

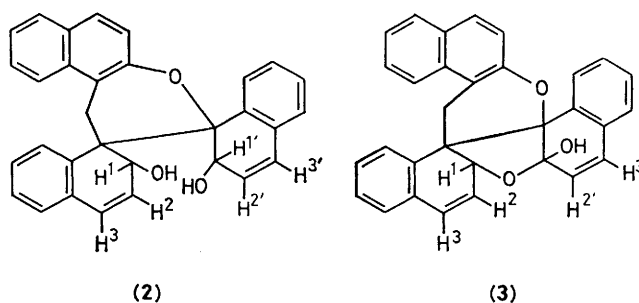
## Novel Intramolecular Reductive C–C Coupling during Borohydride Reduction of a Bi-enone

Tirumalai R. Kasturi\* and Gonibella J. Raju

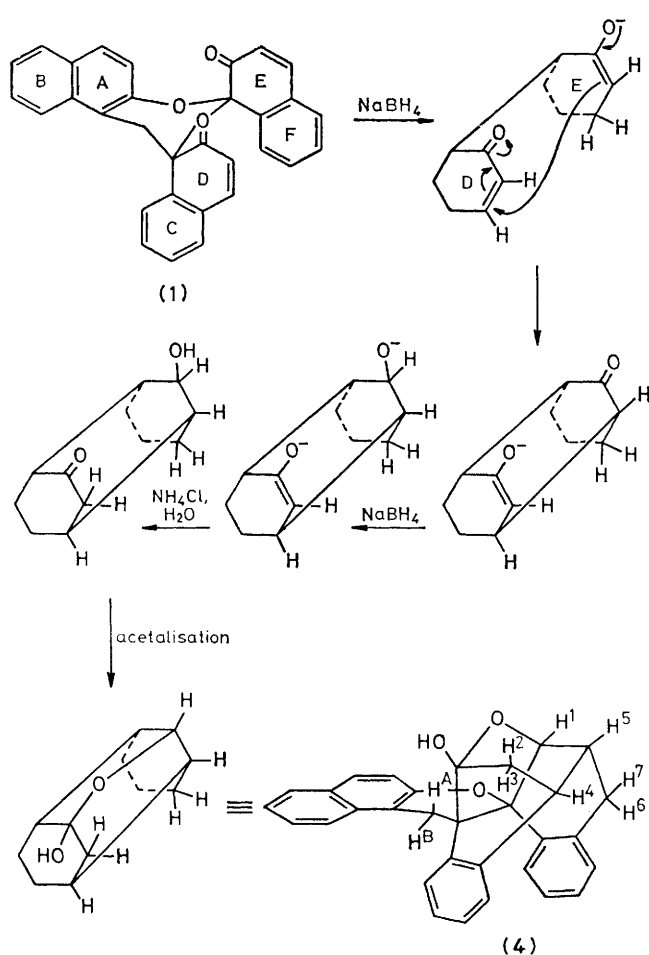
*Department of Organic Chemistry, Indian Institute of Science, Bangalore-560012, India*

Borohydride reduction of the bi-enone (**1**) gave the structurally and mechanistically interesting compounds (**4**) and (**5a–c**) resulting from intramolecular carbon–carbon coupling.

Intramolecular photocycloaddition in the bienone (**1**) has been reported to be inefficient presumably because of the competing facile  $\beta$  C–C cleavage.<sup>1</sup> With a view to preparing the biallylic alcohol (**2**), required for further studies of intramolecular photocycloadditions, we reduced the bienone (**1**) with sodium borohydride in tetrahydrofuran (THF). The biallylic alcohol (**2**) (m.p.† 212–215 °C; *m/e* 444) was obtained in only 15% yield. The major products were the hemiacetal (**3**) (35%;



† All the compounds decomposed near their m.p.s. Satisfactory elemental analyses were obtained for the new compounds.

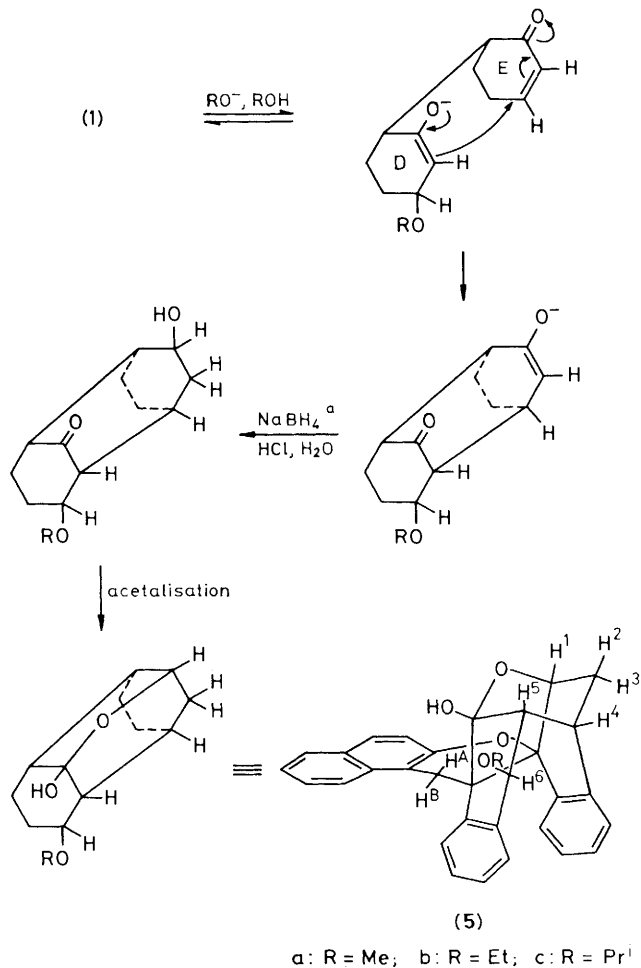


Scheme 1

m.p. 231 °C; *m/e* 442) and the novel intramolecularly C-C coupled hemiacetal (4) (30%, m.p. 230 °C; *m/e* 444). Under very dry conditions and with excess of borohydride, the yield of (4) increased considerably (55%), whereas in THF-methanol or aqueous THF, only the hemiacetal (3) was obtained, with a very minor amount of the allylic alcohol but with no trace of (4). When the reduction was carried out in the presence of sodium hydroxide<sup>2</sup> in aqueous THF, (3) was obtained with traces of (4) and (2). However, reduction in methanol-THF containing sodium hydroxide gave the novel methoxy C-C coupled hemiacetal (5a) (65%; m.p. 272 °C; *m/e* 474) along with (3) (20%). Similarly, the ethoxy C-C coupled hemiacetal (5b) (60%; m.p. 264 °C; *m/e* 488) and the isopropoxy C-C coupled hemiacetal (5c) (30%; m.p. 242 °C; *m/e* 502) were obtained.

The structures of all the compounds were established by <sup>13</sup>C and <sup>1</sup>H n.m.r. spectroscopy,† the off-resonance decoupled <sup>13</sup>C n.m.r. spectrum of (4) shows three triplets and three doublets, while that of (5) shows two triplets and four doublets < 90.0 p.p.m., clearly indicative of intramolecular C-C coupling

† The <sup>13</sup>C and <sup>1</sup>H n.m.r. were taken in CDCl<sub>3</sub> with Me<sub>4</sub>Si as internal standard with a Bruker 270 MHz Fourier transform instrument. Selected <sup>1</sup>H n.m.r. data (δ-values): (2) 1-, 1'-H 4.82 (m), 5.16 (m); OH 3.14 (d), 3.40 (d); 2-, 2'-H 5.76 (dd), 5.93 (dd); 3-, 3'-H 5.63br. (d), 6.24br. (d); (3) 1-H, 4.77 (d); OH 4.70 (s); 2-, 2'-H 6.06 (dd), 5.75 (d); 3-, 3'-H 5.96 (d), 6.72 (d); (4) 1-H 4.75 (d); 2-, 3-H 1.64 (dd), 2.25 (dd); 5-, 4-H 2.62 (m), 3.13 (m); 6-, 7-H 2.80 (d), 3.22 (dd); OH 2.67 (s); (5a), 1-H 4.72 (m); 2-, 3-H 1.57, 2.43 (each 8-line m); 5-, 4-H 2.86 (dd), 3.3 (m); 6-H 4.15 (d); OH 5.33 (s); OMe 3.52 (s).



a: R = Me; b: R = Et; c: R = Pr<sup>1</sup>

**Scheme 2.** <sup>a</sup> Since rings D and E are parallel in (1), the orientation of the alkoxy-group is fixed, and so both sides of saturated C=O group in the intermediate are hindered. Thus, either the enolate is reduced in preference to the ketonic function (for reduction of enolates with borohydride see ref. 4b and P. L. Southwick, N. Latif, B. M. Fitzgerald and N. M. Zaczek, *J. Org. Chem.*, 1966, **31**, 1) or the resulting ketone is reduced during work-up.

between the D and E rings. The occurrence of intramolecular C-C coupling in (4) and (5) between benzylic and nonbenzylic carbon atoms was established by their <sup>1</sup>H n.m.r. spectra. Of the two alternative structures, that with coupling between the D ring benzylic carbon atom and the E ring nonbenzylic carbon atom was assigned to (4), on the basis of the OH resonances in (2)–(4) and theoretical arguments on the difference in the reactivities of the two enone systems in (1). There are significant differences in the <sup>1</sup>H n.m.r. spectra of (4) and (5); in particular the 1-H [d in (4); m in (5)] and 2,3-H resonances [dd in (4); 'ABq' in (5)]. The variation in the OH resonance position with the alkoxy-group in (5) [R = Me, δ 5.33; Et, 5.43; Pr<sup>1</sup>, 5.50; cf. (4), δ 2.67] indicates that the hydroxy-group is on the same side as the alkoxy-group, and probably hydrogen-bonded to it. These facts, as well as the significant differences in the number and nature of the shielded aromatic protons [6 in (4); 7 in (5)], indicate the structure shown for compounds (5) rather than structures similar to (4).

The intramolecular C-C coupled products are believed to arise by hydride attack [compound (4)] and alkoxide attack<sup>3</sup> [compounds (5)] on the β-carbon atom of the enone as shown in Schemes 1 and 2. The more reactive enone carbonyl group (ring D) is perhaps protected in the alkaline medium.<sup>2</sup> In

either case, the enolate ion, acting as the Michael addend, is essential for the intramolecular C–C coupling. The failure to obtain (4) in protic solvents and (5) in alcoholic solvents in the absence of alkali, despite the reported<sup>3</sup> formation of  $\beta$ -alkoxy-products in the borohydride reduction of enones in alcoholic solvents without alkali, is strong evidence for the mechanism proposed.

Intramolecular reductive C–C coupling during borohydride reduction is unprecedented. Apart from the structural novelty of the C–C coupled products, the mechanism of their formation is quite significant owing to the uncertainty still associated<sup>4</sup> with double-bond saturation during the borohydride reduction of enones.

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