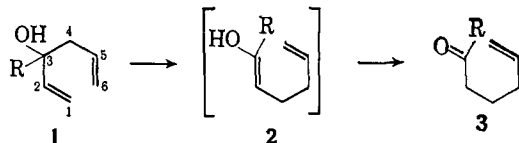


**A Synthesis of Ketones by the Thermal
Isomerization of 3-Hydroxy-1,5-hexadienes.
The Oxy-Cope Rearrangement¹**

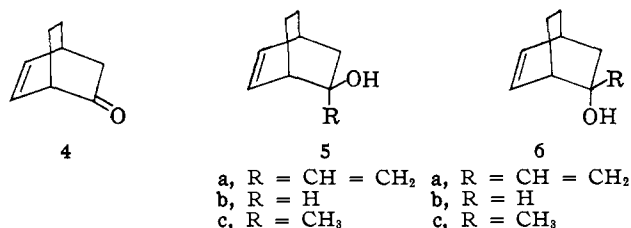
Sir:

Cope rearrangements of 1,5-hexadienes, whether of the double-inversion (C-1-C-6 bond formation)^{2,3} or single-inversion (C-1-C-4 bond formation)⁴ type, generate a new double bond between C-2 and C-3 of the six-atom system. Attachment of a hydroxyl group to C-3 should give the progenitor of an enol, thus permitting the synthesis of carbonyl compounds by ketonization of the rearrangement product (1 → 2 → 3). The present paper reports both double-



inversion and single-inversion examples of this reaction, for which the term "oxy-Cope rearrangement" is proposed.

Bicyclo[2.2.2]oct-5-en-2-one (4)⁵ and vinylmagnesium bromide react to give a 2:1 mixture of 2-endo-vinyl-2-*exo*-hydroxybicyclo[2.2.2]octene (5a)⁶ and the 2-*exo*-vinyl-2-*endo*-hydroxy epimer 6a.⁶ The isomers are separated by vapor chromatography (v.p.c.); each absorbs 2 moles of hydrogen to give 2-ethylbicyclo[2.2.2]octanol-2,⁶ m.p. 39.5–42.5°, identical with



an authentic sample prepared from 2-bicyclo[2.2.2]octanone and ethylmagnesium iodide. The infrared method which formed the basis for the assignments of stereochemistry to the bicyclo[2.2.2]octenols 5b and 6b⁷ does not distinguish between 5a and 6a, but the configurations of the latter compounds follow from their chemical behavior and their nuclear magnetic resonance (n.m.r.) spectra. The methine hydrogen of the vinyl group of the major isomer (5a) from the Grignard addition absorbs as a multiplet centered further upfield (τ 4.30) than the corresponding absorption (at τ 4.17) of the minor isomer (6a),⁸ suggesting

(1) This work was supported in part by the Directorate of Chemical Sciences, Air Force Office of Scientific Research Grant No. AF-AFOSR 389-63, and by funds provided by the Wisconsin Alumni Research Foundation.

(2) A. C. Cope and E. M. Hardy, *J. Am. Chem. Soc.*, **62**, 441 (1940), and later papers by Cope and co-workers.

(3) For a review, see S. J. Rhoads in "Molecular Rearrangements," P. de Mayo, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963.

(4) (a) G. S. Hammond and C. D. De Boer, *J. Am. Chem. Soc.*, **86**, 899 (1964); (b) D. J. Trecker and J. P. Henry, *ibid.*, **86**, 902 (1964).

(5) Prepared according to K. Mislow and J. G. Berger, *ibid.*, **84**, 1956 (1962).

(6) Elemental analysis establishes the empirical composition.

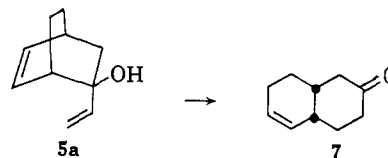
(7) H. L. Goering, R. W. Greiner, and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1391 (1961).

(8) Similar results are observed⁹ with methyl Grignard reagent, the major isomer (probably 6c) showing the methyl singlet n.m.r. peak further upfield than that of the minor isomer.

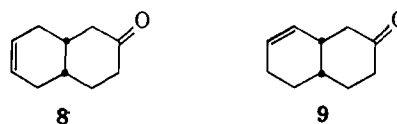
(9) J. A. Berson and N. Kundu, unpublished observations.

diamagnetic shielding by the π -electrons of the *endo*-cyclic double bond¹⁰ in 5a.

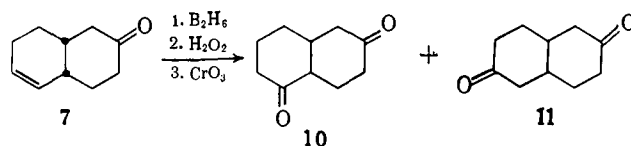
Heating 5a in the gas phase at 320° in an ammonia-washed, evacuated glass tube gives *cis*- $\Delta^{5,6}$ -octalone-2 (7)⁶ as the major product (90% of the volatile material, 50% isolated yield). The infrared spectrum of 7 (λ_{\max} 1720 and 1650 cm.⁻¹) suggests a nonconjugated unsaturated ketone. Hydrogenation gives pure *cis*- β -decalone, uncontaminated by the *trans* isomer. The n.m.r. spectrum shows two olefinic hydrogens,



which, taken with the previous evidence, restricts the structure of the rearrangement product to *cis*- $\Delta^{5,6}$ -octalone-2 (7) and the $\Delta^{6,7}$ (8) and $\Delta^{7,8}$ (9) isomers.

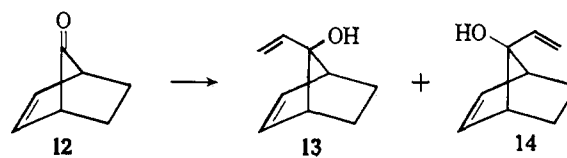


The latter two structures are highly unlikely on mechanistic grounds and are eliminated from consideration by conversion of the rearrangement product *via* hydroboration and oxidation to a mixture of two diketones in the ratio of 7:3. The major diketone isomer has a v.p.c. retention time and infrared spectrum identical with those of authentic 1,6-decalindione (10)¹¹; its disemicarbazone, m.p. 233–234° dec., does not depress the melting point of authentic material on admixture. Only 7 of the three octalones can give 10 by this sequence. The second diketone isomer is presumably 11.



The 5a → 7 reaction is formulated as a Cope rearrangement of the double inversion type, leading to the enol of 7, followed by ketonization. Detailed consideration of the mechanism is deferred.¹²

7-Norbornenone¹³ (12) reacts with vinylmagnesium bromide to give a 4:1 mixture of *syn*-7-vinyl-*anti*-7-hydroxynorbornene (13),⁶ m.p. 58.2–59.8°, and *anti*-7-vinyl-*syn*-7-hydroxynorbornene (14).⁶ Each of the



(10) If these assignments are correct, Grignard additions show a stereochemical preference opposite to that of lithium aluminum hydride reductions of 4, since the latter reaction gives^{9,7} more 6b than 5b.

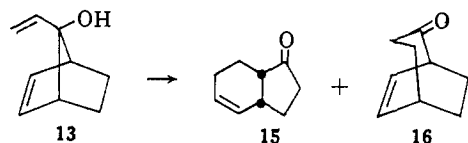
(11) W. S. Johnson, D. S. Allen, Jr., R. R. Hindersinn, G. N. Sausen, and R. Pappo, *J. Am. Chem. Soc.*, **84**, 2181 (1962). We thank Professor Johnson for kindly supplying a sample of 10.

(12) (a) Cf. J. A. Berson and M. Jones, Jr., *ibid.*, **86**, 5017 (1964). (b) The formula numbers correspond to those of the accompanying paper.^{12a}

(13) P. G. Gassman and P. G. Pape, *J. Org. Chem.*, **29**, 160 (1964).

alcohols consumes 2 moles of hydrogen to give 7-ethyl-7-norbornanol,⁶ m.p. 65.5–66.5°, independently prepared from 7-norbornanone and ethylmagnesium iodide. Infrared studies show that the major isomer (**13**) does not have an intramolecular hydrogen bond while the minor isomer (**14**) does. The preference for *syn* addition of the vinyl Grignard reagent to **12** is in accord with the observed¹⁴ course of the reaction of methyl Grignard reagent with **12**.

Pyrolysis of the *syn*-vinyl compound **13** at 250° gives the double-inversion product *cis*-bicyclo[4.3.0]nonen-2-one-7 (**15**)⁶ corresponding to **7**, but this mode of rearrangement now is subordinate (10% of the volatile materials) to the single-inversion path which leads to bicyclo[3.2.2]nonen-6-one-2 (**16**),⁶ m.p. 89–90.8° (84% of the volatile products, 66% isolated yield). An additional 5–6% of minor products is formed.^{12b}



The structure of **16** is established by the infrared spectrum (λ_{\max} 1708 cm^{-1}), by a concordant (but not uniquely decisive) n.m.r. spectrum, and by hydrogenation to 2-bicyclo[3.2.2]nonanone,⁶ m.p. 152.5–154.5°, which is also formed⁹ by pyrolysis of the barium salt of *cis*-4-carboxycyclohexanepropionic acid. Compound **15** can be hydrogenated to *cis*-1-hydrindanone, has an infrared maximum at 1740 cm^{-1} (non-conjugated cyclopentanone), and shows n.m.r. absorptions as multiplets at τ 4.35 (area 2), 7.18 (area 1), and 7.7–8.4 (area 9). Of the seven possible 7-*cis*-bicyclo[4.3.0]nonenones, all but **15**, **17**, and **18** may be eliminated on the grounds of obvious incompatibility with the gross spectral data. The latter two are both mechanistically improbable and furthermore are not in accord with the details of the n.m.r. spectrum, as will be described in the full paper.



The **13** → **16** isomerization provides one of the simplest entries into the bicyclo[3.2.2]nonane system, and the general sequence of vinylation and thermal rearrangement suggests a new synthetic route for conversion of β, γ -unsaturated ketones to bis-homologous δ, ϵ -unsaturated ketones.

(14) R. K. Bly and R. S. Bly, *J. Org. Chem.*, **28**, 3165 (1963).

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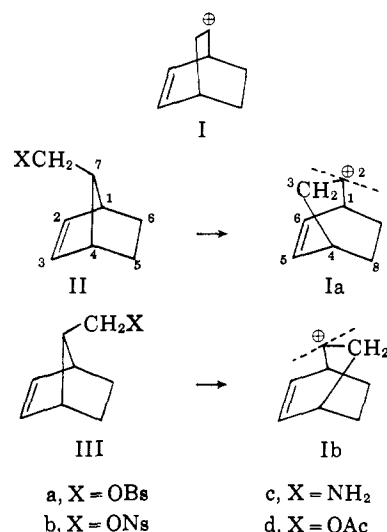
RECEIVED SEPTEMBER 25, 1964

Isomeric Carbonium Ions. Ring Expansion of the *syn*- and *anti*-2-Norbornene-7-carbinyl Systems¹

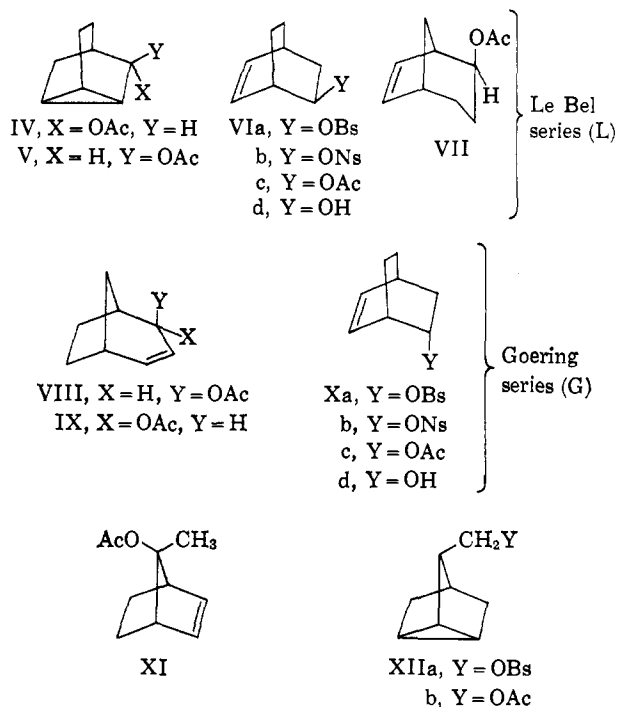
Sir:

The ring expansions² of *syn*-2-norbornene-7-carbinyl derivatives (II) involve intermediates distinctly different from those given by *anti* precursors III.

(1) This work was supported in part by a grant from the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment



The products of acetolyses (at reflux in the presence of 10–20% excess sodium acetate) of the *p*-bromo- and *p*-nitrobenzenesulfonates (IIa, IIb, IIIa, IIIb) of the *syn* and *anti* series, as well as those obtained from the nitrosative deamination in glacial acetic acid at 25° of the amines (IIc and IIIc),³ fall into three main



categories: (i) the "Le Bel" series (L), IV, V, VIc, VII, previously observed⁴ to result from carbonium

is made to the donors of this fund. We are also indebted for support to the Wisconsin Alumni Research Foundation.

(2) For previous studies of other systems, see J. A. Berson and P. Reynolds-Warnhoff, *J. Am. Chem. Soc.*, **84**, 682 (1962); **86**, 595 (1964); J. A. Berson and D. Willner, *ibid.*, **84**, 675 (1962); **86**, 609 (1964).

(3) (a) Previous studies of the acetolysis of IIa at 115° reported products IIId (91%), XIIb (8%), and the remainder unidentified; IIIa was reported to give 90% IIId, 4% XIIb, and the remainder unidentified.^{3b} Acetolyses of IIa and IIIa (OBs = OTs) were reported to give "essentially unrearranged" products.^{3c} (b) R. K. Bly, R. S. Bly, and J. E. Goldberg, Abstracts, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan., 1964, p. 6C; (c) R. R. Sauers and R. M. Hawthorne, Jr., *J. Org. Chem.*, **29**, 1685 (1964).

(4) (a) N. A. Le Bel and J. E. Huber, *J. Am. Chem. Soc.*, **85**, 3193 (1963). (b) *cf.* R. R. Fraser and S. O'Farrell, *Tetrahedron Letters*, 1143 (1962). (c) Product V, formed in very small yield in our system, was not observed in the previous case but would have escaped detection there if present in comparable amount.^{4a}