Regiocontrolled Synthesis of Furans by a Mercury(II) Catalysed Isomerisation of 1-Alkynyl-2,3-epoxyalcohols

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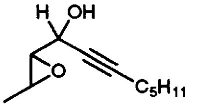
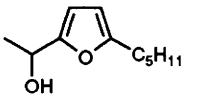
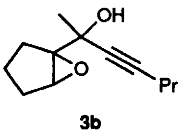
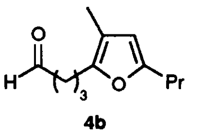
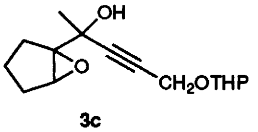
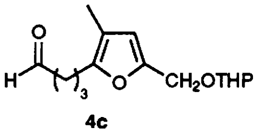
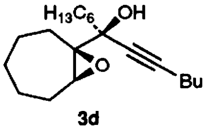
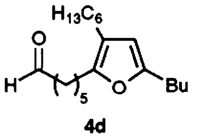
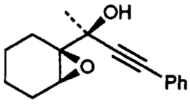
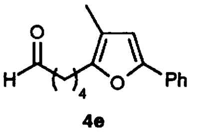
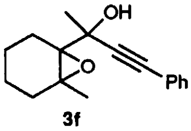
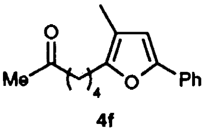
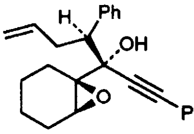
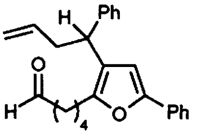
2,3,5-Trisubstituted furans are formed by the reaction of 1-alkynyl-2,3-epoxyalcohols with a catalytic amount of mercury(II) prepared from HgO and dilute sulfuric acid.

The ubiquity of furans in nature, and the variety of pharmaceuticals and compounds of notable flavour and fragrance that contain the furan ring underlies the importance of furans.[1] Additionally, furans serve as diverse intermediates in synthetic organic chemistry.[2] Consequently, the construction of the furan ring, a venerable area of organic synthesis, enjoys continued development of new methods.[1,3–5]

Acetylenic epoxides have been shown to isomerise to furans in both acidic[6] and basic[7] media, and such reactions have been extensively employed in the synthesis of natural products.[3] Esters of 1-alkynyl-2,3-epoxyalcohols undergo reductive elimination to 2-alken-4-yn-1-ols which, by 5-*exo-dig* cyclisation, afford the corresponding furans.[4] In contrast to the above, we report herein an isomerisation of secondary and tertiary 1-alkynyl-2,3-epoxyalcohols **3** to substituted furans **4**, which possess additional oxygenated functionality. The reaction has potential use in the synthesis of biologically active natural products such as furanoid fatty acids[8] and calicogorins[9].

Table 1

Epoxide[a]	*Syn* : *Anti*[b]	Furan	Yield (%)
 **3a**	5 : 4	 **4a**	73
 **3b**	18 : 1	 **4b**	85
 **3c**	3 : 2	 **4c**	55
 **3d**	1 : 0	 **4d**	82
 **3e**	1 : 0	 **4e**	81
 **3f**	13 : 1	 **4f**	75
 **3g**	1 : 0	 **4g**	78

[a] Stereochemistry refers only to relative configurations. [b] For definition see ref. 12.

Reaction of an α,β-unsaturated carbonyl compound **1** with an alkynyllithium (generated by addition of 1.3 equiv. of BuLi to the alkyne at 20 °C) afforded the corresponding enynol **2**. The alcohols **2** were epoxidised with Bu^tOOH (1.5 equiv.) in benzene at 20 °C using $VO(acac)_2$ as the catalyst[10,11] to give a mixture of *syn*- and *anti*-epoxyalcohols **3** (Table 1).

The tertiary cyclic alkynyl epoxides **3b–3g** (*syn* : *anti* mixture;[12] Table 1) were efficiently isomerised to the corresponding furans **4b–4g** upon treatment with mercury(II) in very dilute sulfuric acid.† Under the same conditions, the secondary acyclic epoxide **3a** afforded the furan **4a** as the sole isolated product.

The formation of both **4a** and **4b–g** can be rationalised by invoking an intermediate of the form **5**. Furan **4a** would then arise by dehydration of **5** (R^3 = H), presumably *via* the corresponding oxonium cation. For the alicyclic examples **3b–3g**, direct dehydration is blocked, and the alternative fragmentation with aromatisation occurs, giving the furans **4b–4g**, each containing a carbonyl group at a position determined by the size of the alicyclic ring in the epoxyalcohol **3**. In the present examples no evidence was obtained that the yield of the furan depended upon the ratio of epoxide diastereoisomers used.

The isolation of furan **4e** (55%), containing both tetrahydropyranyl and aldehydic groups, exemplifies the scope of the reaction, and the mild conditions involved. The mechanistic features of this new regiocontrolled route to furans, and its application to the synthesis of furanoid natural products is currently under investigation.

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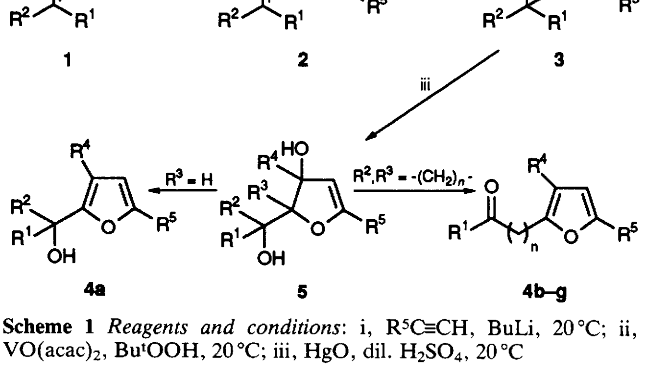

Scheme 1 *Reagents and conditions*: i, $R^5C{\equiv}CH$, BuLi, 20 °C; ii, $VO(acac)_2$, Bu^tOOH, 20 °C; iii, HgO, dil. H_2SO_4, 20 °C

Footnote

† All compounds gave satisfactory spectral data (NMR, IR, MS), and all new compounds gave satisfactory analytical data (HRMS). The procedure is described for **4d**: A solution of 7-(1,2-epoxycyclohept-1-enyl)tridec-5-yn-7-ol (0.3 g, 0.98 mmol) in acetone (30 ml, HPLC grade) was treated with a 0.1 mol dm^{-3} solution of HgO in 2.5% (v/v) H_2SO_4 (0.25 ml). The mixture was stirred for 15 min and neutralised by addition of solid sodium hydrogen carbonate. Filtration and concentration *in vacuo* afforded an oil to which water (3 ml) and diethyl ether (5 ml) were added. Extraction and chromatography (silica; petroleum ether/ethyl acetate) afforded furan **4d** as a colourless oil.

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12 For an explanation, and definition, of *syn* and *anti* as used herein see C. M. Marson, D. W. M. Benzies and A. D. Hobson, *Tetrahedron*, 1991, **47**, 5491.