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Novel Deuteration via Acetylene Bond Migration

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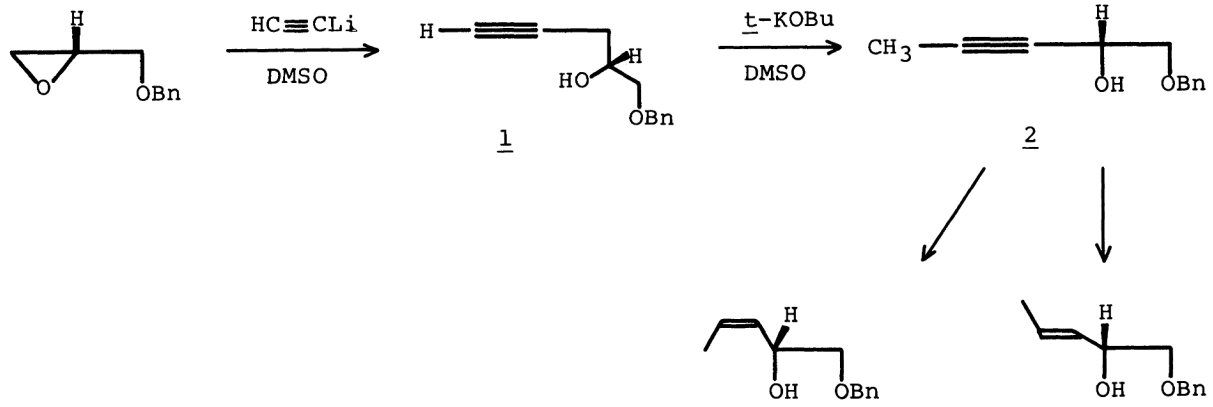
Optically active terminal-β,γ-acetylenic alcohol rearranges to β-trideuteriomethyl-α,β-acetylenic alcohol, an useful chiral building block for the synthesis of a variety of natural products, on exposure to potassium t-butoxide in dimethyl sulfoxide-d_6.

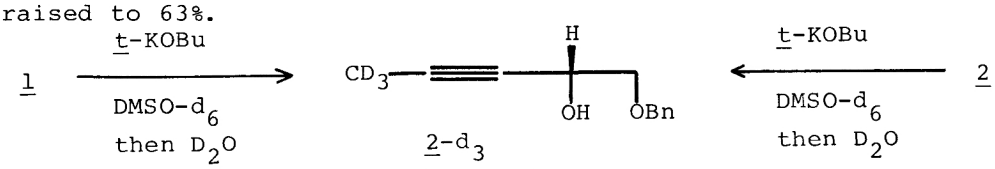
Recently we reported the synthesis of some potentially useful chiral building blocks[1] bearing a secondary methyl group from the optically active terminal-β,γ-acetylenic alcohol **1** via the base induced triple bond migration as key stage.[2] In the reaction, terminal β,γ-acetylene bond of **1** was smoothly migrated to the α,β-position to give the internal acetylenic alcohol **2** without loss of the original chiral integrity when it was briefly treated with potassium t-butoxide in dimethyl sulfoxide.[2] The chiral acetylene **2** was then converted selectively into the allyl alcohols, cis-**3** and trans-**4**, which were successfully transformed into the chiral building blocks for the synthesis of a variety of natural products.[1] We describe here a novel synthesis of this important key acetylenic precursor **2** in a trideuterated form from the non-deuterated alcohol **1** employing the same triple bond migration.



Scheme 1. **3** **4**

Treatment of the terminal acetylenic alcohol[1] **1**, prepared in 89% yield from (S)-O-benzylglycidol,[3] with two equivalents of potassium t-butoxide in dimethyl sulfoxide-d_6 (DMSO-d_6) at room temperature for 2 h afforded a deuterated internal acetylene **2** in 82% yield after exposure to diluted hydrochloric acid. Complete triple bond migration occurred under these conditions, however, deuterium incorporation of the product was found to be 54%. When the reaction was quenched by

deuterium oxide in place of diluted hydrochloric acid, the incorporation was a little raised to 63%.



Scheme 2.

Table 1. Deuterium Incorporation of **2-d$_3$**

Entry	Substrate	Amount of base (equiv.)	Work-up	Yield/%	Deuterium incorporation[a]/%
1	**1**	2	D_2O	82	63
2	**1**	2	10%HCl	80	54
3	**1**	4	D_2O	84	84
4	**1**	6	D_2O	84	85
5	**1**	8	D_2O	89	93
6	**1**	8	10%HCl	86	80
7	**1**	10	D_2O	79	92
8	**2**	2.5	D_2O	67	50
9	**2**	8	D_2O	78	92

a) Determined by ^{1}H-NMR (90 MHz).

No significant improvement was observed by exposure of **1** to two equivalents of n-butyllithium prior to treatment with potassium t-butoxide. It was finally found that the incorporation was greatly affected by amounts of the base used and when **1** was exposed to eight equivalents of potassium t-butoxide at room temperature for 2 h, the rearranged product **2** containing 93% of deuterated product **2-d$_3$** was obtained in 89% yield after quenching with deuterium oxide (Table 1).

Interestingly, it was also found that facile deuterium incorporation occurred with the internal acetylene **2** under the same conditions. When **2** was exposed to two equivalents of potassium t-butoxide, 50% deuterium incorporation was observed and was raised to 90% with eight equivalents of the base.

A typical procedure is as follows: To a solution of (R)-5-benzyloxy-4-hydroxypent-1-yne **1** (503 mg, 2.65 mmol) in DMSO-d_6 (99.9%, 3 ml) was added potassium t-butoxide (2.37 g, 21.16 mmol) portionwise with stirring at room temperature under argon. After stirring for 2 h at room temperature, the mixture was treated with deuterium oxide (99.8%, 5 ml) at 0 °C and was extracted with benzene (3 x 20 ml). The extract was washed (5% aq. $NaHCO_3$ and brine), dried ($MgSO_4$), and evaporated. The residual oil was purified by silica gel chromatography (20 g, hexane/Et_2O 4:1) to give **2-d$_3$** (454.3 mg, 89%) as a colorless oil: $[\alpha]_D^{24}$ +4.30° (c 1.11, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): δ 7.32 (s, 5H), 4.58 (s, 2H), 4.72-4.38 (m, 1H), 3.72-3.37 (m, 2H), 2.43 (brs, 1H, exchangeable), 1.88-1.68 (m, 0.21H).

References

1) S. Takano, Y. Sekiguchi, and K. Ogasawara, J. Chem. Soc., Chem. Commun., 1987, 555.
2) S. Takano, Y. Sekiguchi, N. Sato, and K. Ogasawara, Synthesis, 1987, 139.
3) S. Takano, M. Akiyama, and K. Ogasawara, Synthesis, 1985, 503.

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