A New Stereospecific Route to α-Alkylidene γ-Lactones

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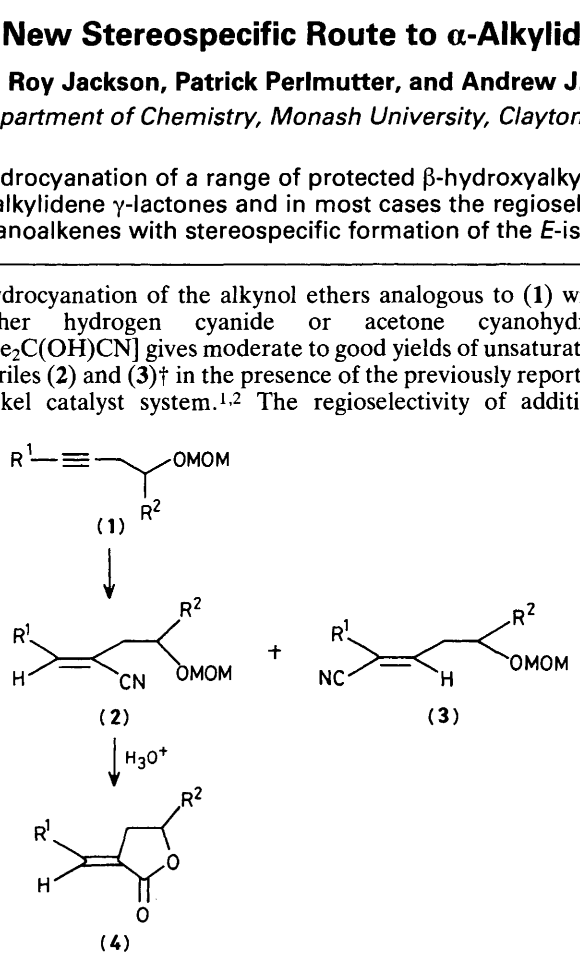
Hydrocyanation of a range of protected β-hydroxyalkynes gives unsaturated nitriles which can be cyclised to α-alkylidene γ-lactones and in most cases the regioselectivity of hydrocyanation can be controlled giving the desired cyanoalkenes with stereospecific formation of the *E*-isomer.

Hydrocyanation of the alkynol ethers analogous to (**1**) with either hydrogen cyanide or acetone cyanohydrin [$Me_2C(OH)CN$] gives moderate to good yields of unsaturated nitriles (**2**) and (**3**)† in the presence of the previously reported nickel catalyst system.[1,2] The regioselectivity of addition favours formation of the desired nitrile (**2**) for terminal alkynes (R^1 = H). The regioselectivity could also be controlled by the presence of a bulky substituent, *e.g.* R^1 = Ph, to give either (**2**) or (**3**), as has been demonstrated previously.[1,2] In all cases the minor isomer was easily removed by chromatography. Where the substituent R^1 was of comparable size to the alkoxyalkane residue, *e.g.* R^1 = 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 cyano alkenes (**2**) were hydrolysed and cyclised to the desired



MOM = $MeOCH_2$

Table 1. Hydrocyanation of alkoxyalkynes (**1**) and cyclisation of the product (**2**) to give α-methylene γ-lactones (**4**).[a]

R^1	R^2	% Yield[b] (**2**) + (**3**)	Ratio (**2**):(**3**)	% Yield[b] (**2**)→(**4**)
H	H	79(55)[c]	90:10	65
Ph	H	77(77)[c]	85:15	83
H	Me	53	90:10	75
Me	H	78(55)[c]	50:50	56

[a] Conditions similar to those in ref. 1. [b] Yield of distilled product. [c] Reaction carried out under identical conditions to those in (a) but with acetone cyanohydrin in place of HCN.

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† All new compounds reported here gave satisfactory spectroscopic and elemental analyses.

α-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 = Me, R^2 = 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[3] (**4**; R^1 = Me, R^2 = H) was isolated by chromatography in moderate yield (56%).‡

Reactions of the parent alkynols with hydrogen cyanide have also been investigated.[4] 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 α-alkylidene-γ-lactones complements and extends methods based on the cyclocarbonylation of alkynols which are restricted to reactions of terminal alkynols.[5,6]

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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‡ Based on the amount of (**2**) in the isomeric mixture.

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