2-Bromomethylprop-2-en-1-yl Acetate; Synthesis and Applications

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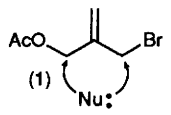
Fluoride-ion-mediated elimination of hydrogen bromide from 3-bromo-2-bromomethylpropyl acetate gave the title compound, the bromine atom of which was specifically substituted by various nucleophiles to yield the corresponding phenyl sulphone, dimethyl malonate, diethylamine, and benzyl sulphide derivatives.

Bifunctional allylic compounds are valuable precursors for the synthesis of rings as well as open-chain compounds.[1] The recent syntheses by Trost *et al.* of *exo*-methylene tetrahydrofurans and -cyclopentanes were based on the novel synthon 2-trimethylsilylmethylprop-2-en-1-yl acetate, which has structural features similar to compounds reported here.[1a,2] Other examples of bifunctional 1,1-disubstituted alkenes have been reported.[3]

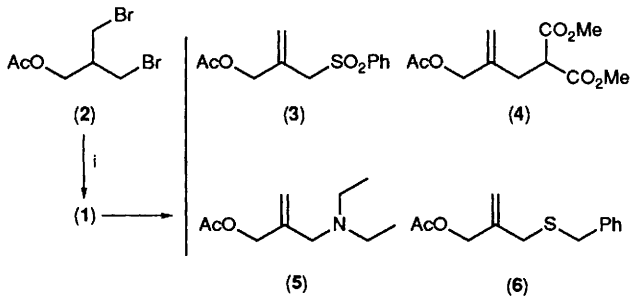
Trost's isobutene derivative carries functionalities that render the two allylic positions potentially nucleophilic and electrophilic, respectively. The present investigation describes the synthesis and use of the novel bis-allylic compound (**1**), which carries functionalities that make both the allylic positions electrophilic.

While investigating general routes for the synthesis of glycoconjugates, 2-bromomethylprop-2-en-1-yl glycosides were prepared as intermediates.[4] However, these allylic bromides were quite reactive and bound irreversibly to silica gel on attempted chromatographic purification. In contrast, the acetate (**1**) is stable and allows both chromatography and distillation. Furthermore, (**1**) was kept at room temperature in the dark for over two months without deterioration as evidenced by gas chromatographic analysis. It seems that the acetate group makes the allylic bromide less reactive.

Compound (**1**) was synthesized by treatment of the known 3-bromo-2-bromomethylpropyl acetate[5] (**2**) with tetrabutylammonium fluoride in acetonitrile. Fluoride ion is a strong base under these conditions and the elimination of hydrogen bromide was complete within 20 min at room temperature. Concentration of the reaction mixture caused the formation of small amounts of 2-fluoromethylprop-2-en-1-yl acetate, presumably due to nucleophilic displacement of the allylic bromide by fluoride ion. A similar reaction was used for the preparation of 2-fluoromethylprop-2-en-1-yl lactoside.[4] The formation of 2-fluoromethylprop-2-en-1-yl acetate was avoided by quenching the reaction with saturated aqueous calcium nitrate which gave an insoluble precipitate of calcium fluoride prior to removal of the solvent. Normal work-up of the reaction mixture, followed by distillation [b.p. ~50 °C/1 torr (1 torr = 133.322 Pa)] of the crude product gave (**1**) in 76% yield.†



† *Spectral data* for (**1**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H, Me), 4.01 (d, 2H, *J* 0.8 H_z, CH_2Br), 4.71 (2 × s, 2H, CH_2O), 5.27 (q, 1H, *J* ~1 Hz, 5''-H), 5.38 (q, 1H, *J* ~1 Hz, 5'-H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 20.8 (Me), 32.5 (CH_2Br), 64.3 (CH_2O), 118 (C-5), 140 (C-4), 170 (C=O).



Scheme 1. *Reagents and conditions:* i, Bu_4NF/MeCN, 25 °C, 17 min.

The bromine atom of (**1**) was specifically substituted by various nucleophiles (Scheme 1). Treatment of (**1**) with sodium benzenesulphinate (*N*,*N*-dimethylformamide; 25 °C; 15 h), dimethylmalonate/sodium hydride (tetrahydrofuran; 25 °C; 2 h), diethylamine (acetonitrile; 80 °C; 25 min), and benzyl mercaptan/caesium carbonate (acetonitrile; reflux; 30 min) and chromatographic purification gave compounds (**3**) (73), (**4**) (83), (**5**) (69), and (**6**) (95%), respectively.

Compound (**1**) is unique in the sense that it is a 1,3-bisallylic four-carbon building block with allylic positions of differing electrophilicities. Therefore, (**1**) has potential for stepwise nucleophilic substitution under base and transition metal catalysis, similar to the 1,4-bisallylic chloroacetates developed by Bäckvall *et al.*[6] A further advantage is that (**1**) should give the same product regardless of the mechanism (S_N2 or S_N2') of the nucleophilic substitution.

The sulphone-acetate (**3**) is 'umpoled' compared to (**1**) in the sense that the allylic position α to the sulphone grouping is a potentially nucleophilic site. Alkylation, followed by elimination of benzenesulphinic acid[7] should give rise to many useful 1,3-dienes. A sulphone-carbonate similar to (**3**) was used by Tsuji for the synthesis of *exo*-methylene cyclopentanes.[1]

In conclusion, compounds (**1**) and (**3**) are potentially valuable tools for use in organic synthesis. Investigations of the scope and limitations of (**1**) and its derivatives as general synthons are in progress.

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