

## New Entry to the Perhydrofuro[2,3-*b*]furan Ring System

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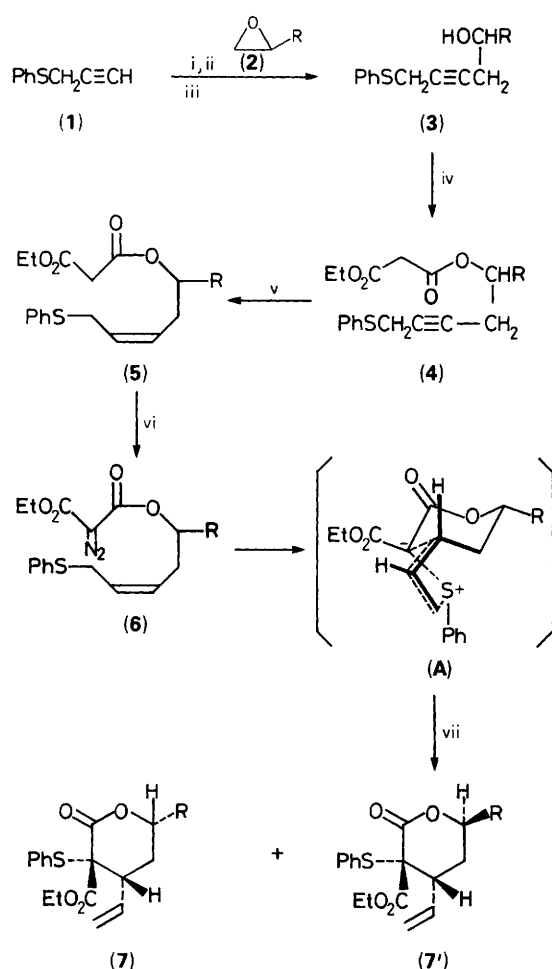
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Treatment of the  $\alpha$ -diazomalonate (**6**) with  $\text{Rh}_2(\text{OAc})_4$  stereoselectively provided substituted valerolactones (**7**) and (**7'**) via the [2,3]sigmatropic rearrangement of a nine-membered cyclic allylsulphonium ylide; the rearrangement product was converted to 5-alkylperhydrofuro[2,3-*b*]furan (**12**) by ozonolysis followed by acid treatment.

Recently we reported a highly efficient and stereoselective synthesis of contiguously substituted butyrolactones by the [2,3]sigmatropic rearrangement of eight-membered cyclic sulphonium ylides.<sup>1</sup> This result prompted us to extend the rearrangement to a nine-membered sulphonium ylide giving

rise to vinylvalerolactone and to examine further conversion to 5-substituted perhydrofuro[2,3-*b*]furan.

The first step was alkylation of the lithium salt of phenyl propargyl sulphide (**1**), prepared with BuLi (1.2 equiv.) in tetrahydrofuran (THF) at  $-35^\circ\text{C}$ , with the epoxide (**2**) (1



**Scheme 1.** Reagents: i, BuLi; ii, THF; iii, BF<sub>3</sub>·Et<sub>2</sub>O; iv, HOCOCH<sub>2</sub>-CO<sub>2</sub>Et, dicyclohexylcarbodiimide, 4-*N,N*-dimethylaminopyridine, CH<sub>2</sub>Cl<sub>2</sub>; v, H<sub>2</sub>, Pd-BaSO<sub>4</sub>, MeOH; vi, TsN<sub>3</sub>, Et<sub>3</sub>N, MeCN; vii, Rh<sub>2</sub>(OAc)<sub>4</sub>, PhH.

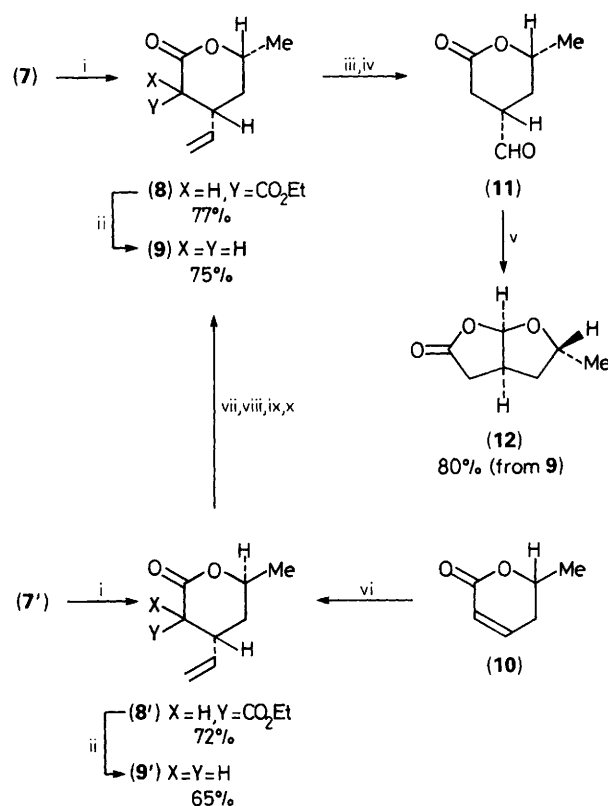
**Table 1.**

R	Yield of product/%				
	(3)	(4)	(5)	(6)	(7) + (7')
Me	93	83	80	87	75(79:21) <sup>a</sup>
Bu	81	95	77	94	74(74:26) <sup>a</sup>
PhCH <sub>2</sub> O	91	90	81	92	80(74:26) <sup>a</sup>

<sup>a</sup> Values in parentheses show the product ratio based on separated diastereoisomers.

equiv.) at -78 °C followed by the immediate addition of BF<sub>3</sub>·Et<sub>2</sub>O (1.2 equiv.),<sup>2</sup> affording the alcohol (3)† in excellent yield (Scheme 1, Table 1). Esterification of (3) thus obtained with ethyl malonyl chloride and pyridine in THF at 0 °C<sup>3</sup> or with malonic acid monoethyl ester, dicyclohexylcarbodiimide, and 4-*N,N*-dimethylaminopyridine in dichloromethane at room temperature<sup>4</sup> provided the malonate (4) in high yield. After hydrogenation of the triple bond of (4) on 5% Pd-BaSO<sub>4</sub> stereoselectively affording the *Z*-alkene (5), reaction of the alkene with toluene-*p*-sulphonyl azide and tri-

† All new compounds reported herein gave satisfactory spectral and microanalytical data.



**Scheme 2.** Reagents: i, Zn, HOAc; ii, NaCl, aq. dimethylsulphoxide; iii, O<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>; iv, Me<sub>2</sub>S; v, *p*-TsOH (Ts = OSO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>-Me), THF; vi, CH<sub>2</sub>=CHMgBr, CuI, THF; vii, K<sub>2</sub>CO<sub>3</sub>, MeOH; viii, N<sub>2</sub>(CO<sub>2</sub>Et)<sub>2</sub>, Ph<sub>3</sub>P, PhCO<sub>2</sub>H; ix, KOH, aq. MeOH; x, conc. HCl, MeOH.

ethylamine in acetonitrile at 40–45 °C over 40 h<sup>3</sup> gave the corresponding diazo-ester (6) in good yield. Treatment of (6) with catalytic Rh<sub>2</sub>(OAc)<sub>4</sub> in refluxing benzene resulted in formation of a stereoisomeric mixture of the valerolactone (7) and its diastereoisomer (7') in high yield. While the stereochemistry of substituents on the lactone ring of (7) was predictable in consideration of the favourable conformation (A) in the transition state of rearrangement, it was unambiguously proved by chemical correlations of (7) and (7') as well as an unequivocal synthesis of the latter.<sup>5</sup>

Reductive desulphurisation of lactones (7) (R = Me) and (7') (R = Me) with zinc powder in acetic acid at 60 °C affording esters (8) and (8') and successive de-ethoxycarbonylation of the resulting esters with sodium chloride in aqueous dimethyl sulphoxide at 150 °C provided lactones (9) and (9') in good overall yields, respectively (Scheme 2).<sup>6</sup> On the other hand, a vinylated lactone was obtained in the well-documented *trans* stereoselective manner by copper(I) salt-catalysed conjugate addition of vinylmagnesium bromide to the lactone (10)<sup>7</sup> and the addition product was identical with (9') derived from (7'). A sequence of reactions of (9'); (i) methanolysis with potassium carbonate in methanol, (ii) Mitsunobu inversion of the resulting hydroxy acid with benzoic acid-diethyl azodicarboxylate-triphenylphosphine,<sup>8</sup> (iii) alkaline hydrolysis of a benzoate formed, and (iv) acid lactonization of a hydroxy acid obtained, provided an isomeric lactone which was identical with the lactone (9) derived from (7). Stereochemical alignment was thus confirmed to be *cis* in (9) with respect to its alkyl and vinyl groups.

Ozonolysis of (9) in dichloromethane at -78 °C followed by reduction with dimethyl sulphide afforded the aldehyde (11),

which was smoothly converted to the 5-methylperhydro-furo[2,3-*b*]furan-2-one (**12**) by catalytic toluene-*p*-sulphonic acid in THF at room temperature. Similar results were obtained with other substrates (**7**) and (**7'**) (*R* = Bu).

Received, 6th November 1989; Com. 9/04766B

## References

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- 2 Though it was alleged that in advance of an epoxide,  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  was added to a lithium acetylide solution to form a presumed alkynylborane (M. Yamaguchi and I. Hirao, *Tetrahedron Lett.*, 1983, **24**, 391), in our case this procedure produced low yields of (**3**). Much better results were obtained by reverse addition in the manner described here. Details of this reaction are now under investigation.
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- 5 The stereochemistry of the phenylthio and vinyl groups depicted for (**7**) and (**7'**) was assigned by analogy with results previously reported (see ref. 1).
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