Effects of Neighbouring Hydroxy-groups in Metal–Ammonia Reductions of αβ-Unsaturated Carbonyl Compounds

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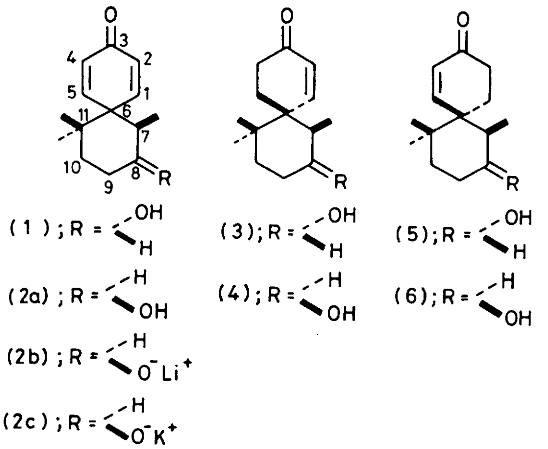
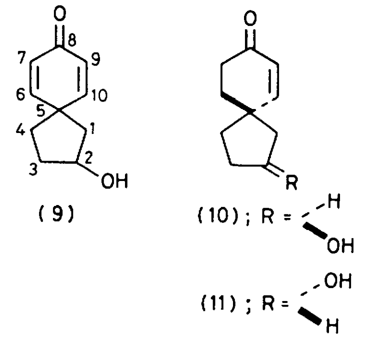
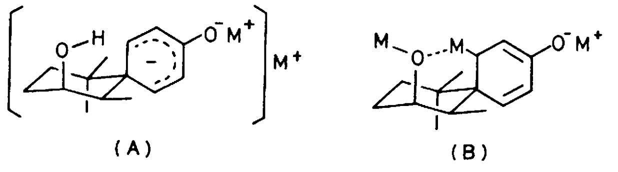
Summary The regiospecific metal–ammonia reductions of both *cis*-8-hydroxy-7,11,11-trimethylspiro[5.5]undeca-1,4-dien-3-one (**2a**) and its metal alkoxides (**2b**) and (**2c**) could be achieved as a result of the proximity of the hydroxy-group to afford *t*-8-hydroxy-*t*-7,11,11-trimethyl-(6*r*C^1)-spiro[5.5]undec-1-en-3-one (**4**) in high yield.

ALTHOUGH metal–ammonia reductions of $\alpha\beta$-unsaturated carbonyl compounds are well known, the influence of neighbouring functional groups on the stereochemistry of β-protonation has not been explored in detail.[1] Recently, McMurry and co-workers[2] described the stereochemical influence of the lithium carboxylate function in the metal–ammonia reduction of 1-carboxy-9-methyl-Δ^4-3-octalone. In conjunction with our work on the total synthesis of spirosesquiterpenes, we have also studied the metal–ammonia reductions of *trans*- and *cis*-8-hydroxy-7,11,11-trimethylspiro[5.5]undeca-1,4-diene-3-one, (**1**) and (**2**)[3] respectively, and 2-hydroxyspiro[4.5]deca-6,9-dien-8-one (**9**), and here report the results of their regioselective reductions, which might be attributed to the proximity of the hydroxy-group.[4]

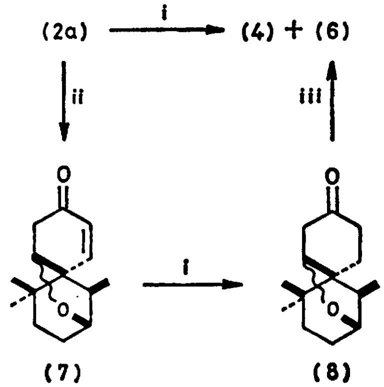






M = metal

Reduction of (**1**) (115 mg) with lithium (8·7 mg) at −70 °C afforded a *ca* 1 : 1 mixture[5] of compounds (**3**) and (**5**).† In contrast, reduction of (**2a**) under the same conditions afforded only *t*-8-hydroxy-*t*-7,11,11-trimethyl-(6*r*C^1)-spiro[5.5]undec-1-en-3-one[6] (**4**) in 89% yield; ν (CHCl$_3$) 3612, 3450, 1664, and 1617 cm^{-1}; δ (CDCl$_3$) 0·97 (3H s), 1·01 (3H, d, *J* 6·8 Hz), 1·03 (3H, s), 1·4—2·6 (10H, m), 3·88 (1H, br q, *J* 4 Hz), 6·00 (1H, d, *J* 10·2 Hz), and 6·65 (1H, d, *J* 10·2 Hz). The stereochemistry of (**4**) was assigned from the presence of the two signals at δ 6·00 and 6·65, due to 2-H and 1-H, respectively, of the $\alpha\beta$-unsaturated ketone moiety. These signals appeared at the normal positions. In contrast, the n.m.r. spectrum of (**6**)‡ showed two signals at δ 6·11 (2-H) and 7·30 (1-H). The signal was shifted to lower field because of the proximity of the hydroxy-group.



SCHEME. i, H$_2$/Pd–C, AcOEt, ii, NaNH$_2$–NH$_3$, iii, NaOMe–MeOH.

The enone (**6**) was prepared as follows (Scheme). Catalytic hydrogenation (H$_2$,Pd–C) of (**2a**) gave (**4**) and (**6**) (1 : 1) in 30—40% yield; treatment of (**2a**) with sodamide in liquid ammonia gave the tricyclic compound (**7**) [ν (CHCl$_3$) 1681 cm^{-1}; δ (CCl$_4$) 0·80 (3H, s), 0·9—1·9 (10H, m, with s at 1·12 and d, *J* 7·0 Hz, at 1·30), 2·21 (1H, q, *J* 7·2 Hz), 2·42 (1H, dd, *J* 16·6 and 10·2 Hz), 2·76 (1H, dd, *J* 16·6 and 8·4 Hz), 4·00 (1H, br d, *J* 3·8 Hz), 4·43 (1H, dd, *J* 10·2 and 8·4 Hz), 6·00 (1 H, d, *J* 10·2 Hz), and 6·54 (1H, d, *J* 10·2 Hz);

TABLE. Metal–ammonia reductions of the dienones (**1**), (**2**), and (**9**).

Substrate	Metal	Product	% Yield
(**1**)	Li	(**3**) and (**5**) (*ca.* 1 : 1)	40
(**2a**)	Li	(**4**)	89
(**2b**)	Li	(**4**)	88
(**2c**)	Li	(**4**)	87
(**2c**)	K	(**4**)	82
(**9**)	Li	(**10**) and (**11**) (7:1)	52

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† Satisfactory analytical and spectral data were obtained for all new compounds.

‡ Data for (**6**): ν (CHCl$_3$) 3608, 3450, 1665, and 1620 cm^{-1}; δ (CDCl$_3$) 0·88 (3H, s), 1·00 (3H, s), 1·13 (3H, d, *J* 6·8 Hz), 1·4—2·7 (10H, m), 3·84 (1H, q-like, *J* 4 Hz), 6·11 (1H, d, *J* 11·0 Hz), and 7·30 (1H, dd, *J* 11·0 and 2·0 Hz); *m/e* 222 (M^+); for (**10**): ν (CHCl$_3$) 3610, 3450, 1675, and 1610 cm^{-1}; δ (CDCl$_3$) 1·3—2·9 (11H, m), 4·44 (1H, m), 5·79 (1H, d, *J* 10·0 Hz), and 6·65 (1H, d, *J* 10·0 Hz); for (**11**): ν (CHCl$_3$) 3605, 3450, 1675, and 1610 cm^{-1}; δ (CDCl$_3$) 1·3—2·9 (11H, m), 4·46 (1H, m), 5·79 (1H, d, *J* 10·0 Hz), and 6·95 (1H, d, *J* 10·0 Hz).

m/e 220(M^+); hydrogenation of (**7**) over 10% palladium on charcoal in AcOEt gave (**8**) which, on treatment with sodium methoxide in methanol, yielded the enone (**6**).

Reduction of (**2b**) or (**2c**) under the same conditions afforded only the product (**4**) in high yield. Similarly, reduction of the alcohol (**9**) afforded compounds (**10**)‡ and (**11**)‡ (7 : 1) in good yield (Table). The n.m.r. spectrum of (**10**) showed a signal at δ 6·65 (6-H), whereas that of (**11**) showed a 6-H signal at δ 6·95, shifted to lower field by the hydroxy-group.

These regioselective metal–ammonia reductions strongly suggest the following reaction processes: the reduction of (**2a**) proceeds *via* intramolecular protonation of an intermediate (**A**), and the reductions of (**2b**) and (**2c**) proceed *via* a metal-chelated intermediate (**B**).

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[6] For an explanation of the nomenclature used here, see J. A. Marshall and P. C. Johnson, *J. Org. Chem.*, 1970, **35**, 192, footnote 16d.