

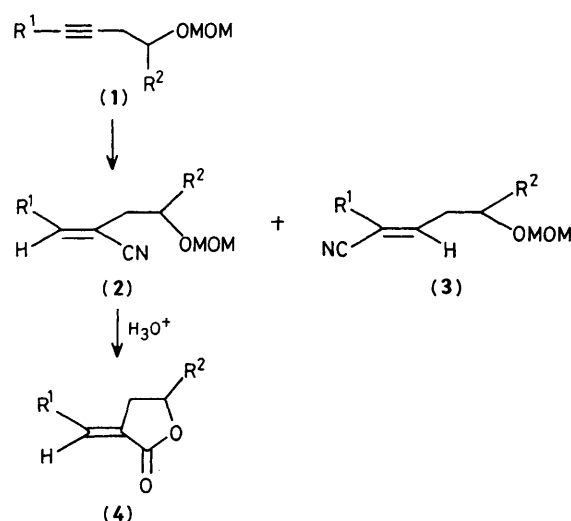
## A New Stereospecific Route to $\alpha$ -Alkylidene $\gamma$ -Lactones

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Hydrocyanation of a range of protected  $\beta$ -hydroxyalkynes gives unsaturated nitriles which can be cyclised to  $\alpha$ -alkylidene  $\gamma$ -lactones and in most cases the regioselectivity of hydrocyanation can be controlled giving the desired cyanoalkenes with stereospecific formation of the *E*-isomer.

Hydrocyanation of the alkynol ethers analogous to (1) with either hydrogen cyanide or acetone cyanohydrin [ $\text{Me}_2\text{C}(\text{OH})\text{CN}$ ] gives moderate to good yields of unsaturated nitriles (2) and (3)<sup>†</sup> in the presence of the previously reported nickel catalyst system.<sup>1,2</sup> The regioselectivity of addition



MOM =  $\text{MeOCH}_2$

favours formation of the desired nitrile (2) for terminal alkynes ( $\text{R}^1 = \text{H}$ ). The regioselectivity could also be controlled by the presence of a bulky substituent, *e.g.*  $\text{R}^1 = \text{Ph}$ , to give either (2) or (3), as has been demonstrated previously.<sup>1,2</sup> In all cases the minor isomer was easily removed by chromatography. Where the substituent  $\text{R}^1$  was of comparable size to the alkoxyalkane residue, *e.g.*  $\text{R}^1 = \text{Me}$ , no regioselectivity was shown, indicating that chelation control by the MOM ether was not operating in the transition state. The cyanoalkenes (2), which could be purified by distillation, were obtained in moderate to good yields using either hydrogen cyanide or acetone cyanohydrin as hydrocyanating reagent in the presence of a tetrakis(triphenyl phosphite)-nickel(0)-triphenyl phosphite catalyst system. The cyanoalkenes (2) were hydrolysed and cyclised to the desired

**Table 1.** Hydrocyanation of alkoxyalkynes (1) and cyclisation of the product (2) to give  $\alpha$ -methylene  $\gamma$ -lactones (4).<sup>a</sup>

$\text{R}^1$	$\text{R}^2$	% Yield <sup>b</sup> (2) + (3)	Ratio (2) : (3)	% Yield <sup>b</sup> (2) $\rightarrow$ (4)
H	H	79(55) <sup>c</sup>	90 : 10	65
Ph	H	77(77) <sup>c</sup>	85 : 15	83
H	Me	53	90 : 10	75
Me	H	78(55) <sup>c</sup>	50 : 50	56

<sup>a</sup> Conditions similar to those in ref. 1. <sup>b</sup> Yield of distilled product.

<sup>c</sup> Reaction carried out under identical conditions to those in (a) but with acetone cyanohydrin in place of HCN.

<sup>†</sup> All new compounds reported here gave satisfactory spectroscopic and elemental analyses.

$\alpha$ -methylenelactones by heating with methanolic hydrochloric acid. Good yields (65–83%) of these sensitive compounds were obtained when the purified isomers (**2**) were cyclised (Table 1). The MOM ether of pent-3-yn-1-ol (**1**;  $R^1 = \text{Me}$ ,  $R^2 = \text{H}$ ) gave equal amounts of the cyanoalkenes (**2**) and (**3**). The mixture was not separated but heated with methanolic hydrochloric acid and the desired lactone<sup>3</sup> (**4**;  $R^1 = \text{Me}$ ,  $R^2 = \text{H}$ ) was isolated by chromatography in moderate yield (56%).<sup>‡</sup>

Reactions of the parent alkynols with hydrogen cyanide have also been investigated.<sup>4</sup> Although the reactions showed evidence of regiocontrol by chelation to the hydroxy group, yields were always <30% and significant amounts of phenol were released from the phosphite based catalyst system.

This hydrocyanation route to  $\alpha$ -alkylidene- $\gamma$ -lactones complements and extends methods based on the cyclocarbonylation of alkynols which are restricted to reactions of terminal alkynols.<sup>5,6</sup>

<sup>‡</sup> Based on the amount of (**2**) in the isomeric mixture.

We thank the Australian Research Grants Scheme for support and the Australian Government, Department of Education, for a Postgraduate Research Award (to A. J. S.).

Received, 12th July 1985; Com. 994

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