Facile and stereospecific synthesis of 1,1-dihalogenoalk-1-enes from 1-halogenoalk-1-ynes by hydroboration

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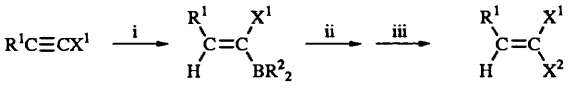
1-Halogenoalk-1-ynes upon hydroboration with dialkylborane followed by treatment with copper(II) halides in the presence of a small amount of water in polar aprotic solvents give both mixed 1,1-dihalogenoalk-1-enes of defined stereochemistry and single isomers in reasonable yield.

Although the synthetic potential of homogenous 1,1-dihalogenoalk-1-enes, readily obtained from aldehydes,[1,2] and stereochemically defined mixed 1,1-dihalogenoalk-1-enes, prepared from 1-halogenoalk-1-ynes[3a] or 1-halogenoalk-1-enylsilanes,[3b] has been demonstrated, more general syntheses of such compounds are of interest in view of the problems, inapplicability† or inconvenience,‡ associated with the published methods.

Recently we found that stereochemically pure (*E*)-1-chloro(or bromo)alk-1-enes were produced highly efficiently by treatment of (*E*)-alk-1-enyldialkylborane [derived from alk-1-yne by hydroboration with dialkylborane in tetrahydrofuran (THF)] with simple reagents; copper(II) chloride [or copper(II) bromide–copper(II) acetate] in the presence of a small amount of water, in a polar aprotic co-solvent [hexamethylphosphoric triamide (HMPT)].[5] In these reactions the halogenation step proceeded with retention of configuration, giving almost pure *E*-isomers. This suggested that such methodology could be employed in convenient and stereospecific syntheses of 1,1-dihalogenoalk-1-enes, without steric hindrance, from 1-halogenoalk-1-ynes (readily available from alk-1-ynes).[3] We were encouraged, therefore, to examine the reaction, in the expectation of complementing earlier described syntheses with a more efficient one.[3]

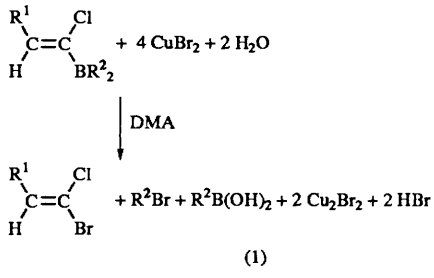
Reaction of (*Z*)-1-chlorohex-1-enylbis(1,2-dimethylpropyl)-borane (1 equiv.) [prepared by hydroboration of 1-chlorohex-1-yne with bis(1,2-dimethylpropyl)borane in THF][6] with copper(II) bromide (2 equiv.) in the presence of co-solvent (HMPT) and a little water (1 equiv.) gave (*E*)-1-bromo-1-chlorohex-1-ene in only moderate yield, with much 2-bromo-3-methylbutane; this contrasted with earlier work.[5] However, a repeat reaction employing a large excess (4 equiv.) of copper(II) halide and 2 equiv. of water gave the mixed dihalogenoalkene in high yield (GC, 96%), with no competing 1,2-dimethylpropyl group transfer from boron to the adjacent C-atom.[3b] Since the desired product and by-product could be separated easily by column chromatography, the present reaction has synthetic potential. The employment of *N*,*N*-dimethylacetamide (DMA) in place of HMPT [an undesirable solvent for regular use (*i.e.*, suspected carcinogenic)] gave almost identical results. In the absence of these polar aprotic solvents or water, little product was formed (*ca.* 8%).[5] In accord with our expectations, the reaction employing 1-chloro-3,3-dimethylbut-1-yne, the corresponding product [(*E*)-1-bromo-1-chloro-3,3-dimethylbut-1-ene] was similarly produced in fairly good isolated yield (84%) and almost complete isomeric purity (> 99%). The corresponding *Z*-isomers were also obtained successfully using 1-bromoalk-1-ynes and copper(II) chloride in similar manner. Some representative results obtained by reactions depicted in Scheme 1 are shown in Table 1. Thus, in the present reactions



Scheme 1 *Reagents and conditions:* i, $R^2{}_2BH$, THF, −15 °C then 0–5 °C; ii, Me_2NCOMe [or $(Me_2N)_3P(O)$], $CuCl_2$ (or $CuBr_2$), H_2O and THF, −15 °C then 0–5 °C; iii, 20 °C. X^1 = Cl [or Br (or I)]. X^2 = Cl (or Br). R^1 = alkyl, R^2 = 1,2-dimethylpropyl.

highly pure (*E*)- or (*Z*)-1-bromo-1-chloroalk-1-enes, (*Z*)-1-bromo (or chloro)-1-iodoalk-1-enes and 1,1-dibromo (or chloro)alk-1-enes were provided in sufficiently good yields.

The above results suggest that the present reactions proceed by way of activation of the halogenoalkenyl moiety by a polar aprotic co-solvent,[7] with retention of configuration, in the halogenation step. Although the detailed reaction mechanism is not, at present, clear, it is likely that it proceeds as shown in eqn. (1).



(1)

In summary, (*E*)-1,1-dihalogenoalkenes are more easily prepared by the described reaction than by the previous procedure,[3b] and specifically that compounds containing a bulky alkyl substituent can be formed in defined stereochemistry by the present procedure.

Experimental

Typical experimental procedure: preparation of (*E*)-1-bromo-1-chloro-3,3-dimethylbut-1-ene

In an argon-flushed flask, (*Z*)-1-chloro-3,3-dimethylbut-1-enylbis(1,2-dimethylpropyl)borane (20 mmol) in THF was

† The *trans*-hydroalumination–bromination (or iodination) sequence entirely from 1-chloroalk-1-ynes proceeded with retention of configuration to afford (*Z*)-1-bromo (or iodo)-1-chloroalk-1-enes,[3a] and the other methodology *via* hydroboration–bromination–elimination from 1-chloro (or bromo)alk-1-ynes gave inversion products, (*Z*)-1-bromo-1-chloroalk-1-enes and 1,1-dibromoalk-1-enes, exclusively.[3b]

‡ The bromination–desilicobromination of (*E*)-1-chloroalk-1-enylsilanes or chlorination–desilicochlorination of (*Z*)-1-bromoalk-1-enylsilanes afforded (*E*)-1-bromo-1-chloroalk-1-enes.[3b] However, an increase in the size of the alkyl substituent in the 1-halogenoalk-1-enylsilanes had a detrimental effect on the isomeric purity of the dihalogenoalkenes.[3b] In addition the starting 1-halogenoalk-1-enylsilanes were not always readily available.[4]

Table 1 Syntheses of 1,1-dihalogenoalk-1-enes from 1-halogenoalk-1-ynes by hydroboration with dialkylborane

Halogenoalkyne	Product	% Yield[a] GC	% Yield[a] Isolated[b]	$E:Z$[e]
BuC≡CCl	$BuCH{=}CCl_2$	93[c] (95)[d]	83[c]	
	(*E*)-BuCH=CCl(Br)	92[c] (96)[d]	(85)[d]	100
BuC≡CBr	(*Z*)-BuCH=CBr(Cl)	91[c] (96)[d]	82[c]	100
	$BuCH{=}CBr_2$	92[c] (95)[d]	(86)[d]	
BuC≡CI	(*Z*)-BuCH=CI(Cl)	93[c] (95)[d]	85[c]	< 1 : > 99
	(*Z*)-BuCH=CI(Br)	92[c] (93)[d]	84[c]	< 1 : > 99
Bu^{t}C≡CCl	$Bu^tCH{=}CCl_2$	92[c] (96)[d]	(86)[d]	
	(*E*)-Bu^{t}CH=CCl(Br)	93[c] (88)[d]	84[c]	> 99 : < 1
Bu^{t}C≡CBr	(*Z*)-Bu^{t}CH=CBr(Cl)	77[c] (80)[d]	(72)[d]	< 1 : > 99
	$Bu^tCH{=}CBr_2$	85[c] (91)[d]	(83)[d]	

[a] All yields are for the overall process, and are based on starting halogenoalkynes. [b] On flash column (silica gel; pentane). GC purity is 95–98%. [c] Co-solvent is DMA. [d] Co-solvent is HMPT. [e] On a glass capillary column.

prepared by the successive reactions of borane (20 mmol) in THF (15 cm^3) with 2-methylbut-2-ene (2.81 g, 40 mmol) in THF (5 cm^3) at −15 °C for 30 min and then 0–5 °C for 2 h[8a] and 1-chloro-3,3-dimethylbut-1-yne[8b] (2.33 g, 20 mmol) in THF (5 cm^3) at −15 °C for 30 min and then 0–5 °C for 30 min (in the case of 1-halogenohex-1-yne, additionally at 20 °C for 2 h).[3b,6] To the solution, DMA (20 cm^3), copper(II) bromide (17.9 g, 80 mmol), water (0.720 g, 40 mmol) and THF (10 cm^3) were added successively at −15 °C under argon, after which the mixture was stirred at 0–5 °C for 2 h and then at 20 °C for 15 h. The contents of the flask were washed with brine and extracted with pentane. The extract was concentrated and the residue oxidized with 3 mol dm^{-3} aq. sodium hydroxide (5 cm^3), 30% hydrogen peroxide (5 cm^3) and THF (10 cm^3) with stirring at 0–20 °C for 4 h. The mixture was washed with brine and extracted with pentane, and the extract was treated with a few crystals of 2,6-di-*t*-butyl-4-methylphenol (BHT, to inhibit isomerization)[3] after which it was dried (Na_2SO_4), filtered and concentrated. Chromatography of the organic residue (consisting of the dihalogenoalkene, 1,2-dimethylpropyl bromide, and 3-methylbutan-2-ol derived from the residual alkylboryl group by above oxidative treatment) on a flash chromatography column (silica gel; pentane) gave highly pure (*E*)-1-bromo-1-chloro-3,3-dimethylbut-1-ene (eluted first, followed by removal of pentane in the presence of a few crystals of BHT) (3.32 g, 84%); ν_{max}(neat)/cm^{-1} 1602 (C=C) and 835 (=CH); δ_H(90 MHz; $CDCl_3$) 1.18 (9 H, s, 3 × Me) and 6.14 (1 H, s, =CH); δ_C(22.4 MHz; $CDCl_3$) 29.15 (3 × Me), 35.18 (C), 103.02 (=C) and 143.66 (=CH); *m/z* 197.9648 (M^+) ($C_6H_{10}{}^{81}Br^{35}Cl$ requires 197.9634). GC [OV-1 glass capillary column (75 m)] analysis showed >99% stereochemical purity, contrasting with the retention time of (*Z*)-1-bromo-1-chloro-3,3-dimethylbut-1-ene prepared *via* hydroalumination of 1-chloro-3,3-dimethylbut-1-yne followed by bromination.[3a]

For (*E*)-1-bromo-1-chlorohex-1-ene; ν_{max}(neat)/cm^{-1} 1607 (C=C) and 840 (=CH); δ_H(90 MHz; $CDCl_3$) 0.91 (3 H, deformed t, Me), 1.15–1.65 [4 H, m, $(CH_2)_2$], 2.00–2.35 (2 H, m, $=CCH_2$) and 6.08 (1 H, t, *J* 7.3, =CH); GC [OV-1 glass capillary column (75 m)] analysis showed 100% stereochemical purity, contrasting with the retention time of the prepared authentic (*Z*)-1-bromo-1-chlorohex-1-ene.[3a]

For (*Z*)-1-bromo (or iodo)-1-chloro (or bromo)alk-1-enes, the products gave satisfactory spectral data (IR, ^1H NMR, ^{13}C NMR, mass), and the GC (similar glass capillary column) retention times were consistent with those of the prepared authentic samples respectively [except for (*Z*)-1-bromo-1-iodohex-1-ene].[3a]

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