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REVERSAL OF THE REGIOSELECTIVITY OF THE BIRCH REDUCTION OF XYLENES

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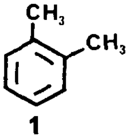
Summary: The "Photo-Birch" reduction of o-, m-, and p-xylene, using $NaBH_4$, 1,3-dicyanobenzene, and photolysis, gives 1,4-dienes as products. The regioselectivity of these reactions is greatly different from the normal Birch reduction.

The Birch (dissolving metal) reduction of aromatic compounds is a powerful tool for the synthesis of complex functionality. Its high regioselectivity[1] apparently arises because the protonation of the radical anion intermediate occurs preferentially at the position bearing the highest negative charge density[2]. Thus, the reduction of o-, m-, and p-xylene (1-3) leads to "exclusive" formation of 4-6, respectively, rather than the alternative reduction products 7-9, which are coincidentally less thermodynamically stable. We wish to report that a "Photo-Birch" reduction using sodium borohydride, 1,3-dicyanobenzene, and light leads to reversal of the regioselectivity so as to preferentially form compounds 7-9.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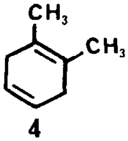
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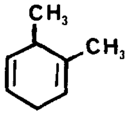
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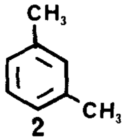
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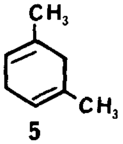
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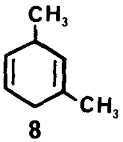
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6


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Irradiation[3] of any of the xylenes in the presence of 1,3-dicyanobenzene apparently leads to a transient charge-transfer species,[4] with radical cation character being borne by the xylene. A hydride transfer from sodium borohydride would be expected to occur preferentially at a site of high positive charge (a carbon bearing an alkyl substituent), giving a radical, and subsequently a radical anion after an electron transfer from the dicyanobenzene radical initially formed. Protonation at the central atom (as in a Birch reduction) leads to a 1,4-dihydro product.

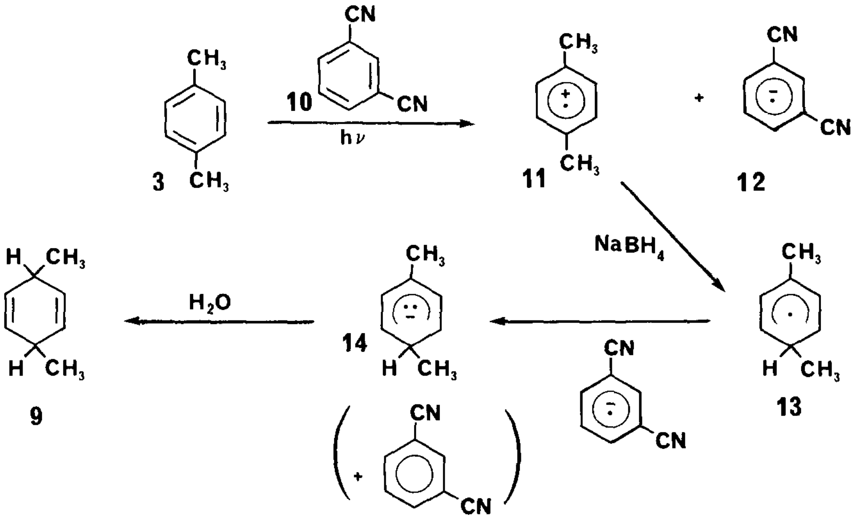

Table 1 shows typical yields[5] for reaction of 1-3. Products were isolated by preparative gas chromatography[6], and structures determined by comparison of their ^{1}H-NMR spectra with those of authentic compounds.[7]

Table 1. Product Distribution[a] from "Photo-Birch" Reduction of Xylenes.

Reactant	"Birch" Product, %	"Photo-Birch" Product, %	Bicyclic[b] Products, %
1	7.2 (4)	86.5 (7)	3.6
2	13.9 (5)	81.5 (8)	4.9
3	46.7 (6)	47.7 (9)	5.6

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[a] based on consumed starting material (typically 85% conversion with 8 hr photolysis

[b] dimethylbicyclo[3.1.0]hexenes

As can be seen from Table 1, with both 1 and 2 there is a clear-cut preference for the formation of the less stable diene, unlike the course of a normal Birch reduction. With 3 the "Photo-Birch" product, 9, is formed in about the same amount as 6, the sole product in a "normal" Birch reduction. The Photo-Birch reduction of 3 gives a 50:50 mixture of the two stereoisomers of 9. The reasons for the higher regioslectivity in the reduction of 1 and 2 are not yet apparent, but may reflect contributions of reactivity from other mechanistic pathways, such as electron transfer to neutral 3 by 14 or sodium borohydride[8], followed by subsequent attack on the xylene radical anion or ion pair.

The Photo-Birch reduction proceeded quite cleanly, with the dihydrobenzenes as virtually the only products. (Analytical gas chromatography using mesitylene as an internal standard confirmed the absence of unsuspected losses of material). Minor amounts of dimethylbicyclo[3.1.0]hexenes were observed in each instance (from sensitized photolysis of the products by unreacted xylene.[9]

In light of the difficulty of alternative reduction routes to dihydrobenzenes, we are continuing to investigate the versatility of this novel one-step approach.

ACKNOWLEDGMENT. We are grateful to the University of Connecticut Research Foundation and the National Institutes of Health (GM33867) for financial support of this work.

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(1) (a) Birch, A. J. Quart. Rev. **1950**, 4, 69-93.
(b) Birch, A. J.; Smith, H. ibid **1958**, 12, 17-33.
(c) Watt, G. W. Chem. Rev. **1950**, 46, 317.

(2) Fleming, I., "Frontier Orbitals and Organic Chemical Reactions", Wiley, New York, **1976**, pp. 200-202.

(3) Typically, 0.350 g (3.28 mmol) of a xylene, 0.350 g (2.73 mmol) of 1,3-dicyanobenzene, and 3.50 g (90.4 mmol) sodium borohydride were irradiated in 75 mL of acetonitrile:water (9:1) using an Osram HNS 10 W/U OFR low pressure mercury lamp (principally 254 nm). The light passed through a quartz insert. The solution was stirred with a stream of nitrogen, and was cooled in an ice bath during irradiation. Irradiation for 8 hours gave greater than

50% conversion.

Large scale irradiations (10-fold scale-up) proceeded similarly. These involved irradiation of 3.5 g of a xylene, 20 g of sodium borohydride, 2.0 g of 1,3-dicyanobenzene, and 750 mL of 90% acetonitrile:water (9:1). A Hanovia 450W medium-pressure mercury lamp, filtered through a vycor sleeve, was used as the irradiation source.

(4) Mizuno, K.; Okamoto, H.; Pac, C.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* **1975**, 839-840.

(5) Products were generally isolated from the photolysate by dilution with an equal volume of salt water, extraction with three 5-mL portions of pentane, washing the pentane extracts with five 30-mL portions of salt water, and drying the pentane phase over molecular sieves.

(6) Column 20 ft x 1/4 in 16% OV-1 on 100-120 mesh Anakrom Q, at 75°.

(7) (a) Wiley Organics (compounds **4**-**5**).

(b) "Atlas of Spectral Data and Physical Constants for Organic Compounds", J. G. Grasselli, ed., CRC Press, Cleveland Ohio, **1973** (compound **6**).

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(8) Klinger, R. J.; Mochida, K.; Kochi, J. K., *J. Am. Chem. Soc.* **1979**, **101**, 6626-37.

(9) A full study of the photoreactivity of the dimethylcyclohexadienes will be the subject of a subsequent report.

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