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A NEW SYNTHESIS OF ACYCLIC 1, 5-DIENES

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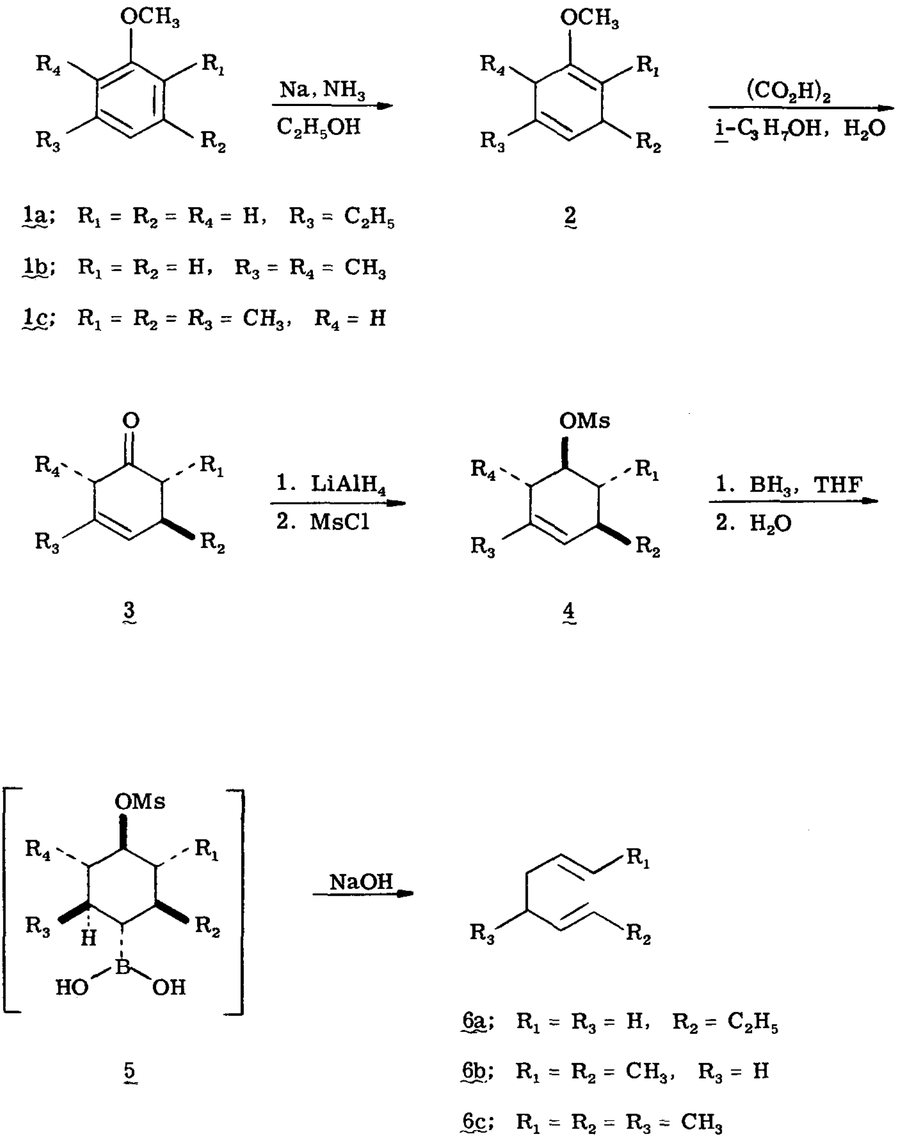
The widespread natural occurrence of acyclic 1, 5-dienes has stimulated interest in the design of efficient synthetic routes to such compounds.[2] In considering potential solutions to this challenging problem we were struck by the simplicity of the scheme outlined in Chart I.[3] In the case of symmetrical 1, 5-dienes (eg, $R_1 = R_2 = R_3 = R_4$), this scheme appears straightforward and unambiguous. However, for unsymmetrical olefins (eg, $R_1 \neq R_2 \neq R_3 \neq R_4$) the question arises as to which of the two equivalently oriented β,γ-cyclohexane ring bonds in the boronic mesylate **5** would be more readily broken. As a consequence of some related studies[4] we had reason to believe that the more highly substituted of the aforementioned C-C sigma bonds would preferentially cleave, although the magnitude of this preference could not be estimated for the systems contained in Chart I. Our preliminary studies have now shown that ring substituents on cyclohexaneboronic mesylates such as **5** strongly control the directional specificity of the ring cleavage reaction and that this directing influence can be gainfully applied to the synthesis of unsymmetrical acyclic 1, 5-dienes.

The general scheme outlined in Chart I was applied to the indicated methoxybenzene derivatives[5] whereupon the 1, 5-dienes could be isolated in 50-60% overall yield. In all cases only those products arising *via* cleavage of the more substituted carbon-carbon bond of the

Chart I



1a; $R_1 = R_2 = R_4 = H$, $R_3 = C_2H_5$

1b; $R_1 = R_2 = H$, $R_3 = R_4 = CH_3$

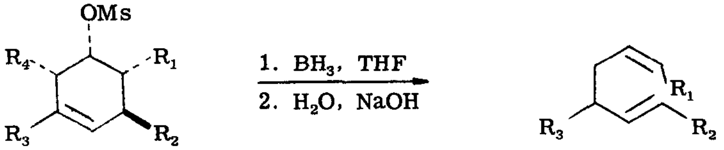
1c; $R_1 = R_2 = R_3 = CH_3$, $R_4 = H$

6a; $R_1 = R_3 = H$, $R_2 = C_2H_5$

6b; $R_1 = R_2 = CH_3$, $R_3 = H$

6c; $R_1 = R_2 = R_3 = CH_3$

presumed boronate intermediate 5 could be detected.[6] The mesylates 4b and 4c derived from methoxybenzenes 1b and 1c also contained the corresponding epimers 7b and 7c (7b:4b ~ 2.5). These substances gave rise to the related *trans*, *cis*-dienes 8b and 8c in the hydroboration-fragmentation sequence.[7]



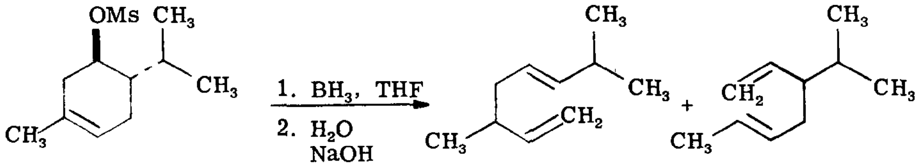
7b; $R_1 = R_2 = H$, $R_3 = R_4 = CH_3$

7c; $R_1 = R_2 = R_3 = CH_3$, $R_4 = H$

8b; $R_1 = R_2 = CH_3$, $R_3 = H$

8c; $R_1 = R_2 = R_3 = CH_3$

Finally, when the cleavable (β, γ) carbon-carbon bonds were equally substituted, as in the case of mesylate 9, both isomeric 1,5-dienes (10:11 = 3) were formed upon hydroboration-fragmentation. It therefore appears as though C-C bond strength exerts a profound influence on the course of fragmentation reactions in a variety of systems.[8]



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1. National Institutes of Health Predoctoral Fellow, Division of General Medical Sciences.
2. *Cf.* W. S. Johnson, *et.al.*, *J. Amer. Chem. Soc.*, **92**, 741 (1970); E. H. Axelrod. G. M. Milne and E. E. van Tamelen, *ibid.*, **92**, 2139 (1970) and references cited therein.
3. J. A. Marshall, *Rec. Chem. Prog.*, **30**, 3 (1969).
4. J. A. Marshall and J. H. Babler, *J. Org. Chem.*, **34**, 4186 (1969).
5. These ethers were prepared *via* methylation (Me_2SO_4-NaOH) of the corresponding phenols secured from the Aldrich Chemical Company, Inc., Milwaukee, Wisconsin.
6. The dienes and cyclohexenols were purified *via* preparative gas chromatography using 0.25 in. columns of 5% Carbowax 20-M on 60-80 mesh Chromosorb W or 4% Dow Corning 550 Silicone Oil on 60-70 mesh Chromosorb W. Structures were assigned by means of infrared and nmr spectra and, where appropriate, comparison with authentic samples. Satisfactory analytical data were obtained for all new dienes and the cyclohexenol precursors.
7. In the case of **7b** the fragmentation was carried out on a purified sample of the mesylate. A 60:40 mixture of mesylates **4c** and **7c** afforded a 66:34 mixture of dienes **6c** and **8c**.
8. For further examples, see M. Geisel, C. A. Grob, and R. A. Wohl, *Helv. Chim. Acta.*, **52**, 2206 (1969).