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ISOMER CONTROL IN THE REDUCTION OF A NORTRICYCLYMERCURIAL

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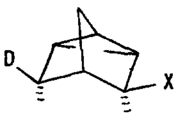
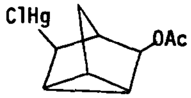
In the course of our investigations leading toward the synthesis of a nortricyclene derivative with a single label with known stereochemistry relative to another functional group (e.g., I), it seemed that a relatively facile route involved the reduction of organomercurial 5-exo-acetoxy-3-exo-nortricyclymercuric chloride, II[1]. Previous reports[2,3] indicate that substantial homoallylic and Wagner-Meerwein rearrangement accompany the borohydride reduction of II, i.e., acetates III, IV and V are formed. In addition, borodeuteride reduction of II results in V in which the label is incorporated in a non-stereoselective manner. Since this reduction reaction appears to involve equilibrating free radical intermediates (VI-VIII) leading to rearranged products, it seemed that stereospecific label incorporated (no Wagner-Meerwein rearrangement) would occur only when clean retention of carbon skeleton (no homoallylic rearrangement) was achieved in the reduction of II[2-6].



I



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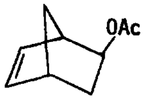

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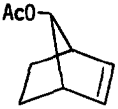

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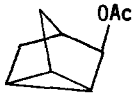
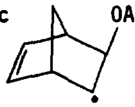


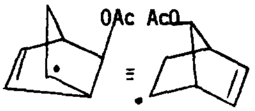
V

A reagent that has been used for reductive cleavages is the radical-anion sodium naphthalene[7] ($Ar^{\dot{-}}$). This reagent seemed especially pertinent in view of the known ability to control isomer composition in reductions in these systems (e.g., of nortricyclyl choride) by adjusting conditions of the radical-anion reaction[8a]. Table I displays the results of sodium naphthalene reductions of II carried out in tetrahydrofuran (THF). The products consist of a mixture of acetates and alcohols (IV, V, IX, X); essentially complete carbon skeleton retention (only V and IX from II) results when the reduction is carried out with radical-anion in excess (from the start) and at low temperatures. These product control techniques are essentially those that had been reported for alkyl chlorides earlier[8a]. The yields from these radical anion reductions were found to be modest (4-25%). A reasonable mechanism for the radical anion reductions would appear to be the following:

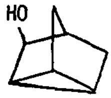
VI



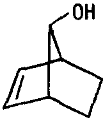
VII



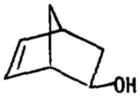
VIII



IX



X



XI

$II + Ar^{\cdot -} \longrightarrow RHgX^{\cdot -} + Ar$ (1)

$RHgX^{\cdot -} \longrightarrow R\cdot + Hg + X^{-}$ $(R\cdot = VI)$ (2)

$R\cdot + Ar^{\cdot -} \longrightarrow R:^{-}$ (3)

$R:^{-} + HSol \longrightarrow RH + Sol^{-}$ (RH = V, HSol = solvent) (4)

$VII \rightleftharpoons R\cdot \rightleftharpoons VIII$ (5)

$Ar^{\cdot -} + VII \longrightarrow VII^{-} \xrightarrow{HSol} III$ (6)

$Ar^{\cdot -} + VIII \longrightarrow VIII^{-} \xrightarrow{HSol} IV$ (7)

Evidence has been accumulated that indicates that carbanions are involved in analogous reductions of alkyl halides[8]. The ability to influence the product ratio by temperature (Table I) implies that the activation energy for the rearrangement process (5) is higher than that for the (second) electron transfer process (3,6,7). In addition, excess radical anion throughout the course of the reaction kinetically favors reduction without rearrangement (3,4) over rearrangement (5).

An alternative reduction, that resulted in more substantial yields (51-59%), is the photolytic procedure of Table II. Irradiation of organomercurial II in THF-deuterium oxide resulted in acetates which were predominately of retained carbon skeleton (maximum 88%). This procedure, however, does not give as complete carbon skeleton retention as does the radical-anion procedure and the deuterium incorporation was modest (24%).

The results of Table II are taken to mean that reductive <u>homolytic</u> processes alone are not sufficiently rapid to give complete retention of carbon skeleton. Radicals are being

Table I. Sodium Naphthalene Reductions[a] of II

Temp.	Stoichiometry Eq. rad. an.: Eq. II	Product Acetates[b] % IV	% V	Product Alcohols[b] % X	% IX	% Carbon Skeleton Retention[c]	Yield[b]
0°	2.5:1.0	11.6	23.5	15.6	49.3	72.8	--
25°	2.5:1.0	3.3	11.1	17.3	68.3	79.4	--
-78°	7.5:1.0	---	93.1	---	6.9	100	--
-78°	7.5:1.0	2.7	97.3	---	---	97.3	14%[d]
-78°	7.5:1.0	2.0	92.5	---	5.5	98.0	17.3%

[a] Reduction reagents were *ca.* 1.0 M in THF; substrate (II) was added to radical-anion and water was added after *ca.* 5 min. Product contact with water varied resulting in various acetate-alcohol mixtures[9].

[b] Glc analyses by comparison to known samples[3,11]; yields were determined by external glc standards.

[c] Compounds III and XI were not observed as products. %V + %IX = % retained carbon skeleton.

[d] Yields are maximized when all reagents are pre-cooled.

reduced less readily than carbanions; i.e. equation 8 competes poorly with rearrangement (5).

$$R\cdot \; + \; HSol \longrightarrow RH \; + \; Sol\cdot \qquad (8)$$

Table II. Photolytic Reductions[a] of II

Irradiation Time (hr.)	Temp.	Acetate Products[b] % IV	% V	Yields
40	ambient	12.0	88.0	---
72	"	12.4	87.6[c]	---
40	"	13.2	86.8	51%
18	"	12.6	87.4	59%
5	0°	28.0	72	---
0.5[d]	ambient	30.0	70	---

[a] 450 Watt Hanovia lamp, pyrex sleeve unless noted otherwise; solutions were 0.1 M in II and water (or deuterium oxide) in *ca.* 10 ml. of THF.

[b] Glc analyses; see Table I: footnotes b and c.

[c] Sample (glc collection) of V subjected to mass and n.m.r. spectral analyses[11]: 24% of one deuterium observed.

[d] No pyrex sleeve (all quartz set-up).

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9. We have found in all of our work and in the repeat of borohydride reductions[3,4] that the products are alcohol-acetate mixtures; this includes application of the procedures of Brown and Geohegan[3,10]. The products are solely acetates only if the water content (in the THF) is less than 10%.
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