Reaction of (*Z*)-1-bromoalk-1-enyldialkylboranes with DMSO: regio- and stereo-selective formation of internal (*E*)-alkenyl bromides

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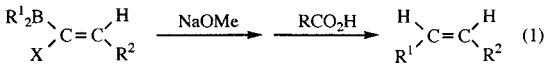
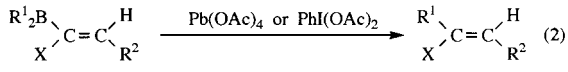
Treatment of (*Z*)-1-bromoalk-1-enyldialkylboranes 1 with DMSO results in 1,2-migration of an alkyl group from the boron to the α-carbon without elimination of bromine to give internal (*E*)-alkenyl bromides 2 with excellent stereoselectivity (> 99%).

(*Z*)-1-Haloalk-1-enylboranes, which can be prepared by hydroboration of 1-haloalk-1-ynes with borane derivatives, are versatile and potential precursors of alkenes.[1] For example, the reaction of (*Z*)-1-haloalk-1-enyldialkylboranes with MeONa followed by protonolysis with carboxylic acids offers regio- and stereo-selective syntheses of internal (*E*)-alkenes where one of the alkyl groups on the boron atom is introduced into the α-alkenyl carbon atom with elimination of a halogen atom [eqn. (1)].[2] This strategy could be applied to the synthesis of



(1)

prostaglandin analogues.[3] On the other hand, we reported that a similar alkyl group migration was performed without elimination of the halogen atom by treatment of (*Z*)-1-haloalk-1-enyldialkylboranes, whose alkyl groups were derived from a relatively hindered alkene, with lead(IV) acetate or (diacetoxyiodo)benzene giving internal (*Z*)-alkenyl halides in a highly stereoselective manner (95–98% for *Z*) [eqn. (2)].[4] Ster-

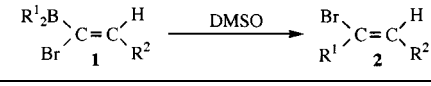


(2)

eodefined alkenyl halides are important substrates, especially as coupling partners of transition metal mediated cross-coupling reactions to give alkenyl units stereoselectively.[5] For example, (11*Z*)-retinal[6] and rapamycin[7] were synthesized using the above coupling reaction. In these reactions the purity of the haloalkene is important. This prompted us to investigate the alkyl group transfer reaction in the hope of obtaining highly pure internal alkenyl halides. We report here a new type of synthesis of internal (*E*)-alkenyl bromides **2** from (*Z*)-1-bromoalk-1-enyldialkylboranes **1** with excellent stereoselectivity (> 99%), on which DMSO has a decisive influence.

The reactions of **1** with DMSO were carried out under reaction conditions optimised using (*Z*)-1-bromohex-1-enyldicyclohexylborane **1a** as a typical substrate. Thus, **1a** was treated with 2 equiv. of DMSO in $ClCH_2CH_2Cl$ at 0 °C to room temperature for 18 h (Scheme 1). After work-up† (*E*)-1-bromo-1-cyclohexylhex-1-ene **2a**‡ was obtained in 73% yield and in > 99% isomeric purity (entry 1, in Table 1). The stereochemistry of **2a** was assigned the *E* configuration by comparing GC and ^1H and ^{13}C NMR analyses of **3a** (Scheme 2)

Table 1 Reaction of (*Z*)-1-bromoalk-1-enyldialkylboranes **1** with DMSO[a]



Entry	R^1	R^2	Product	Yield (%)
1	Cyclohexyl	Bu	**2a**	73
2	Hexyl[b]	Bu	**2b**	69
3	Pr(Me)$CHCH_2$[b]	Bu	**2c**	70
4	$Bu^tCH_2CH_2$[b]	Bu	**2d**	70
5	Cyclopentyl[b]	Bu	**2e**	68
6	Cyclohexyl	Ph	**2f**	59
7	Hexyl[b]	Ph	**2g**	45
8	Hexyl[b]	Bu^t	**2h**	28
9	Cyclohexyl	$(CH_2)_2CH_2Cl$	**2i**	60

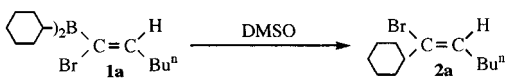
[a] Reactions were carried out in $ClCH_2CH_2Cl$ using 2 equiv. of DMSO unless otherwise noted. [b] Reactions were carried out in CCl_4.

with those of an authentic sample prepared according to the literature.[8]

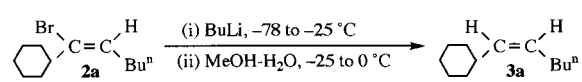
The above example demonstrates that the relatively hindered alkyl group on the boron atom is introduced to the alkenyl moiety of **2** as one of the alkyl substituents in a regio-and stereoselective manner. We next explored the reaction of **1**, which was prepared using a variety of dialkylboranes derived from less hindered alkenes through hydroboration with $BH_2Br{\cdot}SMe_2$,[9] followed by hydridation with $LiAlH_4$.[10] For example, (*Z*)-1-bromohex-1-enyldihexylborane **1b** reacted with DMSO under similar conditions§ to afford isomerically pure (*E*)-6-bromododec-5-ene **2b**¶ in 69% yield (entry 2).

In all cases listed in Table 1, internal (*E*)-alkenyl bromides **2** were obtained in > 99% isomeric purity. Accordingly, the present reaction can be applied not only to the cases of relatively hindered dialkylboranes (entries 1, 6 and 9) but also to the cases of less hindered dialkylboranes (entries 2–5, 7 and 8), demonstrating that a wide variety of compounds **2** can be formed using this strategy.

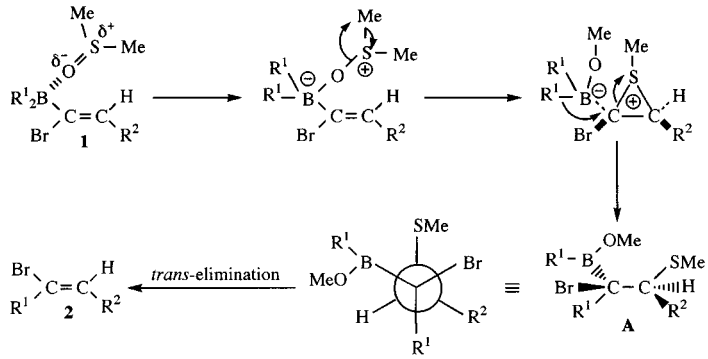
A plausible mechanism for the formation of internal (*E*)-alkenyl bromides **2** is shown in Scheme 3. It was observed that the yields of **2** depended considerably on the solvent employed. In addition, the addition of an equimolar amount of pyridine, a more polar compound than THF, to **1** inhibited completely the present reaction. These results suggest that the reaction is initiated by nucleophilic attack of DMSO. It appears that a concerted reaction, which involves the transfer of a methyl group from sulfur to oxygen and the concomitant formation of methylthio cation, occurs through two-electron oxidation. Then electrophilic addition of the methylthio cation to the carbon–carbon double bond followed by 1,2-migration of an alkyl group from boron to the α-carbon would take place to form intermediate **A**. Finally, intermediate **A** would undergo *trans*-



Scheme 1



Scheme 2



Scheme 3

elimination of an alkylmethoxyboryl group and a methylthio group‖ to yield **2**. In the case of entry 8, the large steric hindrance between R^1 and R^2 could be responsible for the low yield of (*E*)-4-bromo-2,2-dimethyldec-3-ene **2h**.

In summary, we have demonstrated that a variety of compounds **1** react with DMSO to provide the corresponding species **2** in > 99% isomeric purity, and thus both substituents (R^1 and R^2) in **2** can be selected from a wide range of possible groups. It should be noted that the present reaction is carried out under mild and essentially neutral conditions. Further studies on the application of this strategy to different types of species **1** with varying functionality and a similar nucleophilic attack on **1** are now in progress.

Notes and references

† For work-up of the reaction mixture the use of sodium perborate was effective.

‡ *Selected data* for **2a**: δ_H(200 MHz, $CDCl_3$) 0.90 (m, 3H), 1.10–1.88 (m, 14H), 1.98–2.18 (m, 2H), 2.35–2.55 (m, 1H), 5.78 (t, *J* 7.6, 1H); δ_C(50 MHz, $CDCl_3$) 13.8, 22.1, 25.6, 25.8 (2C), 29.1, 31.5, 31.6 (2C), 41.5, 130.9, 133.3; υ_{max}(film)/cm^{-1} 2929, 2854, 1637, 1450, 1377, 893, 648; *m*/*z* (EI) 246 (M^+, 22%), 244 (M^+, 21), 165 (32), 123 (17), 109 (100), 95 (67), 81 (48), 67 (63), 55 (51).

§ After preparation of **1b**, THF was removed under reduced pressure. The residue was extracted with CCl_4 under Ar atmosphere in order to separate **1b** from $LiAlBr_4$, and the extracts were transferred into another flask through a simple filter packed with glass wool.

¶ *Selected data* for **2b**: δ_H(200 MHz, $CDCl_3$) 0.79–1.04 (m, 6H), 1.18–1.62 (m, 12H), 1.90–2.04 (m, 2H), 2.41 (t, *J* 7.2, 2H), 5.84 (t, *J* 7.6, 1H); δ_C(50 MHz, $CDCl_3$) 13.8, 14.0, 22.1, 22.6, 28.0, 28.2, 29.2, 31.4, 31.6, 35.4, 125.9, 132.4; υ_{max}(film)/cm^{-1} 2956, 2927, 2858, 1645, 1463, 1379, 842, 727, 646; *m*/*z* (EI) 248 (M^+, 18%), 246 (M^+, 17), 122 (12), 120 (12), 111 (28), 97 (72), 83 (43), 81 (45), 69 (82), 67 (42), 55 (100).

‖ After hydrolysis of the reaction mixture, there is a characteristic odour of mercaptan.

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