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

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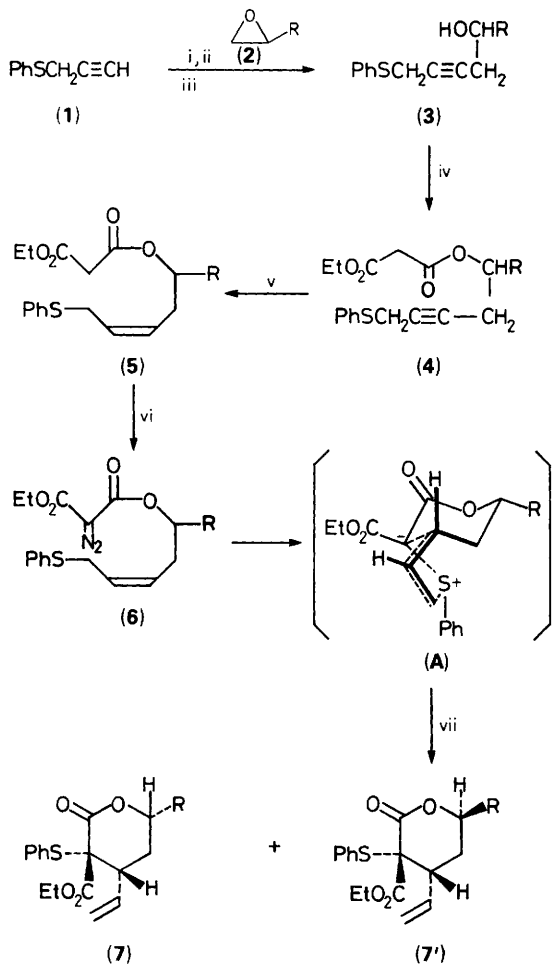
Treatment of the α-diazomalonate (**6**) with $Rh_2(OAc)_4$ stereoselectively provided substituted valerolactones (**7**) and (**7'**) *via* the [2,3]sigmatropic rearrangement of a nine-membered cyclic allylsulphonium ylide; the rearrangement product was converted to 5-alkylperhydrofuro[2,3-*b*]furan (**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.[1] 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 °C, with the epoxide (**2**) (1



Scheme 1. *Reagents:* i, BuLi; ii, THF; iii, $BF_3{\cdot}Et_2O$; iv, $HOCOCH_2CO_2Et$, dicyclohexylcarbodiimide, 4-*N*,*N*-dimethylaminopyridine, CH_2Cl_2; v, H_2, Pd–$BaSO_4$, MeOH; vi, TsN_3, Et_3N, MeCN; vii, $Rh_2(OAc)_4$, PhH.

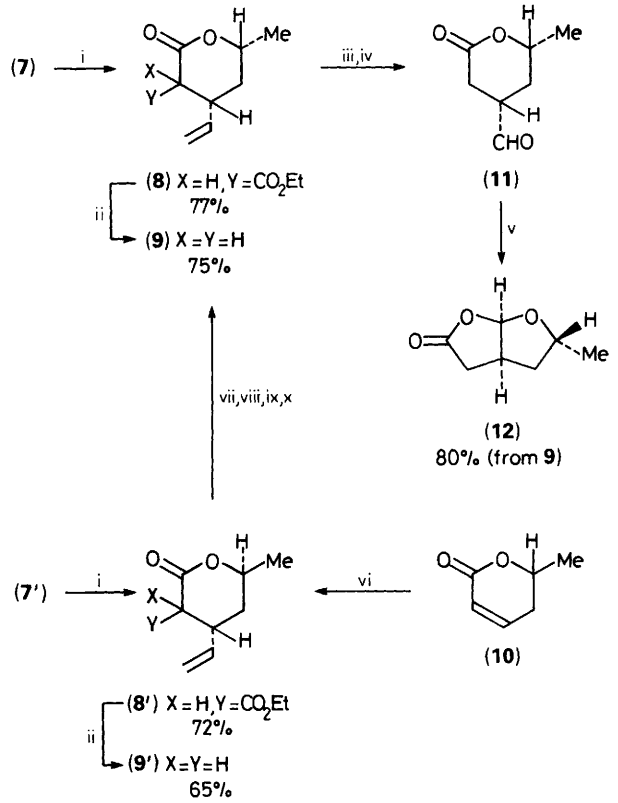
Table 1.

	Yield of product/%				
R	(3)	(4)	(5)	(6)	(7) + (7′)
Me	93	83	80	87	75(79 : 21)[a]
Bu	81	95	77	94	74(74 : 26)[a]
$PhCH_2O$	91	90	81	92	80(74 : 26)[a]

[a] Values in parentheses show the product ratio based on separated diastereoisomers.

equiv.) at −78 °C followed by the immediate addition of $BF_3{\cdot}Et_2O$ (1.2 equiv.),[2] 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[3] or with malonic acid monoethyl ester, dicyclohexylcarbodiimide, and 4-*N*,*N*-dimethylaminopyridine in dichloromethane at room temperature[4] provided the malonate (**4**) in high yield. After hydrogenation of the triple bond of (**4**) on 5% Pd–$BaSO_4$ stereoselectively affording the *Z*-alkene (**5**), reaction of the alkene with toluene-*p*-sulphonyl azide and triethylamine in acetonitrile at 40—45 °C over 40 h[3] gave the corresponding diazo-ester (**6**) in good yield. Treatment of (**6**) with catalytic $Rh_2(OAc)_4$ 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.[5]

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



Scheme 2. *Reagents:* i, Zn, HOAc; ii, NaCl, aq. dimethylsulphoxide; iii, O_3, CH_2Cl_2; iv, Me_2S; v, *p*-TsOH (Ts = $OSO_2C_6H_4$-Me), THF; vi, CH_2=CHMgBr, CuI, THF; vii, K_2CO_3, MeOH; viii, $N_2(CO_2Et)_2$, Ph_3P, $PhCO_2H$; ix, KOH, aq. MeOH; x, conc. HCl, MeOH.

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).[6] 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**)[7] 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,[8] (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-methylperhydrofuro[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, $BF_3 \cdot Et_2O$ 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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