from the "chiral pool"[7] constitutes another approach to the solution of this problem. For instance, a synthesis of **21**, the common precursor for both **22** and **23** can be achieved from D-glucose through a sequence of 10 steps, including three known steps for conversion of D-glucose to **24**;[8] (i) removal of one acetonide protecting group,[9] (ii) conversion of the liberated diol to its thiocarbonate, (iii) olefin formation via desulfurization,[10] (iv) introduction of a terminal hydroxyl group via hydroboration and oxidation,[11] (v) benzylation, (vi) removal of the acetonide, and (vii) sodium borohydride reduction (see Scheme I). Compound **21** is converted in a standard fashion to compound **22**, which has been found to be identical with compound **22a**, derived from **16**, except for signs of rotation. Successive treatments of **21** with sodium metaperiodate and sodium borohydride yield **23**, which in turn is converted to **25**. Compound **25** has also been derived from **19**, thus establishing the absolute configuration of **19**.

In evaluating the two approaches, the reductive epoxide ring opening and sugar routes, the former appears to be applicable to a wider range of target molecules than the latter, and to be more efficient in terms of the number of steps involved. The reductive epoxide ring opening route is also more flexible for the purpose of designing a scheme to synthesize a complex molecule. This work and the preceding paper[1] outlines our approach to the synthesis of both the 1,2- and 1,3-diol systems. The structure of the C(1)–C(19) fragment of amphotericin B (**20**) is indeed tailor-made for the application of the newly developed methodologies, and synthetic work toward this target molecule is in progress.

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Supplementary Material Available: A listing of spectral data and specific optical rotations for all new compounds prepared in this work (4 pages). Ordering information is given on any current masthead page.

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(11) Direct conversion of the thiocarbonate to the primary alcohol via deoxygenation of the secondary alcohol reported by Barton and Subramanian (ref 7b) provided, in our hands, a mixture of the primary and secondary alcohols in a ratio of 3:1.

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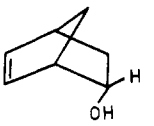
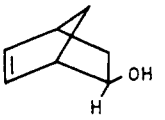
Retro-Diels–Alder Cleavage of *endo*-Bicyclo[2.2.1]hepta-5-en-2-ol

Summary: *endo*-Bicyclo[2.2.1]hepta-5-en-2-ol (**1a**) on reaction with phenylmagnesium bromide was found to yield 1-phenylethanol, arising from a retro-Diels–Alder cleavage into cyclopentadiene and acetaldehyde.

Sir: There are several reports in the literature demonstrating the additions of Grignard reagents to isolated olefins, which also have hydroxyl groups at suitable positions.[1] Thus, the title compound, **1a**, was shown to undergo allylation by the action of allylmagnesium bromide.[1e,g] In the present paper we report a fragmentation reaction of **1a** when phenylmagnesium bromide was used. Such a fragmentation has not been reported by earlier workers in studies with allylmagnesium bromide.



1a



1b

Compound **1a** was refluxed with 2 equiv of phenylmagnesium bromide in ether for 24 h. After the workup, no product corresponding to the phenylation of the double bond was detected. However, 1-phenylethanol (40–50%, based on **1a**) and cyclopentadiene dimer (5%) along with about 50% of unreacted starting material were detected by gas chromatography. The products were isolated by preparative gas chromatography and characterized by IR, NMR, and mass spectra. It was also confirmed that **1a** had not undergone isomerization to the exo isomer **1b** during the reaction. It was suspected that the starting material underwent a retro-Diels–Alder reaction as represented in Scheme I and that the acetaldehyde reacted with excess phenylmagnesium bromide to yield the observed product.

The cleavage of **1a** could be affected also under non-Grignard conditions. Thus, after **1a** was refluxed in ether for 24 h with anhydrous magnesium bromide (1:1 molar ratio) or when the sodium salt of **1a** obtained by the addition of 1 equiv of sodium hydride was refluxed for 24 h in the same solvent, only about 50% of the starting material could be recovered (quantitative analysis by gas chromatography and by NMR spectroscopy with added diphenyl ether as an internal standard). By connecting the top of the reflux condenser to a liquid nitrogen trap, cyclopentadiene (identified as the maleic anhydride adduct) and acetaldehyde (identified as the 2,4-dinitrophenylhydrazone) could be isolated. When **1a** was refluxed with 1 equiv of benzaldehyde and anhydrous magnesium bromide (in the presence of a trace of sodium hydroxide), cinnamaldehyde could be isolated, testifying to the formation of acetaldehyde anion during the reaction. It was further shown that under the reaction conditions the exo isomer, **1b**, was left unaffected.

The reaction is formally similar to a Grob fragmentation, except that the preferred reaction of the endo alcohol

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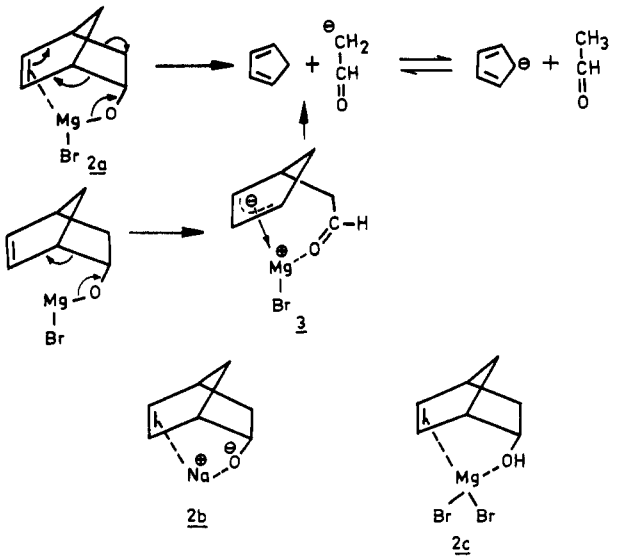
Scheme I



demonstrates the requirement of intramolecular participation by magnesium ion. The reaction need not necessarily be a concerted retro-Diels–Alder cleavage but may involve a Mg^{2+}-stabilized cyclopentenyl anion intermediate (**3**). The stability of the allylcyclopentenyl anion formed by the action of sodium on 5-(chloromethyl)norbornene and other cyclopentenyl anions has been demonstrated.[2] However, in these cases the anions do not undergo further fragmentation. In the present study no product arising from the intermediate **3** could be detected, suggesting that such an intermediate, if formed, is extremely short-lived. Hence the reaction can be formally considered to be a retro-Diels–Alder cleavage involving intermediates of type **2a**, **2b**, or **2c** either in a concerted manner or through a short-lived intermediate similar to **3**.

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Registry No. Ia, 694-97-3; Ia·Na, 80641-17-4; Ib, 2890-98-4; II, 542-92-7; II maleic anhydride adduct, 826-62-0; III, 75-07-0; III hydrazone, 1019-57-4; 1-phenylethanol, 98-85-1; cyclopentadiene dimer, 7313-32-8; cinnamaldehyde, 104-55-2.

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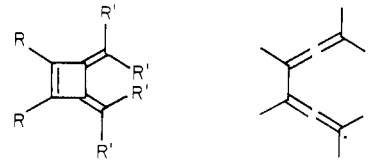
Synthesis of 3,4-Bis(alkylidene)cyclobutenes by the Reductive Dimerization of Propargyl Chlorides

Summary: The treatment of propargyl chlorides with tetrakis(triphenylphosphine)nickel(0) in benzene or tetrahydrofuran solution at 0–25 °C produces the highly reactive 3,4-bis(alkylidene)cyclobutenes in 65–75% yields.

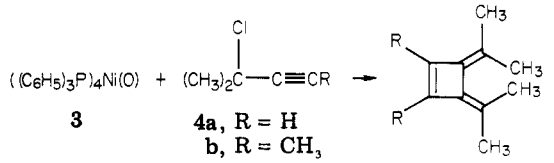
Sir: 3,4-Bis(alkylidene)cyclobutenes (**1**) have received considerable attention from both theorists and experimentalists. Particular interest has been focused on the



1 **2**

electronic properties of **1** relative to the isomeric benzenoid aromatics,[1,2] the thermal isomerization to isomeric structures,[3] the thermodynamic stabilities,[4] and the potential for possessing biradical properties in the ground state.[5] Typical of such interesting systems is the lack of simple methods for their synthesis. 3,4-Dimethylenecyclobutene (**1**, R = R′ = H) has been prepared via multistep pathways[6,7] which are not adaptable to the synthesis of substituted **1**'s. 1,5-Hexadiynes have been converted to **1** in a flow reactor at 335–410 °C at low pressure;[8] a procedure not readily adaptable for large-scale preparations or high-molecular-weight compounds. The thermal ring closure of 1,2,4,5-tetraenes (bisallenes, **2**) also produces **1**;[9] however, no convenient general procedure is available for the synthesis of such tetraenes. In studies in our laboratories on the mechanism of the transition metal (Fe, Co, Ni, and Cu) catalyzed formation of allenes from propargyl chlorides and Grignard reagents[10] we have discovered an exceptionally facile and general procedure for the synthesis of substituted 3,4-bis(alkylidene)cyclobutenes.

The reaction of tetrakis(triphenylphosphine)nickel(0) (**3**) with **4a** and **4b** in benzene or tetrahydrofuran at 0 °C results in the rapid formation of **5a** and **5b**. The product and solvent were removed from the inorganic residue by trap-to-trap distillation on a vacuum line. Analysis of the



3 **4a**, R = H; **b**, R = CH_3 **5a**, R = H; **b**, R = CH_3

residue by NMR showed no characterizable organic material remaining. The dimeric nature of **5a** and **5b** was demonstrated by GC/MS (parent ion *m/e* of 134 and 162, respectively), while the presence of three double bonds was demonstrated by the absorption on 3 molar equiv of hydrogen[11] (over a 10% palladium-on-charcoal catalyst). The structures of **5a** and **5b** were readily assigned on the basis of their ^1H and ^{13}C NMR spectra.[12]

The reaction of 3-chloro-1-butyne with **3** produces a 1:1 mixture of two dimeric products assigned structures **6** and

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(11) The hydrogenation product from **5a** is assigned the structure *cis*-1,2-diisopropylcyclobutane: ^1H NMR ($CDCl_3$) δ 0.83 (d, *J* = 5.7 Hz, 12 H), 1.45–1.85 (br m, 8 H); mass spectrum parent ion calcd. for $C_{10}H_{20}$ *m/e* 140.157, observed *m/e* 140.158.

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