

Preparation of *trans*-3-(Hydroxymethyl)-2-vinyloxetane via Allyloxycarbanion-mediated Carbon–Carbon Bond Formation in Allyl Glycidyl Ether

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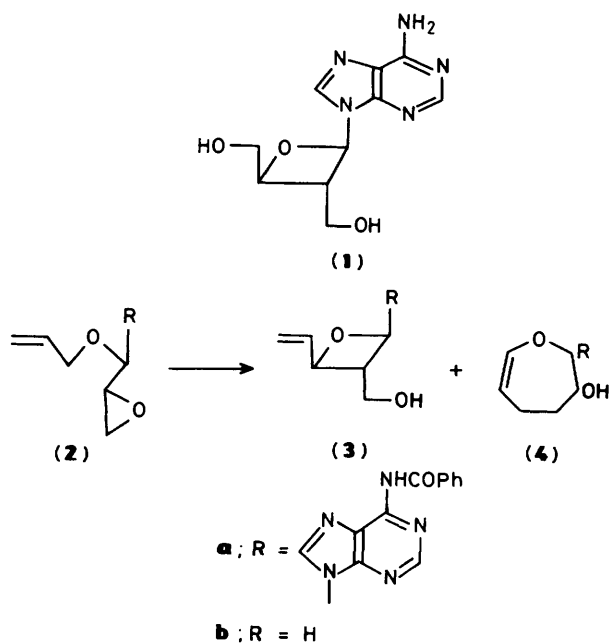
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Reaction of allyl glycidyl ether (**2b**) with Bu^sLi gives vinyloxetane (**3b**) and tetrahydro-oxepine (**4b**).

Oxetanocin is a novel nucleoside having an oxetanosyl-*N*-glycoside structure (**1**) which has interesting biological properties.^{1,2} In particular, it shows appreciable antiviral activity.³ Very recently, we succeeded in the total synthesis of (**1**),^{4,5} the crucial step being the allyloxycarbanion-mediated intramolecular oxetane ring formation. We revealed that the reaction of (**2a**) with a base afforded the desired vinyloxetane (**3a**) and its stereoisomer concomitant with tetrahydro-oxepine (**4a**). In contrast with our result, it has been reported that the reaction

of allyl glycidyl ether (**2b**) with Bu^sLi at –70 °C in the presence of hexamethylphosphoric triamide (HMPT) yielded tetrahydro-oxepine (**4b**) as the sole product and gave no vinyloxetane (**3b**).^{6,7} In this communication, we report the result of our re-examination of the allyloxycarbanion-mediated intramolecular ring closure of (**2b**).

When (**2b**) was treated with Bu^sLi in tetrahydrofuran (THF) at –78 °C, two cyclic compounds, vinyloxetane (**3b**) and tetrahydro-oxepine (**4b**) were produced in 8 and 6% yield,



respectively. In the presence of HMPT, the yields of both compounds were increased to 12% (**3b**) and 27% (**4b**).[†] The structure of this new compound (**3b**) was unequivocally confirmed by 400 MHz ¹H n.m.r. spectroscopic analyses of

[†] *Experimental procedure.* 1.02 M Bu^sLi-cyclohexane (4.9 ml) was added dropwise to a solution of allyl glycidyl ether (**2b**) (0.60 ml) and HMPT (2.6 ml) in anhydrous THF (25 ml) at -78 °C under argon. After stirring for 30 min at the same temperature, the reaction was quenched with phosphate buffer (pH 7; 30 ml). The reaction mixture was saturated with solid NaCl and extracted with ethyl acetate (6 × 30 ml). The combined extract was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure below 25 °C. The resulting mixture was separated by flash chromatography on silica gel. (**4b**) (152 mg) was eluted with ether-hexane (1:1) as eluant and then (**3b**) (69 mg) was eluted with ether-hexane (2:1). The R_f values on t.l.c. (silica gel 60 F₂₅₄) developed with ether-hexane (2:1) were 0.37 for (**4b**) and 0.15 for (**3b**).

(**3b**) and its benzoate.[‡] In conclusion, this work demonstrates that the allyloxycarbanion-mediated intramolecular ring closure of (**2b**) takes place by two routes: the 4-*exo* mode to yield (**3b**) and the 7-*endo* mode to yield (**4b**).⁸ This result is inconsistent with that of the previous paper,⁶ possibly owing to the loss of (**3b**) during isolation of the reaction products, because (**3b**) is not readily extractable from the aqueous reaction mixture.

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[‡] ¹H N.m.r. spectroscopic data (400 MHz, CDCl₃) for (**3b**): δ 2.90 (1H, quint, J 8.0 and 6.2 Hz), 3.07 (1H, br. s), 3.81 (2H, d, J 6.2 Hz), 4.43 (1H, t, J 6.2 Hz), 4.60 (1H, dd, J 8.0 and 6.2 Hz), 4.97 (1H, t, J 6.2 Hz), 5.21 (1H, d, J 10.6 Hz), 5.33 (1H, d, J 17.3 Hz), 6.12 (1H, ddd, J 17.3, 10.6, and 6.2 Hz). The stereochemistry of (**3b**) was assigned as *trans* by comparison with the data reported by A. Balsamo *et al.*⁹

Benzoate of (**3b**): δ 3.20 (1H, quint, J 8.0 and 6.5 Hz), 4.53 (2H, d, J 6.5 Hz), 4.55 (1H, t, J 6.5 Hz), 4.66 (1H, dd, J 8.0 and 6.5 Hz), 5.09 (1H, t, J 6.5 Hz), 5.24 (1H, d, J 10.5 Hz), 5.37 (1H, d, J 17.0 Hz), 6.14 (1H, ddd, J 17.0, 10.5, and 6.5 Hz), 7.46 (2H, t, J 8.0 Hz), 7.59 (1H, t, J 8.0 Hz), 8.05 (2H, d, J 8.0 Hz).

(**4b**): δ 1.78–1.87 (1H, m), 1.92–2.12 (2H, m), 2.14–2.25 (1H, m), 2.61 (1H, d, J 4.0 Hz), 3.91 (1H, dd, J 12.0 and 4.0 Hz), 3.98–4.04 (1H, m), 4.05 (1H, dd, J 12.0 and 2.7 Hz), 4.81 (1H, q, J 6.0 Hz), 6.31 (1H, dt, J 6.0 and 2.0 Hz).