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Note

Sodium borohydride reduction of *E*-3-benzylideneflavanones : Stereoselective formation of 3(*S**)-benzyl-4(*S**)-hydroxy-2(*S**)-flavans

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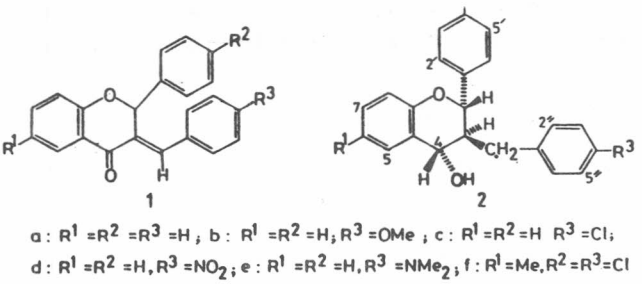
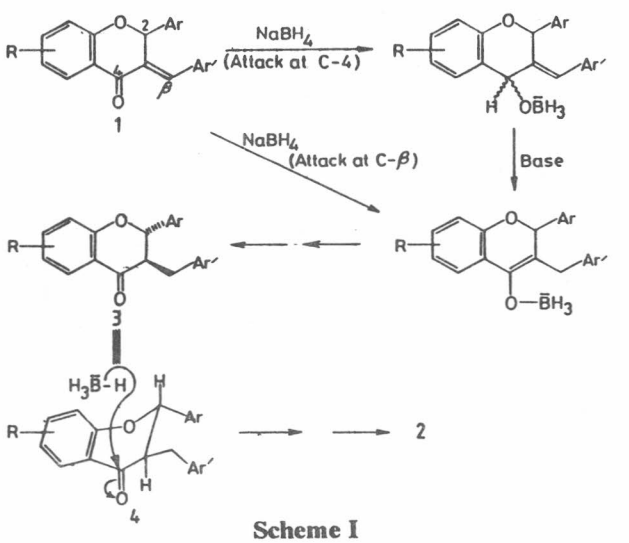
Sodium borohydride reduction of *E*-3-benzylideneflavanones **1a-f** has been found to be highly stereoselective yielding 3(*S**)-benzyl-4(*S**)-hydroxy-2(*S**)-flavans **2a-f** in very good yield. A plausible explanation for the stereoselectivity has been offered.

Recently, we have developed an easy method for the synthesis of *E*-3-benzylideneflavanones[1a] **1** and are interested in studying different reactions of this system[1b,c]. Sodium borohydride reduction of an enone system in alcoholic medium is known to produce a saturated alcohol either solely or in conjugation with an unsaturated alcohol[2]. Considering the structures of the saturated alcohol derived from **1** it is evident that four diastereoisomeric *dl*=pairs are possible for such compounds. We, therefore, undertook the study of sodium borohydride reduction of **1** and the results are presented herein.

Six *E*-3-benzylideneflavanones **1a-f** were reduced with sodium borohydride in methanol. In each case a single product was obtained. The spectral data of the products clearly showed that the same diastereoisomer was formed in all the cases (Table I). Analysis of the coupling constants $J_{2,3}$ and $J_{3,4}$ revealed that the products possess 2,3-*trans*-3,4-*trans* configuration†. The following plausible explanation may be offered for the stereoselectivity.

Owing to weaker hydride donating ability of alkoxyborohydrides compared to alkoxyaluminohydrides, a mechanistic path analogous to that suggested for lithium aluminium hydride reduction of *E*-3-benzylidenechromanones (which leads to stereoselective formation of *trans*-3-benzylchromanols by reduction of the carbonyl group first and then of the exocyclic double bond by intramolecular hydride transfer from the resulting alkoxyaluminohydride moiety from the same side)[5,6] would be improbable in this case. So, by analogy with borohydride reduction of other α,β-unsaturated ketones[2], **1** is possibly transformed first into *trans*-3-benzylflavanones **3** and then to 3(*S**)-benzyl-4(*S**)-hydroxy-2(*S**)-flavans **2** (Scheme I) The preferred conformation of **3** would be **4** and hence during its reduction approach of hydride takes place from the axial side[7] yielding only **2**. This view is supported by the fact that sodium borohydride reduction of *trans*-3-benzylflavanone (prepared by Jones oxidation of





Scheme I

†Reported[3,4] coupling constants for 2,3-*cis*-3,4-*cis* : $J_{2,3}$ ≈1.0 and $J_{3,4}$ ≈ 4.5 Hz; 2,3-*cis*-3,4-*trans* : $J_{2,3}$ = 1-3 and $J_{3,4}$ ≈ 2.5 Hz; 2,3-*trans*- 3,4-*cis* : $J_{2,3}$ ≈ 10 and $J_{3,4}$ ≈ 3.5 Hz; 2,3-*trans*-3,4-*trans* : $J_{2,3}$ = 8.7-9.7 and $J_{3,4}$ = 7-9.7 Hz.

Table I—Characterization data of **2**

Starting Material	Product	m.p.[a] (°C)	Yield (%)	^{1}H NMR($CDCl_3$, δ)[b]
1a	**2a**	158-60	88	1.40(1H,br, O-H)[d], 2.63-2.73 (3H,m,H-3 and –CH_2-), 4.73(1H,br, H-4)[e], 4.90(1H,d, *J*=8.7 Hz,H-2), 6.90-7.43 (14H,m, Ar-H).
1b	**2b**	197-98	81	1.40(1H,d, *J*=8Hz, O-H)[d], 2.50-2.78 (3H,m, H-3, and –CH_2-), 3.76(3H,s, 4″-OCH_3), 4.72 (1H,t, *J*=8.0 Hz, H-4)[e], 4.98(1H,d, *J*=8.0 Hz, H-2), 6.74-7.50 (13H,m,Ar-H)
1c	**2c**	186-87	85	1.30 (1H, d, *J*=9 Hz, O-H)[d], 2.55-2.85 (3H,m, H-3 and CH_2-), 4.65 (1H,br,t, *J*=8.6 Hz, H-4)[e], 4.95 (1H,d, *J*=8.6 Hz, H-2), 6.85-7.45 (13H,m, Ar-H)
1d	**2d**	118-19	78	1.50 (1H, d, *J*=8 Hz, O-H)[d], 2.59-2.65(1H,m, H-3), 2.71 (1H,dd, *J*=13 and 7Hz, H_A-α), 2.95 (1H,dd,*J*=13 and 5 Hz, H_B-∞), 4.70 (1H,t,*J*=8.65 Hz, H-4)[e], 4.91 (1H,d, *J*=8.6 Hz,H-2), 6.88 (1H,d, *J*=8.2 Hz,H-8), 6.99 (1H,dt,*J*=7.6 and 1.0 Hz, H-6), 7.06 (2H, d, *J*=8.65 Hz, H-2″ and 6″), 7.22 (1H,ddd, *J*=8.7, 7.1 and 1.6 Hz, H-7), 7.26-7.30 (5H,m, Ar-H), 7.44 (1H,d, *J*=7.5 Hz, H-5), 7.97-8.00 (2H,m,H-3″ and H-5″)
1e	**2e**	135-36	82	1.43 (1H,d, *J*=6.9Hz, O-H)[d], 2.38-2.40 (1H, m,H-3), 2.56-2.61 (2H,m, -CH_2-), 2.83 (6H,s, NMe_2), 4.68 (1H,t, *J*=6.8, Hz,H-4)[e], 4.89 (1H, d, *J*=7.8Hz, H-2), 6.59 (2H,d, *J*=8.7Hz, H-3″ and H-5″), 6.61-6.90 (2H,m, H-6 and H-8), 6.94 (2H,d, *J*=8.6 Hz, H-2″ and H-6″), 7.13 (1H, dt, *J*=7.9 and 1.4 Hz,H-7), 7.23-7.34 (6H,m, Ar-H)
1f	**2f**	129-30	84	1.39 (1H,d, *J*=8.4Hz, O-H)[d], 2.30 (3H,s, 6-CH_3), 2.56-2.73 (3H,m, H-3 and –CH_2-), 4.64 (1H,t, *J*=7.8Hz,H-4)[e], 4.90 (1H,d, *J*=7.2Hz, H-2), 6.81 (1H,d, *J*=8.4Hz, H-8), 6.98 (2H,d, *J*=8.4 Hz, H-2″ and H-6″), 7.04 (1H,dd, *J*=8.4 and 1.9Hz, H-7), 7.19-7.31 (7H,m, Ar-H)

(a) Uncorrected
(b) 200 MHz machine for **2a, 2c**, 100 MHz for **2b**, 500 MHz for **2d**, 300 MHz for **2e** and **2f.**
(c) Anal. **2a** : C, 83.15; H, 6.20. Calcd for $C_{22}H_{20}O_2$: C, 83.50; H, 6.38%; **2c**: C, 74.96; H, 5.23. Calcd for $C_{22}H_{19}O_2Cl$: C, 75.31; H,5.47%; **2e** : C,79.81; H,6.79. Calcd for $C_{24}H_{25}O_2N$: C,80.18; H,7.02%
(d) Exchangeable with D_2O
(e) Changed to a doublet (*J*≈7.5 Hz) on D_2O shaking

2a) yielded only **2a** in 75% yield. It may be mentioned here that 3-*t*-butylchromanone which exists in only one conformation is reported to give only one product on sodium borohydride reduction[8] while 3-benzylchromanone capable of existing in two conformations in equilibrium gives two products on such reduction[5,9].

Experimental Section

Sodium borohydride reduction of 1: General procedure. To a solution of **1** (1 mmole) in dry methanol sodium borohydride (150 mg) was added in three portions and the mixture kept at room temperature for 48 hr. Usual work-up of the reaction mixture followed by chromatography of **the resulting material gave pure 2**.

Among the reduction products **2a-f, 2a** and **2f** were acetylated (Ac_2O/Py). Acetate of **2a**, m.p. 171-72°; acetate of **2f**, m.p. 136-37°; they showed their acetoxy signals at δ 1.46 and 1.51, respectively, which is noteworthy.

Jones oxidation of 1a. The compound **1a** was oxidised with CrO_3-HOAc (room temperature, 30 min.). The product, *trans*-3-benzylflavanone (colourless oil) showed the following ^{1}H NMR (60 MHz) signals : δ 2.90-3.35 (3H,m, H-3 and –CH_2-), 5.26 (1H,d, *J*=8.4 Hz, H-2), 6.98-7.68 (13H,m, Ar-H) and 7.92 (1H,dd, *J*=8.6 and 1.5 Hz, H-5).

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