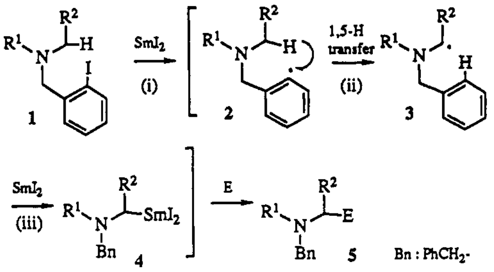
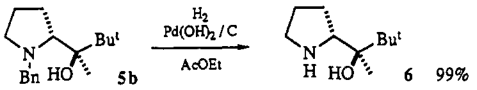
benzylpyrrolidine with iodobenzene and an electrophile) did not afford any C–C bond product. These preliminary mechanistic observations are in accord with a reaction path involving α-amino organosamarium species 4 as a transient intermediate[5] (eq 1). The sequence probably involves the following: (i) deiodination of *o*-iodobenzyl group by SmI_2 giving the corresponding aryl radical 2; (ii) an intramolecular 1,5-hydrogen atom transfer[6,7] producing the α-amino radical 3; and (iii) one-electron transfer from SmI_2 to 3 giving 4. Because of the instability of 4, electrophiles must be present in the reaction medium during its formation.



(eq. 1)

It should be noted that the pendent benzyl group in the product 5 can be removed by hydrogenation to give the secondary amine.[8] Therefore, the reaction provides a useful method for the synthesis of a variety of nitrogen containing compounds including β-amino alcohols and α-amino acid derivatives.



(eq. 2)

Metalation by hydrogen–metal exchange has usually been carried out by abstraction of a proton under strongly basic conditions using an alkyllithium or lithium amide.[1] The present reaction, which constitutes translocation of radical center from the pendent benzyl group to the α-position of an amine and a subsequent one-electron transfer, offers new methodology for amine metalation and subsequent C–C bond formation.

Acknowledgment. This work was supported in part by the Ministry of Education, Science and Culture, Japan (Grant-in-Aid for General Scientific Research (01430017)).

Supplementary Material Available: Experimental details for the synthesis and characterization of **5a–e**, **6**, and **7** and ^{13}C NMR spectra for **5b–d**, **6**, and **7** (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[6] Intramolecular 1,5-hydrogen atom transfer, followed by radical cyclization, has been utilized for synthesis of five- and six-membered carbo- and heterocycles. (a) Bennete, S. M.; Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1986**, 878. (b) Lathbury, D. C.; Parsons, P. J.; Pinto, I. *J. Chem. Soc., Chem. Commun.* **1988**, 81. (c) Borthwick, A. D.; Caddick, S.; Parsons, P. J. *Tetrahedron Lett.* **1990**, *31*, 6911. (d) Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 896. (e) Curran, D. P.; Abraham, A. C.; Liu, H. *J. Org. Chem.* **1991**, *56*, 4335 and references cited therein.

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[8] The stereochemistry of 6 was determined by a ^1H NMR NOE experiment on the corresponding cyclic urethane 7, which is derived from the treatment of 6 with trichloromethyl chloroformate.

Stereoselective Synthesis of Both (*E*)- and (*Z*)-1,2,4-Heptatrien-6-ynes. Formation of an α,3-Dehydrotoluene Biradical, Trapping by an Intramolecular Carbon–Carbon Double Bond, and Decay of the Resulting New Biradical via an Intramolecular Route†

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Summary: Condensation between conjugated allenic aldehydes 3 and γ-(trimethylsilyl)allenylboranes 2 followed by the Peterson olefination reaction afforded enyne–allenes 7 and 8. On heating, 8c underwent a sequence of intramolecular transformations through biradical intermediates.

Recently, simple acyclic (*Z*)-1,2,4-heptatrien-6-ynes were reported to undergo facile cycloaromatization reactions at ambient or even subambient temperatures to produce reactive α,3-dehydrotoluene biradicals,[1] which could mimic the DNA-cleaving mechanisms and properties of the new class of very potent antitumor antibiotics calicheamicins,[2] esperamicins,[3] neocarzinostatin,[4] and dynemicins.[5] The synthetic routes to these conjugated enyne–allenes generally involved acetylene to allene transformation of the corresponding enediyne propargylic alcohols. We report

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† Dedicated to Professor Herbert C. Brown on the occasion of his 80th birthday.

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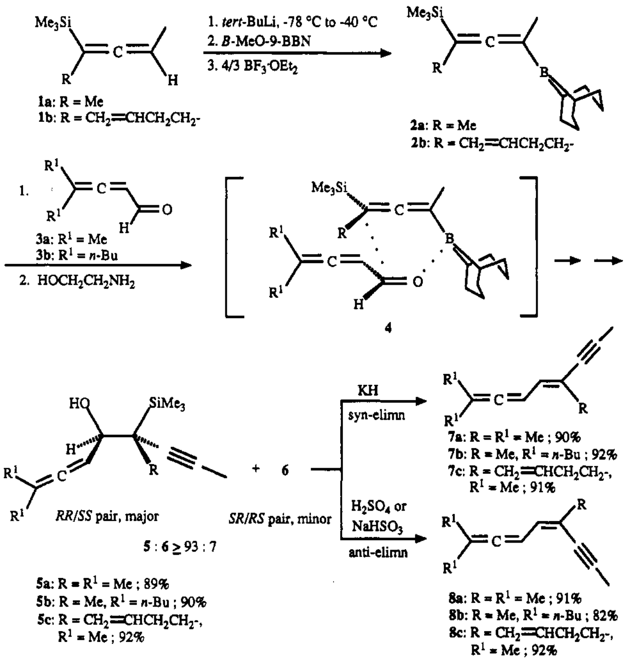
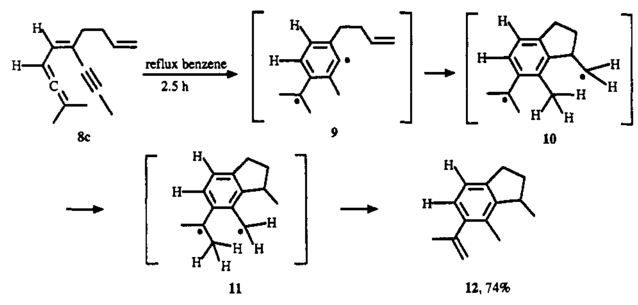
Scheme I



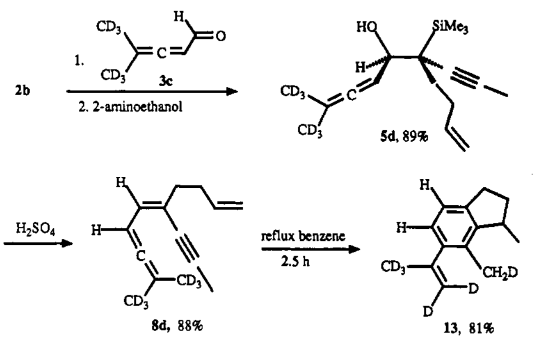
herein an alternative pathway to enyne–allenes by the condensation reaction of γ-(trimethylsilyl)allenylboranes with conjugated allenic aldehydes followed by the Peterson olefination reaction. This new route enabled us to prepare an enyne–allene which underwent a sequence of remarkable intramolecular transformations.

Allenylsilanes **1**[6] were lithiated with *tert*-butyllithium[7] followed by treatment with *B*-methoxy-9-borabicyclo[3.3.1]nonane (*B*-MeO-9-BBN) and 4/3 $BF_3·OEt_2$[8] to produce allenylboranes **2** (Scheme I), which exhibited strong IR signals for allenic structures at 1900 cm^{-1} for **2a** and at 1895 cm^{-1} for **2b** with absence of acetylenic absorptions. Subsequent condensation of **2** with readily available conjugated allenic aldehydes **3**[9] afforded, after treatment with 2-aminoethanol,[10] hydroxypropargylsilanes **5** with high diastereomeric purity (**5**:**6** ≥ 93:7) and in excellent yield. In each case, the *RR*/*SS* pair **5** was assigned as the predominant product on the basis of the geometrical outcome of the resulting double bond after the Peterson olefination reaction.[11] The KH-induced syn elimination of hydroxytrimethylsilane from **5** gave **7** as the major isomer (≥96%), whereas H_2SO_4- or $NaHSO_3$-induced anti elimination produced **8** (≥96%) predominantly.

Scheme II



Scheme III



It is worth noting that if the reaction model proposed by Chodkiewicz et al.[12] is to be employed to explain the stereochemical outcome of the condensation reaction in producing **5** as the major isomer then it would require the reaction to proceed through the pericyclic transition state **4** with the allenic and the trimethylsilyl groups occupying the same side of the six-membered ring. This observation is in sharp contrast to the earlier reports by Yamamoto et al.[13] and Corey et al.[14] in the synthesis of enynes by condensation of other γ-(trialkylsilyl)-substituted allenic organometallics with simple aldehydes. The high diastereoselectivities observed in these earlier cases were attributed to the R group of aldehydes preferentially adopting the side opposite to the trialkylsilyl group in the six-membered cyclic transition states in order to minimize the nonbonded steric interactions. It is possible that acyclic transition states are involved in the current cases because of the potential presence of $BF_3·OEt_2$ which could serve as a Lewis acid in activating the carbonyl group of the allenic aldehydes and the fluoride and methoxide ions which could form complexes with allenylboranes.[15]

Enyne–allene **8c** was synthesized in order to study the possibility of generating α,3-dehydrotoluene **9** by the cycloaromatization reaction and then trapping the benzenoid radical center in **9** by the intramolecular carbon–carbon double bond. Dropwise introduction of a solution of **8c** (0.057 g, 0.31 mmol) in 50 mL of benzene into 300 mL of refluxing benzene under N_2 over a period of 1 h followed by an additional 1.5 h of reflux afforded 0.043 g (0.23

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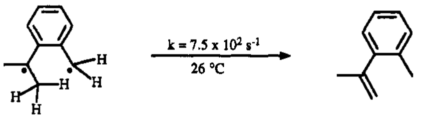
mmol, 74%) of **12** (Scheme II). Apparently, the benzenoid radical center in the initially produced biradical **9** was indeed trapped by the carbon-carbon double bond intramolecularly, forming preferentially a 5-membered ring in a fashion characteristic of the free-radical cyclization reaction,[16] to give a new biradical **10**, which then decayed to afford **12**.

Although on surface a reaction mechanism involving exchange of hydrogen atoms among **10** *intermolecularly* could account for the formation of **12**, this reaction pathway was not what actually occurred. Instead, **10** decayed through an *intramolecular* route with an initial [1,5]-sigmatropic hydrogen shift to form *o*-xylylene **11** followed by a second [1,5]-sigmatropic hydrogen shift to afford **12**. The existence of such an internal decay route was supported by the formation of **13** when deuterated enyne-allene **8d** was utilized (Scheme III). The migration of a deuterium atom to the benzylic position is consistent with the intramolecular pathway.

The transformation from **10** to **11** is likely to be facile; we estimate the heat of formation of **11** to be ca. 13 kcal/mol less than that of **10**, representing the difference in the bond dissociation energies of primary alkyl and benzylic C-H bonds.[17] Furthermore, the rigid structure of **10** should also enhance the rate of the hydrogen shift.[18] Biradical **11**, an *o*-xylylene derivative, is also expected to have a very short life time on the basis of the fact that **14** was reported to have a half-life of only 0.92×10^{-3} s at 26 °C ($k = 7.5 \times 10^{2}$ s^{-1}) (eq 1).[19]



14

(1)

In summary, the reaction sequence outlined in Scheme I provides a facile route to a variety of enyne-allenes by using different combinations of readily available γ-(trimethylsilyl)allenylboranes and conjugated allenic aldehydes. The trapping experiment shown in Scheme II gives further evidence for the formation of α,3-dehydrotoluene species and also demonstrates a way for easy entry to many other new biradicals. Such new biradicals having a longer distance between the two radical centers could potentially exhibit very different DNA-cleaving properties and therapeutic values compared to the original biradicals by abstracting hydrogen atoms from other positions of the sugar-phosphate backbone of DNA.[20] Certainly, any facile intramolecular decay route must be eliminated in order to give these new biradicals a longer life time for hydrogen abstractions from DNA to take place. In addition, it should be noted that other synthetically useful *o*-xylylenes[21] could also be likewise prepared as shown in Scheme II.

Acknowledgment. The financial support of the National Science Foundation for the purchase of a JEOL GX-270 NMR spectrometer (RII-8011453) and an HP 5970B GC/MSD system (CHE-8913626) is gratefully acknowledged.

Supplementary Material Available: Experimental procedures, IR, MS, ^{1}H NMR and ^{13}C NMR spectral data and actual ^{1}H and ^{13}C NMR spectra of **1b**, **5a-d**, **7a-c**, **8a-d**, **12**, and **13** (37 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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A Facile Synthesis of 5-Methylene-1,3-cyclohexadienes (*o*-Isotoluenes) and 1,2,4,6-Heptatetraenes[†]

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Received October 16, 1991

Summary: Condensation between 4-methyl-2,3-pentadienal and γ-(trimethylsilyl)allylboranes **3**, **4**, and **16** followed by the Peterson olefination reaction afforded the corresponding *o*-isotoluenes and diene-allenes.

Since the first synthesis of 5-methylene-1,3-cyclohexadiene (*o*-isotoluene) by Bailey and Baylouny,[1] several different routes to this alicyclic isomer of toluene[2] and its benzologues[3] have been reported. However, almost all of these methods involved multistep synthesis and generally required gas-phase pyrolysis. Only limited quantities could be produced at a time. It is undoubtedly due to the lack of an efficient route to *o*-isotoluenes that a systematic investigation of this class of theoretically interesting and

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[†] Dedicated to Professor Gabor B. Fodor on the occasion of his 75th birthday.

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