(3) C. Elsenbroich, *J. Organomet. Chem.*, **14**, 157 (1968).
(4) A. N. Nesmeyanov, L. P. Yur'eva, and S. N. Levchenko, *Dokl. Akad. Nauk SSSR*, **190**, 118 (1970).
(5) D. N. Kursanov, V. N. Setkina, and B. G. Gribov, *J. Organomet. Chem.*, **37**, C35 (1972).
(6) C. Elsenbroich, F. Gerson, and J. Heinzer, *Z. Naturforsch., B*, **27**, 312 (1972).
(7) M. F. Semmelhack and H. T. Hall, *J. Am. Chem. Soc.*, **96**, 7091 (1974).
(8) E. O. Fischer and W. Hafner, *Z. Naturforsch., B*, **10**, 665 (1955).
(9) P. L. Timms, *Adv. Inorg. Chem. Radiochem.*, **14**, 121 (1972).
(10) P. S. Skell and M. J. McGlinchey, *Angew. Chem. Int. Ed. Engl.*, **14**, 195 (1975).
(11) P. S. Skell, D. L. Williams-Smith, and M. J. McGlinchey, *J. Am. Chem. Soc.*, **95**, 3337 (1973).
(12) R. Middleton, J. R. Hull, S. R. Simpson, C. H. Tomlinson, and P. L. Timms, *J. Chem. Soc., Dalton Trans.*, 120 (1973).
(13) M. J. McGlinchey and T.-S. Tan, *Can. J. Chem.*, **52**, 2439 (1974).
(14) K. J. Klabunde and H. F. Efner, *Inorg. Chem.*, **14**, 789 (1975).
(15) R. E. Banks, "Fluorocarbons and Their Derivatives", Oldbourne Press, London, 1964, p 140.
(16) K. J. Klabunde and H. F. Efner, *J. Fluorine Chem.*, **4**, 115 (1974).
(17) S. S. Dua, R. D. Howells, and H. Gilman, *J. Fluorine Chem.*, **4**, 381 (1974).
(18) T. Birchall, personal communication.
(19) V. S. Khandkarova, S. P. Gubin, and B. A. Kvasov, *J. Organomet. Chem.*, **23**, 509 (1970).
(20) J. L. Fletcher and M. J. McGlinchey, *Can. J. Chem.*, **53**, 1525 (1975).
(21) M. J. McGlinchey and T.-S. Tan, *J. Chem. Soc., Chem. Commun.*, in press.
(22) R. V. Emanuel and E. W. Randall, *J. Chem. Soc. A*, 3002 (1969).
(23) G. M. Bodner and L. J. Todd, *Inorg. Chem.*, **13**, 360 (1974).
(24) V. Graves and J. J. Lagowski, Abstracts, 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973, No. INORG-52.
(25) G. P. van der Kelen, *Bull. Soc. Chim. Belg.*, **72**, 644 (1963).
(26) A. C. Blizzard and D. P. Santry, *J. Chem. Phys.*, **55**, 950 (1971).
(27) B. E. Mann, *Adv. Organomet. Chem.*, **12**, 135 (1974).
(28) B. Nicholls and M. C. Whiting, *J. Chem. Soc.*, 551 (1959).
(29) J. Evans and J. R. Norton, *Inorg. Chem.*, **13**, 3042 (1974).
(30) M. P. Silvon, E. M. Van Dam, and P. S. Skell, *J. Am. Chem. Soc.*, **96**, 1945 (1974).
(31) Previously synthesized by Timms[12] but no data reported.
(32) We have suggested a new simplified nomenclatural system for arene–metal sandwich compounds but this is still sub iudice.: *Inorg. Chem.*, submitted for publication.

# Mechanism of the Sodium Cyanoborohydride Reduction of $\alpha,\beta$-Unsaturated Tosylhydrazones

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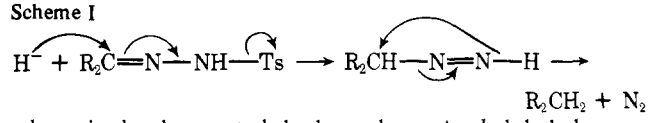
**Abstract:** Through the use of several steroidal cisoid and transoid $\alpha,\beta$-unsaturated tosylhydrazones, it has been possible to establish the course of the $NaBH_3CN$ reduction of such tosylhydrazones. Depending on the nature of the tosylhydrazone, alkane, or alkene (with double bond migration to the site of the carbonyl carbon) or both may be formed. Alkene formation is initiated by hydride reduction of the imminium system, while alkanes are produced by initial Michael-type addition of hydride to the terminus of the conjugated system followed by reduction of the imminium moiety. Supporting evidence is provided by the course of $NaBD_3CN$ reductions and demonstration that in alkene products deuterium is attached to the carbon which bore the original carbonyl group.

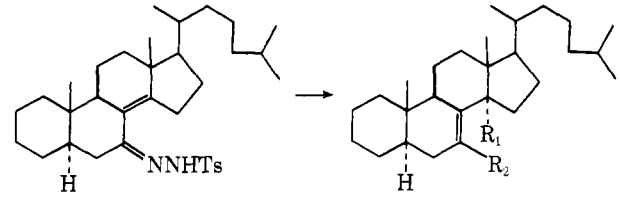
Sodium cyanoborohydride ($NaBH_3CN$) has recently been shown to be a mild, highly selective reagent[1] for the reduction of tosylhydrazone derivatives of aliphatic ketones and aldehydes.[2] As such, this reaction provides a convenient alternative to the Wolff–Kishner and Clemmensen reductions and other direct or indirect deoxygenation methods.[3] It has also been reported that the $NaBH_3CN$ reduction of $\alpha,\beta$-unsaturated tosylhydrazones cleanly produces the alkene resulting from migration of the double bond to the carbon originally bearing the carbonyl group.[2b] This result is in contrast to the observation of Caglioti and Magi[4] that the lithium aluminum hydride reduction of $\alpha,\beta$-unsaturated tosylhydrazones leads to the formation of mixtures of hydrocarbons. In light of these reports and since the labeled reagent sodium cyanoborodeuteride ($NaBD_3CN$) can be readily prepared by exchanging the hydrogens of $NaBH_3CN$ for deuterium,[1b,c] it was decided to investigate the mechanism of the tosylhydrazone reduction with $NaBH_3CN$ and to determine the feasibility of this procedure for selective deuterium labeling.

In particular, as part of our continuing effort to synthesize deuterium-labeled steroids for mass spectrometric studies, it was necessary to synthesize 12,12-$d_2$ steroid hydrocarbons from the corresponding ketones in high chemical and isotopic yields.[5] When the tosylhydrazones of 3- or 12-keto steroids were reduced with $NaBH_3CN$, it was found that pure hydrocarbon product was formed in yields of 75–90%. Use of $D_2O$ in the work-up procedure gave unlabeled product, whereas $NaBD_3CN$ as the reducing agent generated a singly deuterated hydrocarbon. A $d_2$-labeled compound was obtained by deuterium exchange of the hydrogen on the nitrogen of the tosylhydrazone and reduction with $NaBD_3CN$ using deuterated acid catalyst.[6] Therefore, the reduction of saturated tosylhydrazones proceeds operationally and mechanistically in the same fashion as had been demonstrated earlier by us[7] for sodium borohydride (Scheme I).

Scheme I

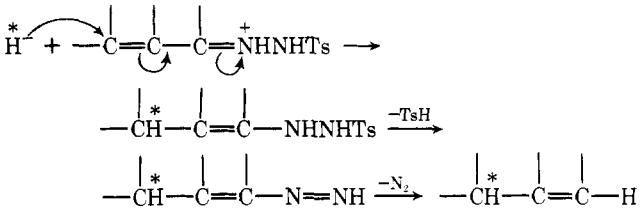



In connection with another project, we needed to synthesize the labeled alkene cholest-7-ene-14$\alpha$-$d_1$ (**2a**). According to the findings of Hutchins and co-workers[2b] 14$\alpha$-cholest-7-ene (**2b**) should be cleanly produced by the $NaBH_3CN$ reduction of cholest-8(14)-en-7-one tosylhydrazone (**1**), and preliminary investigations in our hands




**1** **2a**, $R_1$ = D; $R_2$ = H
**b**, $R_1$ = $R_2$ = H
**c**, $R_1$ = H; $R_2$ = D
**d**, $R_1$ = $R_2$ = D

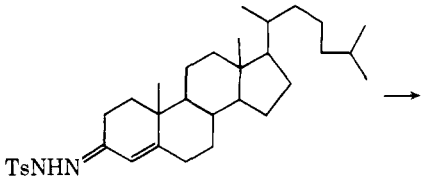
Scheme II



proved this to be true. These workers assumed[2b] that the double bond migration in the acid-catalyzed reduction of tosylhydrazones of $\alpha,\beta$-unsaturated ketones with $NaBH_3CN$ proceeded according to Scheme II, in which case $NaBD_3CN$ reduction should result in the introduction of a deuterium atom into the $\beta$ position of the original ketone (asterisked hydrogen in Scheme II).

In our steroid example **1**, use of $NaBD_3CN$ should, therefore, lead in one step to the desired 14$\alpha$-$d_1$ analog **2a**. However, in actual fact, the product proved to be 14$\alpha$-cholest-7-ene-7-$d_1$ (**2c**), thus showing that the originally postulated[2b] mechanism (Scheme II) involving Michael-type attack of hydride (or deuteride) could not be correct.

Therefore we decided to further investigate the $NaBH_3CN$ reduction of $\alpha,\beta$-unsaturated steroidal tosylhydrazones using the readily available tosylhydrazone of cholest-4-en-3-one (**3**) as a model. In contrast to the relatively simple product composition from the reduction of the cisoid tosylhydrazone **1**, it was found that in this instance a mixture of hydrocarbons was generated which contained not only the expected 5$\alpha$- and 5$\beta$-cholest-3-ene (**4a** and **4b**), but also the saturated products, 5$\alpha$- and 5$\beta$-cholestane (**5a** and **5b**). These results show that not only the mechanism, but



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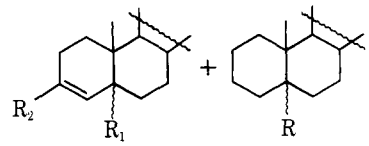


**4a**, $R_1$ = $\alpha$-H; $R_2$ = H
**b**, $R_1$ = $\beta$-H; $R_2$ = H
**c**, $R_1$ = $\alpha$-H; $R_2$ = D
**d**, $R_1$ = $\beta$-H; $R_2$ = D

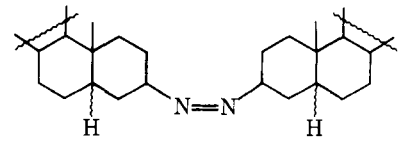
**5a**, R = $\alpha$-H
**b**, R = $\beta$-H

also the nature of the products may differ from earlier assumptions[2b] in the literature.

## Results and Discussion

The reaction conditions used for the $NaBH_3CN$ (or $NaBD_3CN$) reduction of the $\alpha,\beta$-unsaturated steroidal tosylhydrazones were those described by Hutchins and coworkers[2] with the omission of the cyclohexane GLC internal standard. The tosylhydrazone was dissolved in 1:1 DMF–sulfolane, the $NaBH_3CN$ (or $NaBD_3CN$) and a trace of bromcresol green were added, the reaction mixture was acidified by dropwise addition of concentrated HCl (or a DCl–DOAc solution when deuterated acid catalyst was required) until the blue-green indicator color disappeared (ca. pH 3.8), and the solution was heated at 110° for 3–5 h. After work-up, the crude product was purified by chromatography, and the composition of the fractions was monitored by GLC and mass spectrometry.

Reduction of the tosylhydrazone **3** with $NaBH_3CN$ in the indicated manner produced in 71% yield a mixture of hydrocarbons consisting of 6.5% 5$\alpha$-cholest-3-ene (**4a**), 32.5% 5$\beta$-cholest-3-ene (**4b**), 30.5% 5$\alpha$-cholestane (**5a**), 30.5% 5$\beta$-cholestane (**5b**), and a trace of cholest-4-ene (**13**). Further elution of the column gave fractions which were all contaminated with sulfolane. To identify the rest of the reaction product, the reduction was repeated using DMF alone as the solvent. Alumina chromatography of the crude product yielded 70% of a mixture of hydrocarbons having a composition similar to that described above, followed by 8% of one or more 1,2-bis(3-cholestanyl)diazenes (**6**)[8] and ca.



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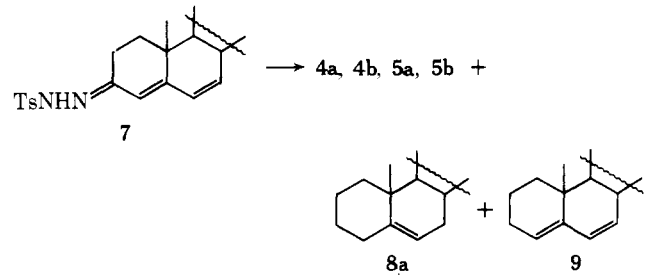
20–22% of a mixture of at least six compounds resulting from hydrolysis of the tosylhydrazone to the starting enone and subsequent reduction by $NaBH_3CN$. A blank experiment showed that such a regeneration of the enone from the tosylhydrazone occurs to a limited extent under the reaction conditions of the reduction.[9]

When **3** was reduced with $NaBD_3CN$ in the presence of hydrochloric acid, the cholest-3-ene mixture consisted predominantly of monodeuterated material (73% $d_1$ vs. 17% $d_2$ and 8% $d_0$), while the major component of the saturated cholestanes was dideuterated (66% $d_2$ vs. 20% $d_1$ and 10% $d_3$). The location of the deuterium atom in 5$\alpha$- and 5$\beta$-cholest-3-ene was established by $^1H$ and $^{13}C$ NMR spectroscopy to be at C-3 (**4c** and **4d**). When the reduction of **3** with $NaBD_3CN$ was catalyzed by deuterated acid, the 5$\alpha$- and 5$\beta$-cholest-3-enes contained predominantly two deuterium atoms (81% $d_2$ vs. 15% $d_1$) and the 5$\alpha$- and 5$\beta$-cholestanes contained up to four deuterium atoms (55% $d_4$ vs. 33% $d_3$ and 7% $d_2$). The use of $D_2O$ in the work-up procedure of the reduction with $NaBD_3CN$ using deuterated acid catalyst caused no appreciable change in the isotopic content of the products.

As a result of the unexpected production of alkanes in the reduction of the tosylhydrazone **3**, the $NaBH_3CN$ reduction of cholesta-4,6-dien-3-one tosylhydrazone (**7**) was investigated to determine whether saturated products would be formed also in this case. The hydrocarbon mixture obtained in 59% yield from this reduction was separated to give 19% of a 1:1 mixture of 5$\alpha$- and 5$\beta$-cholestane (**5a** and **5b**), 28% of cholest-5-ene (**8a**), 10% of a 1:4 mixture of 5$\alpha$- and 5$\beta$-cholest-3-ene (**4a** and **4b**), and 43% of cholesta-4,6-diene (**9**).



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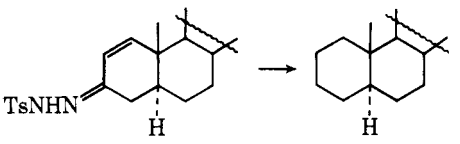
8a 9

The $NaBH_3CN$ reduction of another transoid $\alpha,\beta$-unsaturated tosylhydrazone, 5$\alpha$-cholest-1-en-3-one tosylhydrazone (**10**), which differs from **3** only in the position of the double bond, proceeded in a much more straightforward manner to yield 70% of 5$\alpha$-cholestane (**5a**) with only a trace of cholest-2-ene detected by mass spectrometry. Reduction with $NaBD_3CN$ gave approximately the same isotopic distribution as encountered in the case of the alkane product from the reduction of **3**, i.e., 5$\alpha$-cholestane-$d_2$ when ordi-

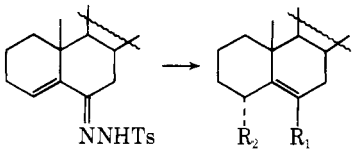



10 5a

nary hydrochloric acid was used and $d_4$ product in the presence of deuterated acid.

When the cisoid $\alpha,\beta$-unsaturated tosylhydrazone of cholest-8(14)-en-7-one (**1**) was reduced with $NaBH_3CN$, 14$\alpha$-cholest-7-ene (**2b**) was generated in 88% yield as the only hydrocarbon, uncontaminated with saturated product. Reduction with $NaBD_3CN$ yielded 14$\alpha$-cholest-7-ene-*7*-$d_1$ (**2c**) of fair isotopic purity (27.4% $d_0$, 56.0% $d_1$, 16.6% $d_2$) which was unchanged when $D_2O$ was used in the work-up procedure. As expected, use of deuterated acid catalyst afforded cholest-7-ene-*7,14*$\alpha$-$d_2$ (**2d**) (68% isotopic purity).

Reduction of another cisoid $\alpha,\beta$-unsaturated tosylhydrazone, cholest-4-en-6-one tosylhydrazone (**11**), with




11 **8a**, $R_1 = R_2 = H$
**b**, $R_1 = D$; $R_2 = H$
**c**, $R_1 = R_2 = D$

$NaBH_3CN$ again produced only the alkene resulting from double bond migration to the original carbonyl carbon, cholest-5-ene (**8a**), in 79% yield, and no detectable alkane product. The use of $NaBD_3CN$ with hydrochloric acid gave cholest-5-ene-*6*-$d_1$ (**8b**) (60% $d_1$ vs. 33% $d_0$), while introduction of deuterated acid afforded dideuterated product of 79% isotopic purity, which was established to be cholest-5-ene-*4*$\alpha$,*6*-$d_2$ (**8c**) by $^1H$ NMR (see Experimental Section).

On the basis of these results, the following conclusions can be drawn concerning the mechanism of the sodium cyanoborohydride reduction of $\alpha,\beta$-unsaturated tosylhydrazones. The deuterium labeling showed that one of the hydrogens involved in the reduction process is provided by the $NaBH_3CN$. When the hydrocarbon product from the reduction with $NaBD_3CN$ is the alkene resulting from migration of the double bond (e.g., **1** → **2**), the deuterium is located exclusively at the original carbonyl carbon (e.g., **2c**). However, these monodeuterated alkenes are of rather poor isotopic purity due to the ability of the $NaBD_3CN$ to undergo hydrogen–deuterium exchange near pH 3[1b,c] (the reduction is run below pH 3.8). There is also a considerable amount of dideuterated product present in these alkenes, which is attributable to exchange of the hydrogen on the nitrogen of the tosylhydrazone with deuterium (Scheme III). It is this hydrogen on the tosylhydrazone nitrogen which is the second hydrogen involved in the reduction process (vide infra). The use of a deuterated acid catalyst in the $NaBD_3CN$ reduction produces a dideuterated alkene, again due to exchange of the hydrogen of the tosylhydrazone nitrogen with deuterium. When alkanes are produced in the reduction of $\alpha,\beta$-unsaturated tosylhydrazones, $NaBD_3CN$ and a proton acid catalyst give dideuterated product resulting from two successive reductions, while $NaBD_3CN$ with a deuterated acid catalyst gives tetradeuterated material. The isotopic purity is also poor in these cases, since with two reductions there is even greater opportunity for hydrogen–deuterium exchange. Some deuteration of the enolizable protons of the tosylhydrazone may also be occurring.[10]

Sodium cyanoborohydride has been found to have a propensity for selectively reducing imminium ions.[1] It is generally assumed that alkyldiazenes, resulting from 1,2-elimination of toluenesulfinic acid from RNHNHTs,[11] are intermediates in the $NaBH_3CN$ reduction of such imminium type ions formed by the protonation of tosylhydrazones (Scheme IV).[2b] It has been established that such alkyldiazenes (as well as aryl- and alkenyldiazenes) undergo a bimolecular decomposition to produce the corresponding alkane (Scheme V) plus other products.[8] However, it does not seem likely that such an alkyldiazene intermediate is possible in the $NaBH_3CN$ reduction of an $\alpha,\beta$-unsaturated tosylhydrazone to produce as the only olefin the alkene resulting from migration of the double bond, since deuterium labeling has shown that initial hydride (or deuteride) attack occurs at the imminium ion carbon. In the reduction of cholest-4-en-6-one tosylhydrazone (**11**), hydride attack at C-6 of the protonated tosylhydrazone followed by loss of toluenesulfinic acid would produce the alkyldiazene **12** (Scheme VI). Decomposition of **12** following a bimolecular pathway such as that shown in Scheme V would be expected to lead to cholest-4-ene (**13**) or a mixture of **13** and cholest-5-ene (**8a**). In actual fact the rearranged alkene **8a** is the only product observed.[12]

Therefore, it seems probable that the reduction of the $\alpha,\beta$-unsaturated tosylhydrazone **11** to give only **8a** occurs in

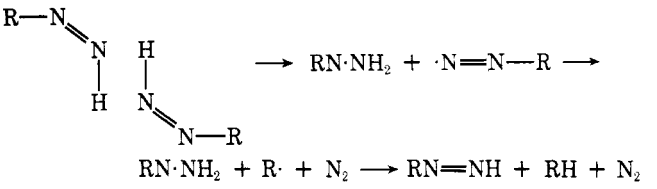
Scheme III

$$^-BD_3CN + H^+ + R_2C{=}NNHTs \longrightarrow {}^-BD_2HCN + D^+ + R_2C{=}NNHTs \longrightarrow {}^-BD_2HCN + H^+ + R_2C{=}NNDTs$$

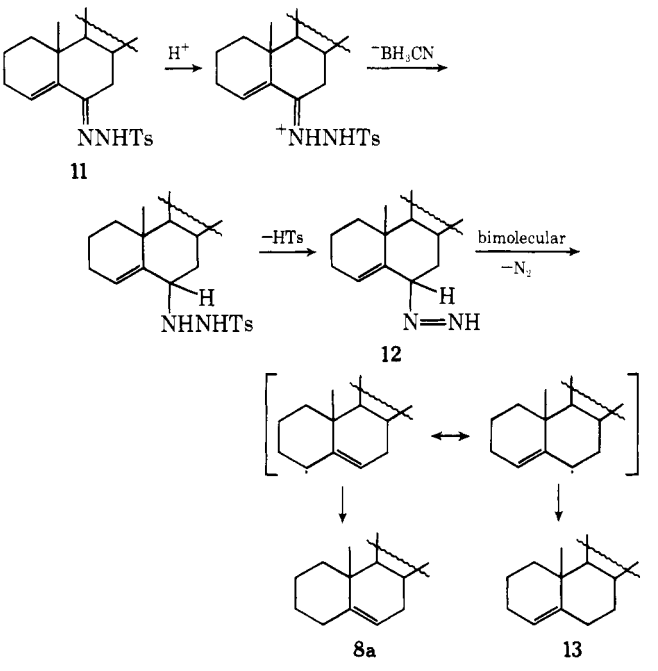
Scheme IV

$$R_2C{=}NNHTs \xrightarrow{H^+} R_2C{=}N^+HNHTs \xrightarrow{^-BH_3CN} R_2CHNHNHTs \xrightarrow{-TsH} R_2CHN{=}NH \longrightarrow N_2 + R_2CH_2$$

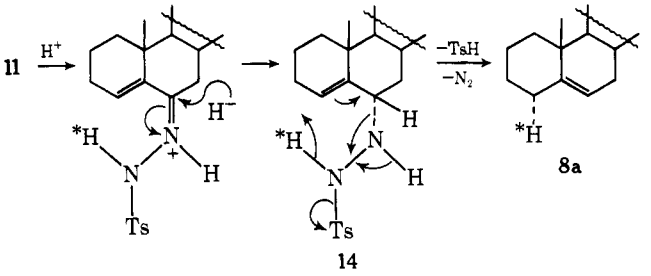
Scheme V



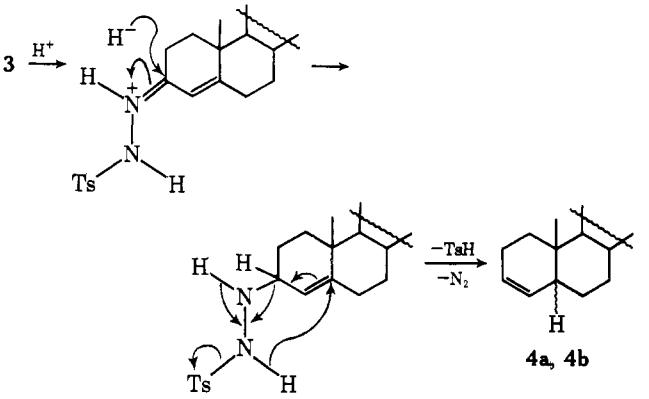

Scheme VI



Scheme VII



Scheme VIII



a concerted manner such as that shown in Scheme VII. Such a reaction pathway is especially attractive for those $\alpha,\beta$-unsaturated tosylhydrazones which have, or can assume, a cisoid conformation, because of the intermediate six-membered cyclic transition state required for delivery of tosylhydrazone hydrogen to the terminus of the conjugated system. Indeed, for the cisoid tosylhydrazones **1** and **11** and all of the $\alpha,\beta$-unsaturated tosylhydrazones reported by Hutchins et al.[2b] that can assume a cisoid conformation, the alkene arising from double bond migration is formed in good yield as the only product.

The stereochemical course of the reduction is completely consistent with Scheme VII since $NaBD_3CN$ treatment of **11** in the presence of deuterated acid led to cholest-5-ene-$4\alpha,6$-$d_2$ (**8c**). Initial hydride attack at C-6 in such systems is known[13] to occur from the $\beta$ side of the molecule and the resulting $6\alpha$-tosylhydrazine intermediate **14** could then deliver the proton attached to nitrogen only from the $\alpha$ side to produce (in the deuterated example) **8c.** It is also noteworthy that in the $NaBH_3CN$ reduction of the tosylhydrazone **1**, the only product formed was $14\alpha$-cholest-7-ene (**2b**) with no $14\beta$ compound detected, indicating complete stereospecific transfer of the hydrogen on nitrogen in this case as well.

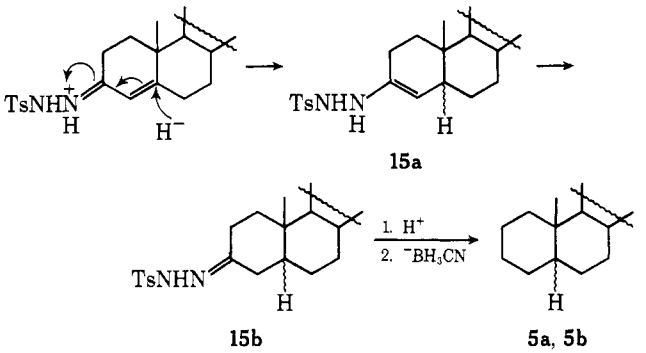
For $\alpha,\beta$-unsaturated tosylhydrazones which are restricted to a transoid conformation by structural rigidity, the results of the $NaBH_3CN$ reduction are not as straightforward as those for cisoid tosylhydrazones. Hutchins and co-workers[2b] report considerably poorer yields for the reductions of such compounds, with the only product reported being the rearranged alkene. As shown above, the $NaBH_3CN$ reductions of the transoid steroidal tosylhydrazones **3, 7,** and **10** produced good yields of hydrocarbons, but a considerable amount (or all, in the case of **10**) of the product was saturated.

In the $NaBH_3CN$ reduction of the tosylhydrazone **3,** the only alkenes generated, **4a** and **4b,** were again the result of double bond migration. These alkenes must also be produced by a mechanism similar to that described in Scheme VII (or ref 12), since the $NaBD_3CN$ reduction of **3** led to alkenes labeled at C-3 (**4c** and **4d**). In this instance, however, the intramolecular proton transfer step (Scheme VIII) is less sterically favorable than for a cisoid tosylhydrazone (Scheme VII) and indeed accounts for only 39% of the hydrocarbon product.

The predominant formation of $5\beta$-cholest-3-ene (**4b**) in the $NaBH_3CN$ reduction of **3** is readily rationalized in terms of the mechanism depicted in Scheme VIII, because favored attack of the $^-BH_3CN$ is expected[14] to proceed from the $\alpha$ face of the molecule. Internal hydrogen transfer from nitrogen to C-5 can then only take place from the $\beta$ side of the molecule via a half-boat intermediate. The small amount of $5\alpha$-cholest-3-ene (**4a**) isolated from the reduction of **3** presumably arises from the minor $3\beta$ attack[14] of hydride to the imminium system.

The generation of alkanes in the $NaBH_3CN$ reduction of **3** must occur through a different mechanism from that described in Scheme VIII for the formation of alkenes **4a** and **4b.** Attack of hydride in a Michael-type addition at the $\beta$ carbon of the protonated tosylhydrazone followed by isomerization of the resulting alkenyltosylhydrazine **15a**[10] to the saturated tosylhydrazone **15b,** reprotonation, and subsequent reduction by a second hydride would produce the saturated cholestanes **5a** and **5b** (Scheme IX). It should be noted that in contrast to the preponderant formation of $5\beta$-cholest-3-ene (**14b**), reflecting the great steric preference[14] for initial $\alpha$ attack by hydride to the imminium system, the alkane mixture consists of equal amounts of $5\alpha$- and $5\beta$-cholestanes (**5a** and **5b**). In this instance, the stereochemical course is controlled by the initial Michael-type attack at C-5 and it is known from other Michael additions to $\Delta^4$-3-keto steroids[15] that such reactions generate approximately equal amounts of $5\alpha$ and $5\beta$ isomers.

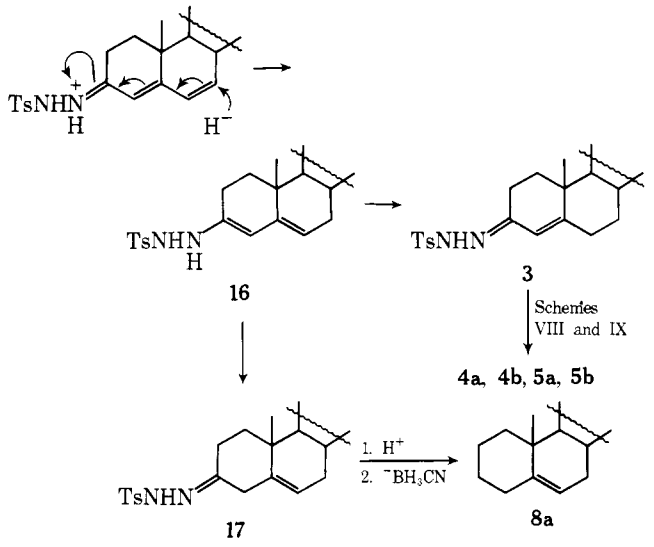
Scheme IX



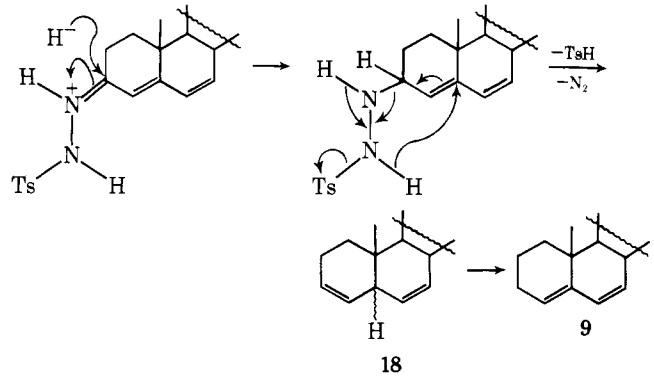
The alkanes **5a** and **5b** formed in the reduction of the dienone tosylhydrazone **7** can be accounted for in a similar manner, assuming again initial Michael-type hydride attack at C-7 (Scheme X). The observed production of cholest-5-ene (**8a**) can be rationalized via isomerization of **16** to the nonconjugated unsaturated tosylhydrazone **17** followed by a second reduction with $NaBH_3CN$. Cholesta-4,6-diene (**9**) must be produced by initial hydride attack at C-3 and internal hydrogen transfer from nitrogen to C-5 similar to Scheme VIII. The resulting nonconjugated diene **18** then isomerizes to the conjugated diene **9** (Scheme XI). This product accounts for 43% of the hydrocarbon mixture, compared to the 39% of alkenes **4a** and **4b** formed in the reduction of **3** by a similar mechanism.

We conclude that alkene formation (with migration of the double bond) is initiated by hydride reduction of the imminium system (Schemes VII and VIII), while alkanes are generated by initial Michael-type addition of hydride to the terminus of the conjugated system (Scheme IX). The relative proportion of alkene vs. alkane product will then depend on extrinsic factors favoring either Michael addition or imminium ion reduction. This is nicely documented in

Scheme X




Scheme XI




the reduction of the 5α-cholest-1-en-3-one tosylhydrazone (**10**) which we found to proceed solely with formation of alkane product, **5a**, i.e., initial Michael-type attack of hydride. It is well known that while the reaction of $NaBH_4$ with cholest-4-en-3-one proceeds almost exclusively by reduction of the carbonyl group,[14a,b] 5α-cholest-1-en-3-one, under similar conditions, undergoes almost exclusive 1,4-addition[16] with production of a saturated rather than an unsaturated analog.

In summary, while the $NaBH_3CN$ reduction of α,β-unsaturated tosylhydrazones is clearly of synthetic utility, caution must be exercised in predicting the nature of the products. Of least utility are those substrates (e.g., cholest-4-en-3-one tosylhydrazone (**3**)) in which the balance between imminium reduction and Michael attack is so delicate that a mixture of alkene and alkane products is obtained.

## Experimental Section

**General.** $NaBH_3CN$ was obtained from Alfa Inorganics and used without purification. $NaBD_3CN$ was prepared by exchanging the hydrogens of $NaBH_3CN$ for deuterium using the procedure of Borch and co-workers.[1c] Sulfolane and DMF were distilled under vacuum from $CaH_2$, mixed in a 1:1 ratio by volume and stored over 4A molecular sieves. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Infrared spectra were recorded for solutions in chloroform on a Perkin-Elmer Model 421 spectrometer, $^1H$ NMR spectra on Varian Model T-60 and Bruker Model HXS-360 spectrometers, and $^{13}C$ NMR spectra on a Varian XLFT-100 spectrometer using deuteriochloroform as solvent and tetramethylsilane as internal reference. Optical rotations were measured for solutions in chloroform using a Perkin-Elmer Model 141 spectropolarimeter. Uv spectra were recorded for solutions in 95% ethanol on a Cary-14 spectrometer. Low-resolution mass spectra were obtained by Messrs. R. G. Ross and R. Conover with AEI MS-9 and Atlas CH-4 instruments using a direct inlet system. Elemental analyses were determined by the Microanalytical Laboratory, Stanford University.

Gas–liquid phase chromatography (GLC) was performed on a Hewlett-Packard Model 402 high-efficiency instrument using 6-ft glass columns packed with 3% OV-25 on Gas-Chrom Q (100–200 mesh) from Applied Science Laboratories, Inc. Column chromatography was done using Merck neutral activity II alumina and TLC was carried out on silica gel $HF_{254}$ plates visualized by spraying with ceric surface solution (2% in 1 M sulfuric acid) followed by heating.

**General Procedure for Tosylhydrazone Preparation.**[2b] A solution of the ketone and a 10–20% molar excess of *p*-toluenesulfonylhydrazine in absolute ethanol (ca. 5–10 ml/mmol of ketone) was heated under reflux for 0.5–1 h. The solution was cooled and the precipitate was collected by suction filtration and washed with 95% ethanol to yield the tosylhydrazone. The products obtained were sufficiently pure that recrystallization was not necessary.

**Cholest-4-en-3-one Tosylhydrazone (3):** yield, 88%; mp 138–140° dec (lit.[4] mp 142°); NMR δ 0.68 (s, 3 H, C-18 $CH_3$), 0.99 (s, 3 H, C-19 $CH_3$), 2.40 (s, 3 H, Ar-$CH_3$), 5.74 (s, 1 H, vinyl), 7.24 (d, $J$ = 8 Hz, 2 H, aromatic), 7.76 (d, $J$ = 8 Hz, 2 H, aromatic).

**Cholesta-4,6-dien-3-one Tosylhydrazone (7):** yield, 87%; mp 175–177° dec; NMR δ 0.72 (s, 3 H, C-18 $CH_3$), 0.89 (s, 3 H, C-19 methyl), 2.40 (s, 3 H, Ar $CH_3$), 5.80–6.07 (m, 3 H, vinyl), 7.29 (d, $J$ = 8 Hz, 2 H, aromatic), 7.88 (d, $J$ = 8 Hz, 2 H, aromatic).

Anal. Calcd for $C_{34}H_{50}N_2O_2S$: C, 74.18; H, 9.09; N, 5.09; S, 5.82. Found: C, 73.88; H, 8.84; N, 5.18; S, 5.95.

**5α-Cholest-1-en-3-one Tosylhydrazone (10):** yield, 75%; mp 167–169° dec (lit.[17] mp 168–170° dec); NMR δ 0.65 (s, 3 H, C-18 $CH_3$), 0.79 (s, 3 H, C-19 $CH_3$), 2.41 (s, 3 H, Ar $CH_3$), 5.91 (d, $J$ = 10 Hz, 1 H, vinyl), 6.38 (d, $J$ = 10 Hz, 1 H, vinyl), 7.28 (d, $J$ = 8 Hz, 2 H, aromatic), 7.78 (d, $J$ = 8 Hz, 2 H, aromatic).

**Cholest-8(14)-en-7-one Tosylhydrazone (1):** yield 66%; mp 134–136° dec; NMR δ 0.64 (s, 3 H, C-19 $CH_3$),[18] 0.83 (s, 3 H, C-18 $CH_3$),[18] 2.40 (s, 3 H, AR $CH_3$), 7.26 (d, $J$ = 8 Hz, 2 H, aromatic), 7.83 (d, $J$ = 8 Hz, 2 H, aromatic).

Anal. Calcd for $C_{34}H_{52}N_2O_2S{\cdot}C_2H_5OH$: C, 72.18; H, 9.77; N, 4.68; S, 5.36. Found: C, 72.07; H, 9.64; N, 4.74; S, 5.29.

**Cholest-4-en-6-one Tosylhydrazone (11):** yield, 69%, mp 155–157° dec; NMR δ 0.55, 0.61, 0.65 (3 H, C-18 $CH_3$), 0.91 (s, 3 H, C-19 $CH_3$), 2.42 (s, 3 H, Ar $CH_3$), 5.71 (m, 1 H, vinyl), 7.30 (d, $J$ = 8 Hz, 2 H, aromatic), 7.84 (d, $J$ = 8 Hz, 2 H, aromatic).

Anal. Calcd for $C_{34}H_{52}N_2O_2S$: C, 73.91; H, 9.42; N, 5.07; S, 5.80. Found: C, 73.87; H, 9.35; N, 5.15; S, 5.98.

**General Procedure for Reduction of the Tosylhydrazones with Sodium Cyanoborohydride (Deuteride).** A mixture of the tosylhydrazone, a fourfold molar excess of $NaBH_3CN$ ($NaBD_3CN$), and a trace of bromcresol green in 1:1 DMF–sulfolane (ca. 5 ml/mmol of tosylhydrazone) was acidified by dropwise addition of concentrated HCl (DCl–DOAc solution[19]) until the blue-green color disappeared. After heating with stirring at 105–110° for 3–5 h, the reaction mixture was cooled, diluted with $H_2O$ ($D_2O$), and extracted three times with ether. The combined ether extracts were washed well with $H_2O$, saturated $NaHCO_3$, and $H_2O$, dried ($MgSO_4$), and concentrated. The resulting product was chromatographed on alumina by eluting with hexane to yield the hydrocarbon.

**Reduction of Cholest-4-en-3-one Tosylhydrazone (3) with Sodium Cyanoborohydride.** The reduction of **3** (200 mg) with $NaBH_3CN$ carried out according to the general procedure yielded after column chromatography 96 mg (71%) of a hydrocarbon mixture as a colorless oil. Further elution with more polar solvents gave fractions which were all contaminated with sulfolane.

Preparative TLC of the hydrocarbon mixture on $AgNO_3$-impregnated silica gel and developing with $CCl_4$ yielded a 1:1 mixture (by GLC) of 5α- and 5β-cholestane (**5a** and **5b**, 43 mg, 61%) and a 1:5 mixture (by GLC) of 5α- and 5β-cholest-3-ene (**4a** and **4b**, 27 mg, 39%) plus a trace of cholest-4-ene (**13**). These compounds were identified by molecular weight (mass spectrometry), NMR, and comparison of GLC and TLC ($AgNO_3$ impregnated silica gel) retention times with authentic samples.[20]

**Reduction of Cholest-4-en-3-one Tosylhydrazone (3) with Sodium Cyanoborohydride in DMF Solvent.** The reduction of **3** (450 mg)

with $NaBH_3CN$ was carried out as described above except that the solvent was pure DMF. Chromatography of the crude reaction product on alumina and eluting with hexane yielded a mixture of hydrocarbons (214 mg, 70%) of similar composition as that above; 30% benzene in hexane eluted a white crystalline compound (25 mg, 8%) thought to be one or more 1,2-bis(3-cholestanyl)diazenes (**6**) which crystallized from ethyl acetate: mp 187–190°; mass spectrum $M^+$ 770 ($\equiv C_{54}H_{94}N_2$).

Anal. Calcd for $C_{54}H_{94}N_2$: C, 84.16; H, 12.21; N, 3.63. Found: C, 83.89; H, 11.92; N, 3.63.

Further elution of the column with ether gave a yellow oil (71 mg, ca. 20–22%) which was found to be a mixture of at least six compounds by TLC and GLC. The ir spectrum of the mixture indicated that there was little, if any, tosylhydrazone present (no peaks at 3290, 3210 (N–H), and only a very small peak at 1150 $cm^{-1}$ ($-SO_2-$)). The ir did show the following peaks: 3685, 3615 (O–H), 1704 (saturated C=O), 1665 (unsaturated C=O), and 1596 $cm^{-1}$ (C=C). The GLC–mass spectrum of this mixture confirmed the fact that it was probably a mixture of 5α- and/or 5β-cholestan-3ξ-ol ($M^+$ 388), 5α- and/or 5β-cholestan-3-one ($M^+$ 386), and a trace of cholest-4-en-3-one ($M^+$ 384), but the resolution of the many peaks on GLC was poor and positive identification was not pursued.

**Partial Hydrolysis of Cholest-4-en-3-one Tosylhydrone (3) under the Conditions of the Sodium Cyanoborohydride Reduction.** A solution of **3** (150 mg) (purified by column chromatography on alumina to remove any traces of underivatized ketone) and a trace of bromcresol green in 1.5 ml of DMF was acidified by adding concentrated HCl dropwise until the blue-green color disappeared. The reaction was heated at 105° for 5 h, then worked up in the usual manner to give 133 mg of yellow semicrystalline material. Chromatography on alumina eluting with hexane and then benzene afforded 33 mg of yellow semicrystalline material shown to be mostly cholest-4-en-3-one by TLC and GLC comparison with an authentic sample.[21] Elution with ether gave an orange oil (62 mg) which was mainly the starting tosylhydrazone as shown by ir, NMR, and TLC comparison with an authentic sample.

**Reduction of Cholest-4-en-3-one Tosylhydrazone (3) with Sodium Cyanoborodeuteride.** The $NaBD_3CN$ reduction of **3** (650 mg) afforded 295 mg (67%) of a hydrocarbon mixture which was separated by preparative TLC on $AgNO_3$ impregnated silica gel by developing with $CCl_4$ to give a 1:1 mixture of 5α- and 5β-cholestane-$d_2$ (113 mg) [mass spectrum $M^+$ 374 ($C_{27}H_{46}D_2$) ($d_0$, 2.8; $d_1$, 20.2; $d_2$, 66.2; $d_3$, 9.6; $d_4$, 0.8; $d_5$, 0.4%] and a 1:6 mixture of 5α- and 5β-cholest-3-ene-3-$d_1$ (**4c** and **4d**, 109 mg) [mass spectrum $M^+$ 371 ($C_{27}H_{45}D$) ($d_0$, 8.2; $d_1$, 73.0; $d_2$, 16.8; $d_3$, 1.0; $d_4$, 1.0%); $^1H$ NMR δ 5.36 (broad s, ca. 1 H, vinyl); $^{13}C$ NMR showed signals at δ 131.2 (corresponding to C-4 of 5α-cholest-3-ene)[22] and 132.1 ppm (which should be C-4 of 5β-cholest-3-ene) in a 1:6 ratio]. There are no signals at 125.1 (C-3 of 5α-cholest-3-ene)[22] or within 2 ppm of 125.1 ppm (which would correspond to C-3 of 5β-cholest-3-ene). Thus the deuterium in **4c** and **4d** is located at C-3.

**Reduction of Cholest-4-en-3-one Tosylhydrazone (3) with Sodium Cyanoborodeuteride Using a Deuterated Acid Catalyst.** The reduction of **3** (100 mg) with $NaBD_3CN$ using the DCl–DOAc acid catalyst produced 50 mg (74%) of a hydrocarbon mixture, which was separated as above to yield a 1:1 mixture of 5α- and 5β-cholestane-$d_4$ (24 mg) [mass spectrum $M^+$ 376 ($C_{27}H_{44}D_4$) ($d_0$, 1.2; $d_1$, 0.9; $d_2$, 6.7; $d_3$, 32.9; $d_4$, 55.1; $d_5$; 2.5; $d_6$, 0.7%] and a 1:7 mixture of 5α- and 5β-cholest-3-ene-$d_2$ (17 mg) [mass spectrum $M^+$ 372 ($C_{27}H_{44}D_2$) ($d_0$, 0.9; $d_1$, 14.7; $d_2$, 81.1; $d_3$, 3.3%); NMR δ 5.32 (broad s, ca. 1 H, vinyl].

**Reduction of Cholest-4-en-3-one Tosylhydrazone (3) with Sodium Cyanoborodeuteride Using a Deuterated Acid Catalyst Followed by a $D_2O$ Workup.** The above reaction was repeated and the reaction mixture was diluted first with 0.5 ml of $D_2O$ followed by the usual work-up and chromatography to give 52 mg (77%) of a hydrocarbon mixture consisting of a 1:1 mixture of 5α- and 5β-cholestane-$d_4$ (27 mg) [mass spectrum $M^+$ 376 ($C_{27}H_{44}D_4$) ($d_0$, 2.6; $d_1$, 1.5; $d_2$, 9.1; $d_3$, 35.1; $d_4$, 42.8; $d_5$, 7.8; $d_6$, 1.1%] and a 1:6 mixture of 5α- and 5β-cholest-3-ene-$d_2$ (17 mg) [mass spectrum $M^+$ 372 ($C_{27}H_{44}D_2$) ($d_0$, 1.0; $d_1$, 14.6; $d_2$, 77.1; $d_3$, 6.3; $d_4$, 1.0%); NMR δ 5.31 (broad s, ca. 1 H, vinyl].

**Reduction of Cholesta-4,6-dien-3-one Tosylhydrazone (7) with Sodium Cyanoborohydride.** The reduction of **7** (200 mg) with $NaBH_3CN$ afforded a mixture of hydrocarbons (160 mg, 59%) which was separated by preparative TLC on $AgNO_3$-impregnated silica gel by developing with chloroform to give the following compounds: a 1:1 mixture (by GLC) of 5α- and 5β-cholestane (**5a** and **5b**, 15 mg, 19%), cholest-5-ene (**8a**, 22 mg, 28%) [mp 95–96° (MeOH) (lit.[23] mp 91–93°); $[\alpha]_D$ −54° (*c* 1.1) (lit.[23] $[\alpha]_D$ −56°); mass spectrum $M^+$ 370 ($C_{27}H_{46}$); NMR δ 0.67 (s, 3 H, C-18 $CH_3$), 0.99 (s, 3 H, C-19 $CH_3$), 5.23 (m, 1 H, vinyl], a 1:4 mixture (by GLC) of 5α- and 5β-cholest-3-ene (**4a** and **4b**, 8 mg, 10%), and impure cholesta-4,6-diene (**9**, 33 mg, 43%) as an oil which would not crystallize (lit.[24] mp 91–92°); $[\alpha]_D$ +4.8° (*c* 0.54) (lit.[24] $[\alpha]_D$ +7°, also +9°, +13°); mass spectrum $M^+$ 368 ($C_{27}H_{44}$); NMR δ 0.71 (s, 3 H, C-18 $CH_3$), 0.90 (s, 3 H, C-19 $CH_3$), 5.43–5.63 (m, 3 H, vinyl); uv $\lambda_{max}$ 245 nm (lit.[24] $\lambda_{max}$ 230, 238, and 245 nm (ε 21 500, 25 800, and 14 500).

**Reduction of 5α-Cholest-1-en-3-one Tosylhydrazone (10) with Sodium Cyanoborohydride.** The reduction of **10** (100 mg) with $NaBH_3CN$ carried out according to the general procedure yielded white crystals of 5α-cholestane (**5a**, 47 mg, 70%). Recrystallization from methanol gave material with mp and mmp 79–81° (lit.[25] mp 79–80°), mass spectrum $M^+$ 372 ($C_{27}H_{48}$) (also traces of unsaturated material $M^+$ 370 and *m/e* 316 corresponding to the retro-Diels–Alder fragmentation of cholest-2-ene). However, this olefin is only a slight impurity not visible by TLC on $AgNO_3$-impregnated silica gel); NMR δ 0.65 (s, 3 H, C-18 $CH_3$), 0.77 (s, 3 H, C-19 $CH_3$).

**Reduction of 5α-Cholest-1-en-3-one Tosylhydrazone (10) with Sodium Cyanoborodeuteride.** The $NaBD_3CN$ reduction of **10** (50 mg) gave 5α-cholestane-$d_2$ (26 mg, 76%) as white crystals which were recrystallized from MeOH; mp 79.5–81°; mass spectrum $M^+$ 374 ($C_{27}H_{46}D_2$) ($d_0$, 10.6; $d_1$, 28.0; $d_2$, 57.8; $d_3$, 3.6%).

**Reduction of 5α-Cholest-1-en-3-one Tosylhydrazone (10) with Sodium Cyanoborodeuteride Using a Deuterated Acid Catalyst Followed by an $H_2O$ or $D_2O$ Workup.** Tosylhydrazone **10** (100 mg) was reduced with $NaBD_3CN$ and the DCl–DOAc catalyst according to the general procedure. After the reduction was complete, the reaction mixture was divided into two portions, one of which was diluted with $H_2O$ and worked up as usual to give white crystals of 5α-cholestane-$d_4$ (12 mg): mp 80–82° (MeOH); mass spectrum $M^+$ 376 ($C_{27}H_{44}D_4$) ($d_1$, 1.6; $d_2$, 7.8; $d_3$, 33.3; $d_4$, 56.1; $d_5$, 1.2%). The second portion of the reaction mixture was diluted with $D_2O$ followed by the usual work-up, yielding cholestane-$d_4$ (33 mg): mp 80–82° (MeOH); mass spectrum $M^+$ 376 ($C_{27}H_{44}D_4$) ($d_1$, 2.3; $d_2$, 7.9; $d_3$, 33.0; $d_4$, 55.5; $d_5$, 1.3%).

**Reduction of Cholest-8(14)-en-7-one Tosylhydrazone (1) with Sodium Cyanoborohydride.** The reduction of **1** (110 mg) with $NaBH_3CN$ yielded white crystals of cholest-7-ene (**2b**, 68 mg, 88%) which were recrystallized from ethanol: mp 86.5–88° (lit.[23] mp 86–87°); $[\alpha]_D$ +8.0° (*c* 1.0) (lit.[23] $[\alpha]_D$ +11°); NMR δ 0.53 (s, 3 H, C-18 $CH_3$), 0.76 (s, 3 H, C-19 $CH_3$), 5.17 (broad, 1 H, vinyl); mass spectrum $M^+$ 370 ($C_{27}H_{46}$).

**Reduction of Cholest-8(14)-en-7-one Tosylhydrazone (1) with Sodium Cyanoborodeuteride.** Reduction of **1** (40 mg) with $NaBD_3CN$ afforded cholest-7-ene-7-$d_1$ (**2c**, 23 mg, 86%); mp 85–87° (EtOH); mass spectrum $M^+$ 371 ($C_{27}H_{45}D$) ($d_0$, 27.4; $d_1$, 56.0; $d_2$, 16.6%); NMR δ 5.17 (small signal, ca. 0.3 H, vinyl).

**Reduction of Cholest-8(14)-en-7-one Tosylhydrazone (1) with Sodium Cyanoborodeuteride Followed by a $D_2O$ Workup.** The above reduction was repeated and the reaction mixture was diluted with 0.5 ml of $D_2O$ followed by the usual workup to yield cholest-7-ene-7-$d_1$ (**2c**, 23 mg, 86%); mp 86–88° (EtOH); mass spectrum $M^+$ 371 ($C_{27}H_{45}D$) ($d_0$, 30.0; $d_1$, 51.9; $d_2$, 18.1%); NMR δ 5.16 (small signal, ca. 0.3 H, vinyl).

**Reduction of Cholest-8(14)-en-7-one Tosylhydrazone (1) with Sodium Cyanoborodeuteride Using a Deuterated Acid Catalyst.** The tosylhydrazone **1** (40 mg) was reduced with $NaBD_3CN$ and the DCl–DOAc catalyst to give cholest-7-ene-7,14α-$d_2$ (**2a**, 23 mg, 86%): mp 85–87° (EtOH); mass spectrum $M^+$ 372 ($C_{27}H_{44}D_2$) ($d_0$, 3.3; $d_1$, 12.3; $d_2$, 67.8; $d_3$, 5.7; $d_4$, 3.1; $d_5$, 4.0; $d_6$, 3.8); $^1H$ NMR showed no vinyl proton signal, and $^{13}C$ NMR showed no signals at δ 117.5 (C-7)[22] or 55.2 ppm (C-14),[22] indicating that these carbons are labeled with deuterium.

**Reduction of Cholest-4-en-6-one Tosylhydrazone (11) with Sodium Cyanoborohydride.** The reduction of **11** (110 mg) with $NaBH_3CN$ according to the general procedure yielded white crystals of cholest-5-ene (**8a**, 53 mg, 79%) which were recrystallized from ethanol: mp 92–94° (lit.[23] mp 91–93°); $[\alpha]_D$ −53° (*c* 1.7)

(lit.[23] $[\alpha]_D$ −56°); mass spectrum $M^+$ 370 ($C_{27}H_{46}$); NMR δ 0.67 (s, 3 H, C-18 $CH_3$), 1.00 (s, 3 H, C-19 $CH_3$), 5.27 (broad d, $J$ = 8 Hz, 1 H, vinyl).

**Reduction of Cholest-4-en-6-one Tosylhydrazone (11) with Sodium Cyanoborodeuteride.** The tosylhydrazone **11** (50 mg) was reduced with $NaBD_3CN$ to give cholest-5-ene-6-$d_1$ (**8b**, 28 mg, 84%): mp 93–95° (EtOH); mass spectrum $M^+$ 371 ($C_{27}H_{45}D$) ($d_0$, 32.8; $d_1$, 59.9; $d_2$, 6.3; $d_3$, 1.0%); NMR δ 5.25 (small signal, ca. 0.3 H, vinyl).

**Reduction of Cholest-4-en-6-one Tosylhydrazone (11) with Sodium Cyanoborodeuteride Followed by a $D_2O$ Workup.** The above reduction was repeated and the reaction mixture was diluted with 0.5 ml of $D_2O$ followed by the usual work-up to yield cholest-5-ene-6-$d_1$ (**8b**, 82%); mp 93–95°; mass spectrum $M^+$ 371 ($C_{27}H_{45}D$) ($d_0$, 22.5; $d_1$, 67.0; $d_2$, 9.6; $d_3$, 0.9%); NMR δ 5.25 (small signal, ca. 0.3 H, vinyl).

**Reduction of Cholest-4-en-6-one Tosylhydrazone (11) with Sodium Cyanoborodeuteride Using a Deuterated Acid Catalyst.** The reduction of **11** (40 mg) with $NaBD_3CN$ and the DCl-DOAc catalyst according to the general procedure afforded cholest-5-ene-4α,6-$d_2$ (**8c**, 23 mg, 86%): mp 93.5–95.5° (EtOH); mass spectrum $M^+$ 372 ($C_{27}H_{44}D_2$) ($d_0$, 0.8; $d_1$, 9.4; $d_2$, 79.4; $d_3$, 7.9; $d_4$, 2.5%); 60-MHz $^1H$ NMR showed no vinyl proton signal and 360-MHz $^1H$ NMR showed only a very small signal for a vinyl proton at δ 5.25, thus locating one deuterium atom at C-6. The 360-MHz $^1H$ NMR spectrum of unlabeled cholest-5-ene (**8a**) separated one allylic proton signal at δ 2.21 (broad t, $J$ = 14 Hz, 1 H) from the other allylic protons centered at 1.97 (broad m, 3 H). In the dideuterated compound, the signal at 2.21 almost completely disappears, indicating a stereospecific replacement of one allylic proton with deuterium. Irradiation of the vinyl proton in the unlabeled compound caused only a slight change in the signal at δ 2.21, while major changes were noticeable in the shape of the signal at 1.97. This means that the signal at 2.21 can be assigned to one of the C-4 protons, which has only a small allylic coupling to the C-6 proton. Two of the protons which resonated at δ 1.97 are then at C-7 and have a larger vicinal coupling to the C-6 proton. The C-4 proton at δ 2.21 (which is replaced by deuterium in the $d_2$-labeled compound) is assigned the α configuration on the basis of its downfield shift from the other allylic protons. The 4α proton lies almost directly in the plane of the double bond and is therefore expected to be more deshielded than the other allylic protons which are out of this plane.[26]

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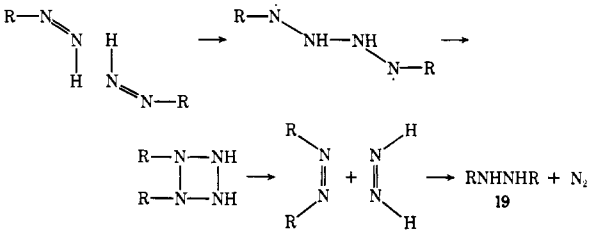
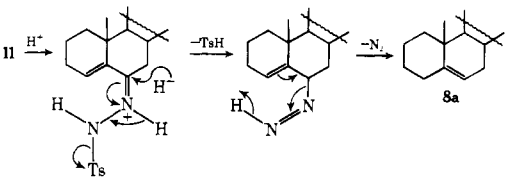
## References and Notes

(1) (a) For a recent review on the selective reductions of $NaBH_3CN$ see C. F. Lane, *Aldrichimica Acta*, **8**, 3 (1975); (b) R. F. Borch and H. D. Durst, *J. Am. Chem. Soc.*, **91**, 3996 (1969); (c) R. F. Borch, M. D. Bernstein, and H. D. Durst, *ibid.*, **93**, 2897 (1971); (d) R. O. Hutchins, B. E. Maryanoff, and C. A. Milewski, *Chem. Commun.*, 1097 (1971).
(2) (a) R. O. Hutchins, B. E. Maryanoff, and C. A. Milewski, *J. Am. Chem. Soc.*, **93**, 1793 (1971); (b) R. O. Hutchins, C. A. Milewski, and B. E. Maryanoff *ibid.*, **95**, 3662 (1973).
(3) For reviews see (a) W. Reusch in "Reduction", R. L. Augustine, Ed., Marcel Dekker, New York, N.Y., 1968, pp 171–211; (b) H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 4.
(4) L. Caglioti and M. Magi, *Tetrahedron*, **19**, 1127 (1963).
(5) Existing methods such as desulfurization of the thioketal with Raney nickel or $LiAlD_4$ reduction of the tosylhydrazone lack one or both of these requirements; see L. Tökes and L. J. Throop in "Organic Reactions in Steroid Chemistry", Vol. I, J. Fried and J. A. Edwards, Ed., Van Nostrand-Reinhold, New York, N.Y., 1972, Chapter 4.
(6) H. Klein and I. Midgley, unpublished results from this laboratory.
(7) M. Fischer, Z. Pelah, D. H. Williams, and C. Djerassi, *Chem. Ber.*, **98**, 3236 (1965).
(8) Kosower and co-workers have shown that part of the product generated in the bimolecular decomposition of monosubstituted diazenes is a symmetrical 1,2-bisdialkyldiazane (**19**) formed as shown below. Such diazanes are known to readily air oxidize; thus **6** could be produced from air oxidation of the corresponding 1,2-bis(3-cholestanyl)diazane. See (a) E. M. Kosower, P. C. Huang, and T. Tsuji, *J. Am. Chem. Soc.*, **91**, 2325 (1969); (b) T. Tsuji and E. M. Kosower, *ibid.*, **93**, 1999 (1971); (c) *ibid.*, **93**, 1992 (1971); (d) E. M. Kosower, *Acc. Chem. Res.*, **4**, 193 (1971); (e) A. Heesing and B.-U. Kaiser, *Tetrahedron Lett.*, 1307 (1971).




(9) For other conditions leading to regeneration of carbonyl compounds from tosylhydrazones, see (a) T.-L. Ho and C. M. Wong, *J. Org. Chem.*, **39**, 3453 (1974); (b) G. Rosini, *ibid.*, **39**, 3504 (1974); (c) A. Bhati, *Chem. Commun.*, 476 (1965).
(10) G. Rosini and G. Baccolini, *J. Org. Chem.*, **39**, 826 (1974).
(11) D. J. Cram and J. S. Bradshaw, *J. Am. Chem. Soc.*, **85**, 1108 (1963).
(12) A bimolecular decomposition route (Schemes V and VI) for the unsaturated diazene is not the only possibility, since an intramolecular process may also intervene:




(13) S. Greenfield, E. Glotter, D. Lavie, and Y. Kashman, *J. Chem. Soc. C*, 1460 (1967).
(14) (a) O. H. Wheeler and J. L. Mateos, *Can. J. Chem.*, **36**, 1049 (1958); (b) J. A. Waters and B. Witkop, *J. Am. Chem. Soc.*, **90**, 758 (1968); (c) H. Nakata, *Bull. Chem. Soc. Jpn*, **38**, 378 (1965); (d) A. von Wartburg, *Helv. Chim. Acta*, **49**, 30 (1966).
(15) (a) W. Nagata, M. Yoshioka, and S. Hirai, *Tetrahedron Lett.*, 461 (1962); (b) H. B. Henbest and W. R. Jackson, *J. Chem. Soc. C*, 2465 (1967).
(16) R. Albrecht and C. Tamm, *Helv. Chim. Acta*, **40**, 2216 (1957); see also D. Lavie, E. C. Levy, and M. K. Jain, *Tetrahedron*, **27**, 3927 (1971).
(17) J. E. Herz, E. Gonzalez, and B. Mandel, *Aust. J. Chem.*, **23**, 857 (1970).
(18) The chemical shift assignments for the angular methyl groups of **1** are based on our observation that the tosylhydrazone substituent seems to have little effect on the chemical shift of C-18 and C-19 protons. The resonances are approximately the same as for the corresponding hydrocarbon. Thus compound **1**, with the C-19 methyl group at 0.64 and C-18 at 0.83, is very similar to cholest-8(14)-ene, with the C-19 methyl group at 0.66 and C-18 at 0.82. See N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964, Chapter 2.
(19) The deuterated acid catalyst was made by the cauticus addition of 0.2 ml of acetyl chloride to 0.5 ml of $D_2O$.
(20) For the preparation of 5α-cholest-3-ene, see "Organic Reactions in Steroid Chemistry", ref 5, p 348, and 5β-cholest-3-ene, see B. R. Davis and P. D. Woodgate, *J. Chem. Soc. C*, 2006 (1966); 5β-cholestane was prepared by reduction of 5β-cholestan-3-one tosylhydrazone with $NaBH_3CN$.
(21) Rosini[9b] reported that in the case of α,β-unsaturated tosylhydrazones, regeneration of ketones from tosylhydrazones does not result in a consistent formation of the parent carbonyl compound, but leads to mixtures of products.
(22) H. Eggert and C. Djerassi, in preparation.
(23) G. M. L. Cragg, C. W. Davey, D. N. Hall, G. D. Meakins, E. E. Richards, and T. L. Whateley, *J. Chem. Soc. C*, 1266 (1966).
(24) M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, **29**, 1131 (1964).
(25) P. M. Jones and W. Klyne, *J. Chem. Soc.*, 871 (1960).
(26) N. S. Bhacca and D. H. Williams, ref 18, pp 88–89.