* 2 Hz, 1H), 6.24 (d, *J* 2 Hz, 1H), 4.77 (s, 1H), 4.43 (d, *J* 2.5 Hz, 2H), 3.00—2.75 (m, 4H), 2.51 (t, *J* 2.5 Hz, 1H), and 2.73—1.90 (m, 6H). (**3a**), i.r., $\nu_{max.}$ 3390 cm^{-1}; ^1H n.m.r., δ($CDCl_3$) 7.10 (t, *J* 1 Hz, 1H), 5.55 (br. d, *J* 4 Hz, 1H) 4.51 (br. dd, *J* 5.5 and 4. Hz, 1H), 3.71—3.18 (m, 2H), 2.82 (dd, *J* 5.5 and 1 Hz, 2H), and 3.03—1.87 (m, 9H). (**4**), i.r., $\nu_{max.}$ 1635 cm^{-1}; ^1H n.m.r., δ($CDCl_3$) 7.19 (t, *J* 2 Hz, 1H), 6.16 (dm, *J* 9.5 Hz, 1H), 5.89 (dm, *J* 9.5 Hz, 1H), 2.89 (s, 3H), 2.85 (s, 3H), 2.60 (s, 2H), and 3.70—1.60 (m, 12H). (**8**), i.r., $\nu_{max.}$ 1665 cm^{-1}; ^1H n.m.r., δ ($CDCl_3$) 7.33 (t, *J* 1.5 Hz, 1H), 3.10—3.11 (m, 10 H), and 1.33 (s, 3H).

Introduction of a methyl group into the angular position of (**3a**) was achieved *via* the Claisen rearrangement (Scheme 3). Heating of (**3a**) and *N*,*N*-dimethylacetamide dimethyl acetal (3 equiv.) in refluxing xylene (140 °C; 30 min) smoothly gave rise to a [3,3] sigmatropic rearrangement[9] leading to (**4**)‡ in 55—60% yield. Diimide reduction[10] of (**4**) gave the amide (**5**)‡ (m.p. 138—139 °C) which was converted into the aldehyde (**6**)‡ by successive reduction ($LiEt_3BH$)[11] and oxidation (Collins reagent).[12] Decarbonylation using Wilkinson's complex[13] gave (**7**)‡ and oxidative cleavage of the dithioacetal unit of (**7**)[14] afforded the tricyclic furan (**8**)‡ as a colourless oil. Considering the concerted nature of the [3,3] sigmatropic rearrangement, the chirality of the alcohol (**3**) may be effectively transferred into the angular position.[15]

The above method provides a simple means for the construction of fused furan ring systems carrying useful functionality, and we are currently studying the synthesis of natural products including the tricyclic furan skeleton (**8**).

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