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NOVEL STEREOCHEMICAL RESULTS IN THE BIRCH REDUCTION OF 4-ALKYL-$\Delta^{1(9)}$-2-OCTALONES

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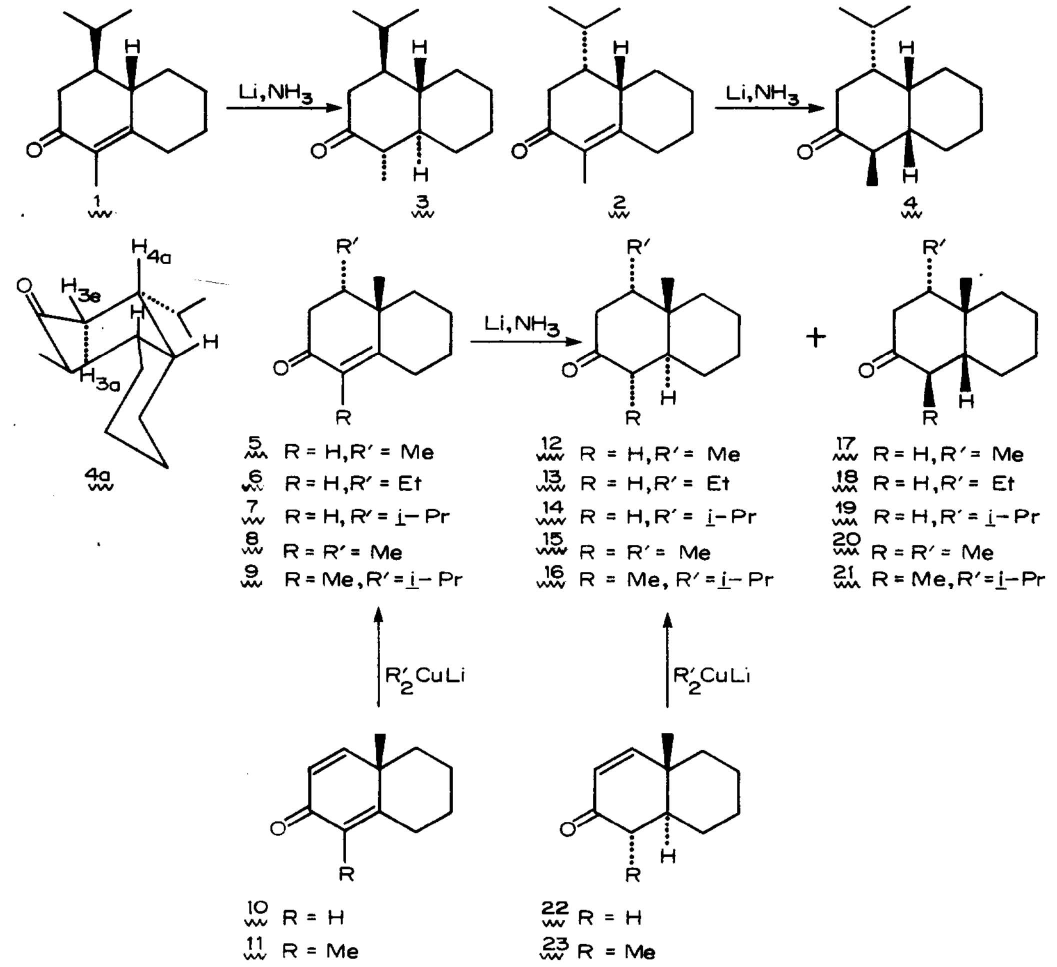
It is well known that the alkali metal-ammonia (Birch) reduction of simply substituted $\Delta^{1(9)}$-2-octalones generally affords, in each case, a high proportion of the corresponding trans-fused 2-decalone.[2-4] The mechanistic details of this type of reduction have received close attention,[5,6] and a number of proposals have been put forth to explain the stereochemical results.[3,4,7] We report in this communication novel stereochemical results obtained in a study of the Birch reduction of the 4-isopropyl-$\Delta^{1(9)}$-2-octalone **2** and of various 4-alkyl-10-methyl-$\Delta^{1(9)}$-2-octalones (**5**-**9**, inclusive).

Condensation of the pyrrolidine enamine of cyclohexanone with trans-2-methylhept-3-en-5-one afforded, after sodium methoxide catalyzed epimerization of the initial product, a mixture of the octalones **1** and **2**, in a ratio of 3:1, respectively (83% yield). These two compounds were readily separated by preparative gas-liquid chromatography (glc).

Although lithium-ammonia reduction of **1** proceeded in a "normal" manner and produced only the trans-fused decalone **3**, a similar reduction of **2** afforded, stereoselectively, the cis-fused decalone **4**. The stereochemistry of the latter was confirmed in the following ways: 1) Hydrogenation of the carbon-carbon double bond of **2** would be expected to take place from the side opposite the alpha isopropyl group and also produce only the cis-fused decalone **4**. This was indeed found to be the case. 2) Internuclear double resonance (INDOR) studies[8] on compound **4** revealed the following proton-proton splittings: H_{3e}-H_{3a}, 13.0 Hz; H_{3e}-H_{4a}, 3.9 Hz; H_{3a}-H_{4a}, 13.0 Hz. These observed splittings are inconsistent with a decalone possessing a trans fusion, but are consistent with structure **4** (cf. **4a**).

The above results revealed that the presence of an alpha substituent at the C_4 position can exert a profound effect on the stereochemical outcome of the Birch reduction of a $\Delta^{1(9)}$-2-octalone. In view of this novel stereochemical result, it was decided to extend the investigation to include the lithium-ammonia reduction of analogous octalone systems possessing an angular



methyl group at C_{10}. In particular, the Birch reduction of octalones **5** - **9**, inclusive,[9] was carried out and, in each case, a high yield of a mixture of the corresponding trans-fused (**12** - **16**, respectively)[13] and cis-fused (**17** - **21**, respectively)[16] decalones was obtained. The results are summarized in the Table.

The typical experimental procedure employed to obtain these results was as follows. To a magnetically stirred solution of lithium metal (55 mg) in liquid ammonia (60 ml) was added, dropwise over a period of 30 min, a solution of the octalone (100 mg) in anhydrous ether (10 ml). After two hours, the reaction was quenched by addition of ammonium chloride, the ammonia was

Table. Stereochemistry of Birch Reduction of 4-Alkyl-$\Delta^{1(9)}$-2-octalones

Expt. No.[a]	Octalone	Yield (%)[b]	Ratio of trans:cis Decalone	Recovered Starting Material (%)
1	**1**	91	>99: 1	--
2	**2**	80	<1:99	--
3	**5**	93	87:13	2
4	**6**	94	75:25	13
5	**7**	98	69:31	14
6	**8**	90	82:18	8
7	**9**	98	65:35	7

[a] All experiments were done at least in duplicate. [b] Yield of distilled product.

allowed to evaporate, and dilute hydrochloric acid was added to the residue. The product, isolated by extraction of the resulting mixture with ether, was distilled under reduced pressure and then subjected to analysis by glc.

A number of interesting conclusions can be drawn from the results tabulated in the Table. Firstly, the results show that the Birch reduction of $\Delta^{1(9)}$-2-octalones possessing an alpha-oriented alkyl substituent at C_4 affords, in each case, a much greater proportion of the corresponding cis-fused decalone than is normally found in reductions of this type.[2-4] Secondly, the presence or absence of an angular methyl group (at C_{10}) in these compounds has a profound effect on the stereochemistry of the reduction (Expt. Nos. 2, 7). Thirdly, the relative amount of cis-fused decalone in the product increases with increasing size of the alpha-oriented C_4 alkyl group (Expt. Nos. 3-5 and 6,7). Finally, the presence or absence of a methyl group (or, presumably, another alkyl group) at C_1 has little effect on the stereochemistry of reduction (Expt. Nos. 3, 5, 6, 7).[17]

Finally, it is pertinent to point out that the work described above has obvious synthetic potential. For example, the formation and Birch reduction of octalones **1** and **2** can obviously be applied, with appropriate modifications, to the synthesis of both cadinane-type[18] and amorphane-type[18] sesquiterpenes.

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9. Compounds **5** - **9** were prepared by conjugate addition of an appropriate lithium dialkylcuprate[10] to the cross-conjugated dienones **10**[11] or **11**[12].
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13. Compounds **12** - **16** were prepared by conjugate addition of an appropriate lithium dialkylcuprate[10,14] to the Δ^3-2-octalones **22**[15] or **23**[15].
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15. Prepared by bromination-dehydrobromination of the corresponding *trans*-fused 2-decalone. *Cf*. C. Djerassi and D. Marshall, *J. Amer. Chem. Soc.*, **80**, 3986 (1958); E.J. Corey and A.G. Hortmann, *ibid*, **87**, 5736 (1965).
16. Compounds **17**-**21** were prepared by hydrogenation (Pd-C, 0.3 N ethanolic potassium hydroxide) of the $\Delta^{1(9)}$-2-octalones **5** to **9**, respectively.
17. Work in this area is continuing. A detailed discussion of mechanism will be given in the full paper.
18. *Cf*. Y. Ohta, K. Ohara, and Y. Hirose, *Tetrahedron Letters*, 4181 (1968).