A Novel Stereospecific Hydrohalogenation Reaction of Propiolates and Propiolic Acid

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(*Z*)-3-Halo-propenoates or -propenoic acids have been synthesized stereospecifically by the reaction of lithium halides in acetic acid with propiolates or propiolic acid, respectively.

3-Halopropenoates have proved to be versatile and valuable intermediates in organic synthesis.[1] They are usually prepared by the addition of hydrogen halides to propiolates in acetic acid,[2,3] and obtained as a mixture of *Z*- and *E*-isomers, with the *E*-isomer predominating. They can also be prepared by the esterification of the corresponding acids[4,5] or by other methods.[6] Pure (*Z*)-3-chloropropenoates have been prepared by esterification of (*Z*)-3-chloropropenoic acid, which was synthesized from the reaction of propiolic acid with CuCl in concentrated hydrochloric acid.[4,7,8] Thus, it is still desirable to develop a new, simple method for the stereospecific synthesis of 3-halopropenoates.

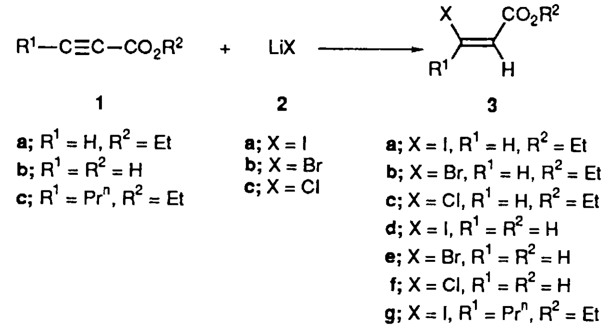
During our study of palladium(II) catalysed cyclization of 4-iodobut-2-enyl propiolate,[9] occasionally it was found that propiolates could be hydrohalogenated stereospecifically by their reactions with lithium halides in acetic acid as shown in Scheme 1.

The results in Table 1 show that propiolates can be hydrohalogenated regio- and stereo-specifically in high yield. The halogen atom attacked the 3-position regioselectively, and the carbon–carbon double bond in the product **3** was in the *Z*-configuration. The assignment of the stereochemistry of the product **3** was based on the coupling constant between the

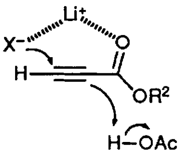
Table 1 Reaction of propiolates or propiolic acid with lithium halides in acetic acid[a]

Entry	Reagents		Product	Reaction time/h	Yield (%)
1	**1a**	**2a**	**3a**	5	75[b]
2	**1a**	**2b**	**3b**	15	91
3	**1a**	**2b**	**3b**	21	85
4	**1a**	**2c**	**3c**	20	80
5	**1b**	**2a**	**3d**	24	89
6	**1b**	**2b**	**3e**	24	93
7	**1b**	**2c**	**3f**	24	89
8	**1c**	**2a**	**3g**	24	22[c]

[a] A mixture of **1** (1 mmol), **2** (1.1 mmol) and HOAc (1 ml) was stirred at 70 °C. [b] 5% of $Pd(OAc)_2$ was added. [c] Based on ^1H NMR spectra.



Scheme 1. *Conditions:* HOAc, 70 °C



(A)

two vicinal vinyl protons (J 8.3–8.6 Hz) in ^{1}H NMR spectra. Z- and E-isomers of such compounds may be separated by TLC on silica gel using light petroleum–ethyl acetate (10:1) as eluent, but we did not detect any E-isomers. GC analysis also showed that the products contained <1% of E-isomers. The substituted propiolate **1c** gave a lower yield (entry 8). Attempts to hydrofluorinate the propiolates with lithium fluoride failed.

The reaction of ethyl propiolate and lithium bromide in acetonitrile under reflux for 24 h followed by hydrolysis with 20% HOAc gave ethyl (Z)-3-bromopropenoate in only 5% yield. The same reaction in the presence of 1 equiv. of HOAc proceeded in 77% yield, implying that the presence of a proton source is necessary. When $MeCO_2D$ was used instead of $MeCO_2H$, ethyl (Z)-3-bromo-2-deuteriopropenoate was isolated in 79% yield after reaction at 70 °C for 20 h.

The high stereoselectivity ruled out the possibility of the addition of hydrogen halides to the propiolates in acetic acid, which is reported to show low stereoselectivity.[2] The halide ion might be present in the solution in the form of a contact ion pair with lithium. The coordination of the lithium ion with the carbonyl oxygen atom and nucleophilic attack of the halide ion on the electron-deficient triple bond[3,10] from the same side would account for the high Z stereoselectivity. The reaction may proceed as shown on structure (A).

(Z)-3-Halopropenoic acids have been reported to have specific cotton defoliating activity.[8,11] The literature methods for 3-halopropenoic acids usually afford a mixture of E- and Z-isomers,[12] except that described in ref. 8. The results in Table 1 (entries 5–7) show that these compounds could also be prepared in high yields and stereospecificity from propiolic acid and lithium halides under milder conditions than those in the literature.[5,8]

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