

ratio, 10.0) were recovered. The keto alcohol **14a** was oxidized¹⁸ to the 26-aldehyde **14b** and decarbonylated¹⁹ to ¹⁴C₄-25-³H-26-norcholestenone (**14c**) (specific activity 4.37 × 10⁵ dpm/mmol of ¹⁴C; ³H:¹⁴C ratio, 11.9).

The decreased (16.6%) specific activity and parallel increase (16.0%) in the ³H:¹⁴C ratio correspond to the loss of nearly one ¹⁴C atom. It follows that the methyl originating from C-2 of MVA was hydroxylated. Since **4a** has the 25*R* configuration, the ¹⁴C₅-26-hydroxycholest-4-en-3-one must have the configuration **14a**. Consequently, cholesterol has the configuration as in **3**. The geometry at the C-24 double bond of lanosterol¹⁻³ is that shown in **1**. Therefore, the reduction of this double bond in rat livers is equivalent to a *trans* addition of two hydrogens, and the methyl originating from C-2 of MVA has the 25-*pro-S* configuration.

It is noteworthy that hydroxylation of the 25-*pro-S*-methyl of cholesterol by *M. smegmatis* contrasts with that in rat livers where the oxygenation of the 25-*pro-R*-methyl (originating from 3' of MVA) is indicated.^{5,6} Also, evidence suggests that the reduction of the Δ²⁴ intermediate in the biosynthesis of tigogenin in *D. lanata*²⁰ differs from that in rat livers. In tigogenin, which has the 25*R* configuration, the methyl originating from 3' of MVA bears the oxygen function. Consequently, the addition of the C-25 proton in *D. lanata* occurs on the opposite side to that in rat liver enzyme systems.

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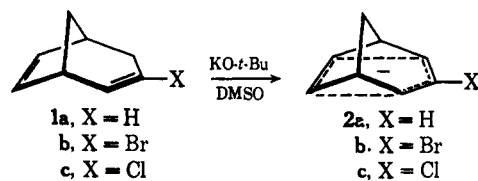
Base-Catalyzed Rearrangement of 3-Bromobicyclo[3.2.1]octa-2,6-diene to *endo*-6-Ethynylbicyclo[3.1.0]hex-2-ene. Possible Intermediacy of a Homoconjugated Carbene

Sir:

Bicycloheptadienes such as **1a** undergo rapid proton exchange in strongly basic media via the "bishomoaromatic"¹ anion **2a**. We now wish to report that **1b**,² the 3-bromo analog of **1a**, under conditions which

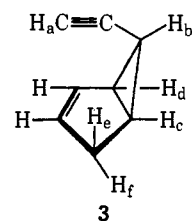
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should form the bromoanion **2b** (potassium *t*-butoxide in DMSO at room temperature), is immediately transformed into a new product (29% isolated yield; >99% pure) in an unusual and deep-seated rearrangement.

The reaction product exhibits acetylenic carbon-carbon and carbon-hydrogen absorptions in the infrared (2130 and 3320 cm⁻¹). After purification by vpc, its mass spectrum shows a parent peak at *m/e* 104, corresponding to overall loss of HBr, with abundant peaks at *m/e* 103, 91, 78, and 63. That the structure of this new material is *endo*-6-ethynylbicyclo[3.1.0]hex-2-ene (**3**) is strongly suggested by its proton nmr spectrum.³ At 220 MHz, signals for eight nonequivalent hydrogens are observed. The acetylenic hydrogen (H_a) is a sharp doublet (*J* = 2 Hz) at 347 Hz downfield from tetramethylsilane (TMS). Cyclopropyl proton H_b appears at 335 Hz as a doubled triplet, coupled to H_c and H_d (*J* ≅ 6 Hz) as well as H_a. The resonance at 390 Hz for H_c is a broadened quartet due to coupling of similar magnitude (*J* ≅ 6 Hz) with H_b, H_d, and H_f and that at 480 Hz (H_d) a slightly doubled (*J* = 2 Hz) triplet. H_e (510 Hz) and H_f (560 Hz) are coupled to one another (*J* = 18 Hz); the latter doubled again by coupling (*J* = 6.5 Hz) to H_c. The two vinyl hydrogens appear as complex and overlapping signals at 1222 and 1228 Hz downfield from TMS.

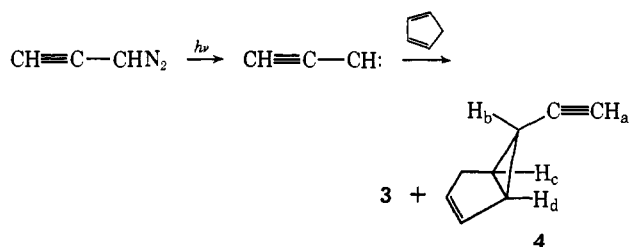


Assignment of structure **3** to the rearrangement product is confirmed by an independent synthesis of the material. Irradiation (λ >3000 nm) of diazopropyne⁴ in the presence of cyclopentadiene gives two major products (ratio ~1:1) which are separable by vapor phase chromatography on a 10 ft × 3/8 in. column packed with 10% UCC-W98 on 60-80 Chromosorb P operated at 120°. On the basis of spectral and analytical data and by analogy with other propargylene additions⁴ these materials are assigned the 6-ethynylbicyclo[3.1.0]hex-2-ene structure. One product has nmr and ir spectra identical with **3**. The other has *exo* stereochemistry (**4**), an assignment made on the basis of the lower coupling constant between H_b and H_c or H_d (*J* = 2.5 Hz).⁵

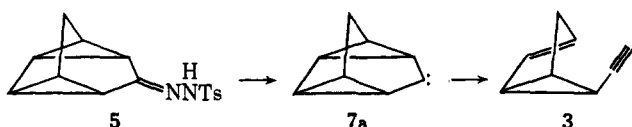
(3) Nmr spectra were determined on a Varian Model HR-220 spectrometer.

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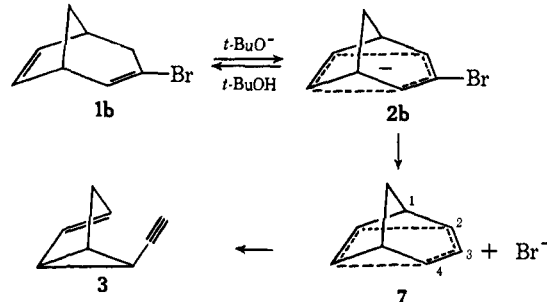
In experiments aimed at the elucidation of the mechanism of this reaction, we have made the following observations. (1) Chlorodiene **1c**⁶ is completely unreactive in 10% DMSO-THF (conditions which convert **1b** to **3**) but does produce **3** in a much more basic medium (0.29 M KO-*t*-Bu in pure DMSO at room temperature). It is not likely that this substantial rate difference is due to decreased acidity of the hydrogen at C-4 (bromo- and chloroacetic acid have identical pK_a 's and Br a slightly lower electronegativity than Cl⁻), and therefore must be interpreted to mean that carbon-halogen bond cleavage occurs in the rate-determining step of the reaction. (2) We have prepared optically active **1b** ($[\alpha]^{25D} +83.1^\circ$ (c 0.0343, CHCl_3)) by asymmetric hydroboration of the racemic material using a deficiency of isopinocampheylborane⁸ followed by recovery of excess bromodiene. When carried to *ca.* 60% conversion to **3** in KO-*t*-Bu-DMSO-THF, recovered **1b** had lost 99.8% of its optical activity and **3** was produced with no detectable rotation ($[\alpha]^{25D}$ 0.00° (c 0.0368, CHCl_3)). This demonstrates that rapid, reversible deprotonation-reprotonation of **1b** occurs (presumably through anion **2b**) at a rate substantially greater than that of rearrangement. (3) We have synthesized the *p*-toluenesulfonylhydrazide (**5**) of tetracyclo[3.2.1.0^{2,7}.0^{4,6}]octan-3-one⁹ and examined the products of its decomposition in 0.926 M NaOCH₃ in tetraglyme at 165°. On the basis of a large number of precedents,¹⁰ these conditions should be sufficient to convert **5** to the corresponding diazo compound **6** and thence to the carbene **7a**. The volatile product formed in this reaction (38% yield) is identical with the rearrangement product **3**.



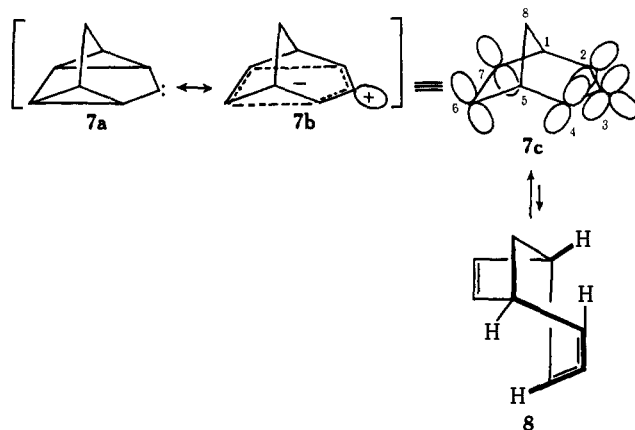
We feel that the mechanism most consistent with these observations is that illustrated in Scheme I. A rapid preequilibrium between bromodiene **1b** and homoconjugate anion **2b** is established, followed by rate-determining loss of bromide ion to produce neutral inter-

mediate **7**. This intermediate then undergoes cleavage to **3**, a reaction typical of cyclopropyl methylenes.¹¹

Scheme I



The most adequate representation of **7** is structure **7c**, which illustrates the basis set of carbon atomic orbitals making up the six-electron pseudo- π system. The rigidity of this structure undoubtedly enforces the stabilizing¹² C-2,C-7 and C-4,C-6 interactions (as it does in anions **2a** and **2b**; hence the term "homoconjugated



carbene"), and in addition probably prevents very much rotation about the C-2,C-3 or C-3,C-4 bonds, a movement which would be necessary to convert **7** to the highly distorted cyclic allene **8**.

Experiments are under way aimed at obtaining direct information concerning the structure and lifetime of **7**, as well as examining other aspects of carbene homoconjugation.

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