instead occur preferentially upon a second molecule of N-PSP, particularly if the reagent is present in large excess. This results in the formation of the diselenide and phthalimide anion, which reacts further with **9** to afford the observed products **6** and **7**. It is not clear whether the product-forming step involves an S_N1 or S_N2 process as both are expected to favor the major stereoisomer **6**. A predominantly S_N2 displacement would result in inversion of configuration at C-3 from β to α, while an S_N1 step would produce an allyl cation which is known to undergo preferential nucleophilic attack from the α-face in the cholestane series.[9]

In contrast to the above results, sterol **3** was smoothly converted to selenides **4a** and **4b** with selenocyanates **1a** and **1b** in yields of 80% and 65%, respectively. Evidently the selenocyanates are less effective than N-PSP in competing with the alkoxyphosphonium ion **9** for available selenolate. Product **4a** was transformed to the rearranged alcohol **5** in 47% yield with *m*-chloroperbenzoic acid;[11] **4b** provided a slightly lower yield.[12] These experiments suggest that selenocyanates are a more prudent choice than N-PSP for the conversion of secondary alcohols to selenides.

Experimental Section

Melting points were determined on an A. H. Thomas hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 467 instrument while NMR spectra were obtained on a Varian XL200 spectrometer at 200 MHz in CDCl$_3$ solution with tetramethylsilane as the internal standard. A Varian MAT CH5 instrument was employed in recording mass spectra and optical rotations were measured on a Rudolph Autopol III polarimeter in CHCl$_3$ solution. Elemental analyses were performed by Dr. W. S. Lin (University of Calgary). Preparative TLC was carried out on Analtech 20 × 20 cm glass plates coated with 1 mm of silica gel GF. Sterol **3** was prepared by a variation of a literature method,[7] via the reduction of the corresponding enone with diisobutylaluminum hydride. Selenocyanates **1a** and **1b**,[14] as well as N-PSP,[15] were obtained by previously reported procedures. Tri-*n*-butylphosphine and *m*-chloroperbenzoic acid were purchased from the Aldrich Chemical Co. and used without further purification.

Reaction of 3β,17β-Dihydroxy-4-androstene 17-(*tert*-Butyldimethylsilyl Ether) (3) with N-PSP and Tri-*n*-butylphosphine. Sterol **3** (203 mg, 0.50 mmol) and N-PSP (302 mg, 1.00 mmol) were dissolved in 3 mL of dry, degassed THF at 0 °C under nitrogen. The phosphine (0.25 mL, 1.0 mmol) was introduced via syringe and the solution was stirred at 0 °C for 2 h. The mixture was then concentrated and filtered through a short column of silica gel with ethyl acetate as the solvent to remove polar byproducts (tri-*n*-butylphosphine oxide, phthalimide), and the remaining products were separated by preparative TLC in 15% ethyl acetate–hexane to afford three principal bands: (A) Diphenyl diselenide: 110 mg (71%); R_f 0.72; identified by comparison with an authentic sample (TLC, mp, NMR). (B) 17β-Hydroxy-3α-phthalimido-4-androstene *tert*-butyldimethylsilyl ether (6): 137 mg (51%); R_f 0.52; mp 152–155 °C (from dichloromethane–methanol); $[\alpha]_D$ +155°; IR (Nujol) 1760, 1715, 1608 cm^{-1}; ^{1}H NMR 7.9–7.7 (m, 4 H), 5.19 (d, *J* = 2.4 Hz, 1 H), 4.78 (m, 1 H), 3.56 (t, *J* = 8 Hz, 1 H), 1.04 (s, 3 H), 0.87 (s, 9 H), 0.73

(s, 3 H); mass spectrum, *m/e* (relative intensity) 533 (M$^+$, <1), 476 (M$^+$ – C$_4$H$_9$, 25). Anal. Calcd for C$_{33}$H$_{47}$NO$_3$Si: C, 74.25; H, 8.88; N, 2.62. Found: C, 74.65; H, 8.88; N, 2.44. (C) The 3β-epimer **7**: 28 mg (10%); R_f 0.46; mp 226–227 °C (from dichloromethane–methanol); $[\alpha]_D$ – 25°; IR (CHCl$_3$) 1768, 1707, 1609 cm^{-1}; ^{1}H NMR 7.9–7.7 (m, 4 H), 5.11 (d, *J* = 1.5 Hz, 1 H), 4.84 (m, 1 H), 3.56 (t, *J* = 8 Hz, 1 H) 1.21 (s, 3 H), 0.88 (s, 9 H), 0.74 (s, 3 H); mass spectrum, *m/e* (relative intensity) 533 (M$^+$, 2), 476 (M$^+$ – C$_4$H$_9$, 61). Anal. Calcd for C$_{33}$H$_{47}$NO$_3$Si: C, 74.25; H, 8.88; N, 2.62. Found: C, 74.22; H, 8.86; N, 2.61.

In a separate experiment the phosphine in 2 mL of THF was added over 1.5 h to the other reactants via a mechanically driven syringe. After workup as above, the yields of **6** and **7** were 168 mg (63%) and 30 mg (11%), respectively.

17β-Hydroxy-3α-[(2-nitrophenyl)seleno]-4-androstene *tert*-Butyldimethylsilyl Ether (4a). Sterol **3** (2.03 g, 5.00 mmol) and *o*-nitrophenyl selenocyanate (**1a**, 1.25 g, 5.50 mmol) were dissolved in 40 mL of dry THF under nitrogen. Tri-*n*-butylphosphine (1.5 mL, 6.0 mmol) was injected via syringe. After 1.5 h at room temperature, the mixture was concentrated and chromatographed over 80 g of silica gel. Elution with 30% benzene–hexane afforded 2.35 g (80%) of the title compound as a bright yellow solid: mp 129–130° (from ether–isopropyl alcohol); $[\alpha]_D$ +194°; IR (Nujol) 1593, 1585, 1565, 1515 cm^{-1}; ^{1}H NMR 8.3–7.25 (m, 4 H), 5.45 (d, *J* = 5 Hz, 1 H), 4.18 (m, 1 H), 3.56 (t, *J* = 8 Hz, 1 H), 1.05 (s, 3 H), 0.88 (s, 9 H), 0.72 (s, 3 H); mass spectrum, *m/e* (relative intensity) 387 (M$^+$ – *o*-NO$_2$PhSe, 28). Anal. Calcd for C$_{31}$H$_{47}$NO$_3$SeSi: C, 63.24; H, 8.05; N, 2.38. Found: C, 63.55; H, 8.31; N, 2.37.

17β-Hydroxy-3α-[(4-nitrophenyl)seleno]-4-androstene *tert*-Butyldimethylsilyl Ether (4b). The title compound was prepared in 65% yield from sterol **3**, selenocyanate **1b**, and tri-*n*-butylphosphine by the same procedure as **4a**, as a pale yellow solid: mp 143–145 °C (from hexane); $[\alpha]_D$ +108°; IR (Nujol) 1595, 1515 cm^{-1}; ^{1}H NMR 8.08 (d, *J* = 9 Hz, 2 H), 7.57 (d, *J* = 9 Hz, 2 H), 5.49 (d, *J* = 5 Hz, 1 H), 4.22 (m, 1 H), 3.56 (t, *J* = 8 Hz, 1 H), 1.03 (s, 3 H), 0.89 (s, 9 H), 0.72 (s, 3 H); mass spectrum, *m/e* (relative intensity) 387 (M$^+$ – *p*-NO$_2$PhSe, 28). Anal. Calcd for C$_{31}$H$_{47}$NO$_3$SeSi: C, 63.24; H, 8.05; N, 2.38. Found: C, 63.01; H, 8.17; N, 2.18.

5α,17β-Dihydroxy-3-androstene 17-*tert*-Butyldimethylsilyl Ether (5). Selenide **4a** (230 mg, 0.39 mmol) was dissolved in 5 mL of THF at 0 °C. *m*-Chloroperbenzoic acid (0.2 g of ca. 85% purity, 1 mmol) was added and the yellow color rapidly faded. After 10 min the solution was diluted with ether, washed 3 times with aqueous K$_2$CO$_3$, dried over anhydrous MgSO$_4$, and purified by preparative TLC (15% ethyl acetate–hexane) to afford 75 mg (47%) of the title compound; R_f 0.51, mp 96–97 °C (from methanol); $[\alpha]_D$ –26°; IR (CHCl$_3$) 3600, 3470 cm^{-1}; ^{1}H NMR 5.73 (dt, *J* = 10, 3 Hz, 1 H), 5.60 (dt, *J* = 10, 2 Hz, 1 H), 3.56 (t, *J* = 8 Hz, 1 H), 0.91 (s, 3 H), 0.87 (s, 9 H), 0.70 (s, 3 H); mass spectrum, *m/e* (relative intensity) 404 (M$^+$, <1), 386 (M$^+$ – H$_2$O, 6). Anal. Calcd for C$_{25}$H$_{44}$O$_2$Si: C, 74.19; H, 10.96. Found: C, 73.85; H, 11.17.

(10) It is interesting to note that geraniol, a primary allylic alcohol, affords the corresponding selenide in 82% yield under similar conditions.[3] This suggests that steric factors are important in determining the course of the reaction.

(11) The use of other oxidants such as hydrogen peroxide and ozone under various conditions failed to provide better yields of **5**.

(12) The stereochemistry of **4a,b** is assumed to be 3α since the conversion of alcohols to selenides with PhSeCN-*n*-Bu$_3$P is known[13] to proceed with inversion of configuration. This in turn results in the 5α-hydroxy stereoisomer **5** upon [2,3]-sigmatropic rearrangement.

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Two-Bond Cleavage in the Oxidation of Acyclic Tertiary 1,4-Diols with *N*-Iodosuccinimide
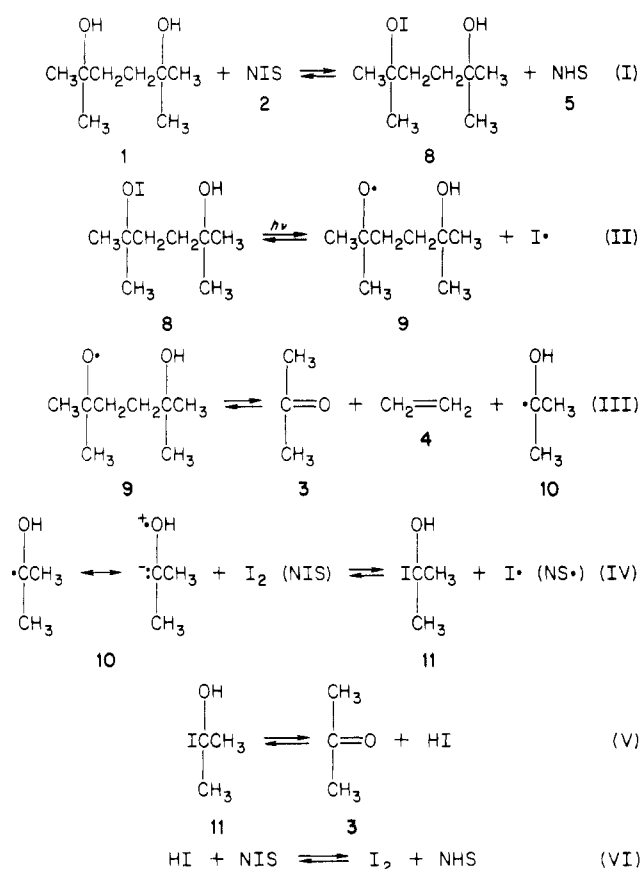
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Recently, we found that 1,2-diols[1] and α-hydroxy carboxylic acids[2] were easily cleaved with *N*-iodosuccinimide

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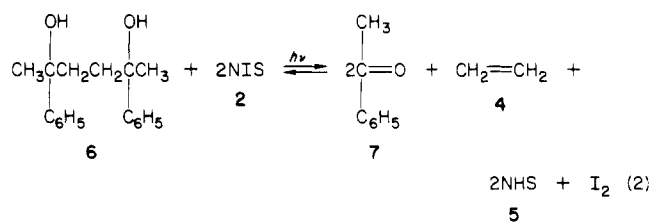
Scheme I

(NIS). Here we describe the novel two-bond cleavage[3] of two acyclic tertiary 1,4-diols with NIS and irradiation. For example, when 2,5-dimethyl-2,5-hexanediol (1) in benzene was treated with NIS (2) and light, acetone (3) was produced in 96–99% yields (assuming 2 mol of acetone for each mol of 1,4-diol). Ethene (4) was obtained in 80–85% yields in separate reactions performed in diphenyl ether with irradiation using a vacuum system. Iodine and succinimide (5) were found in sufficient yields to support the reaction stoichiometry given by eq 1.
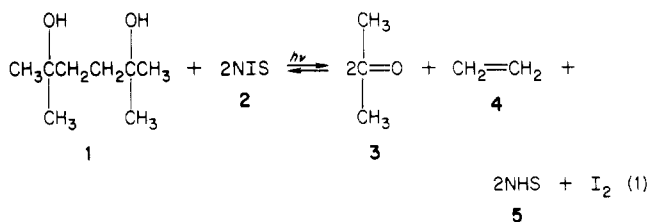
Also, the reaction of 2,5-diphenyl-2,5-hexanediol (6) in benzene with NIS produced acetophenone (7) and ethene (4) as the only cleavage products, in yields of 86–100% and 55–65%, respectively (eq 2). A postulated pathway for

Table I

run	NIS (mmol)	diol (mmol)	% yield[a] (acetone)	time
		Oxidation of 2,5-Dimethyl-2,5-hexanediol with NIS		
1	1.204	0.595	99	1 h 25 min
2	1.240	0.574	99	1 h 10 min
3	0.804	2.045	85	1 h 30 min
4	1.147	0.561	99	1 h
5	0.307	0.092	96	1 h 20 min

run	NIS (mmol)	diol (mmol)	% yield[a] (acetophenone)	time
		Oxidation of 2,5-Diphenyl-2,5-hexanediol with NIS		
1	1.196	0.538	100	6 h
2	1.209	0.538	96	6 h
3	1.164	0.563	91	5 h
4	1.209	0.630	101	6 h
5	1.444	0.644	86	5 h
6[b]	1.302	0.598	3	23 h

[a] Assuming 2 mol of ketone product for each mol of diol. [b] This reaction was done in the dark with ambient temperatures.

the proposed two-bond cleavage of the ditertiary 1,4-diol 1 is given in Scheme I. There is much evidence[4,5] for the formation of alkyl hypoiodites from the reaction of alcohols and N-iodosuccinimide and the subsequent decomposition of the alkyl hypoiodites to produce alkoxy radicals. The two-bond cleavage occurs after the formation of the alkoxy radical 9. Production of the doubly bonded acetone and ethene molecules along with the resonance-stabilized radical 10 permits the easy cleavage of the two carbon–carbon bonds in step III. A second molecule of acetone is formed when the iodohydrin 11 eliminates hydrogen iodide. The hydrogen iodide produced in step V rapidly reacts with NIS to give iodine and succinimide. A similar two-bond cleavage[6] occurs when the cyclic peroxide 12 is irradiated or heated. The dialkoxy radical 13 is postulated as an intermediate.
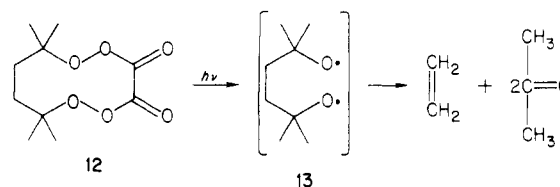

Table I outlines several reactions involving the oxidation of 2,5-dimethyl-2,5-hexanediol and 2,5-diphenyl-2,5-hexanediol with NIS in benzene with irradiation. Reactions performed in the dark give only small percentages of carbonyl products indicating the radical nature of the reaction.

Experimental Section

Analyses were performed on Perkin-Elmer 810VPC and Varian Aerograph Model 700VPC spectrometers. Liquid chemicals used in the reaction mixtures and standard VPC mixtures all had greater than 99.5% purity as determined on a gas chromatograph. The benzene solvent was spectrscopically pure and was used without further purification. VPC analyses were done on 6 ft × 0.25 in. copper columns of 10% SE-30, 7% SE-30 and 3% Carbowax 20-M, and 10% Carbowax 20-M. The 2,5-dimethyl-2,5-hexanediol was used as purchased. The 2,5-diphenyl-2,5-hexa-

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nediol[7] was synthesized from 2,5-hexanedione by using phenylmagnesium bromide. The NIS was determined to have 98.0–99.5% active iodine and was used as purchased. Irradiation of reaction mixtures was effected with GE Projector Spot 150-W, 130-V tungsten lamps.

Oxidation of 2,5-Dimethyl-2,5-hexanediol with NIS and Irradiation. A 5-mL solution of 0.082 g (0.561 mmol) of 2,5-dimethyl-2,5-hexanediol in benzene was added to 0.258 g (1.147 mmol) of NIS contained in a 10-mL flask. A condenser with a drying tube was attached to the flask. The mixture was stirred and irradiated. Reaction time and percentage yields of acetone (assuming 2 mol of acetone for each mol of diol) were as follows: 10 min (15%), 15 min (49%), 35 min (96%), 55 min (99%), 70 min (99%). Elemental iodine determination gave 0.543 mmol (98%). Succinimide was recovered in 88% yield.

Oxidation of 2,5-Diphenyl-2,5-hexanediol with NIS and Irradiation. A 5-mL solution of 0.152 g (0.538 mmol) of 2,5-diphenyl-2,5-hexanediol in benzene was added to 0.269 g (1.196 mmol) of NIS in a 10-mL flask. A condenser with a drying tube was attached to the flask. The mixture was stirred and irradiated. Reaction times and percentage yields of acetophenone (assuming 2 mol of acetophenone for each mol of diol) were as follows: 1 h 15 min (39%), 2 h (64%), 3 h (83%), 4 h (92%), 6 h (100%), 7 h (99%). Succinimide was recovered in 99% yield (1.070 mmol) and elemental iodine was found at 94% (0.506 mmol). Crude acetophenone was recovered, weight 0.131 g (1.090 mmol, 101%). Preparation of a 2,4-dinitrophenylhydrazone derivative of the acetophenone gave 0.255 g (0.849 mmol, 78%) of product (mp 230–235 °C; lit.[8] mp 238–240 °C).

Oxidation of 2,5-Diphenyl-2,5-hexanediol with NIS in the Dark at Ambient Temperatures. A 5-mL solution of 0.164 g (0.598 mmol) of 2,5-diphenyl-2,5-hexanediol in benzene was added to 0.293 g (1.302 mmol) of NIS contained in a 10-mL flask. The flask was covered with aluminum foil in a dark fume hood. The mixture was stirred. After 23 h of reaction time acetophenone was found in 3% yield as determined by VPC.

Collection of Ethene in the Oxidation of 2,5-Dimethyl-2,5-hexanediol with NIS and Irradiation. The diol (2,5-dimethyl-2,5-hexanediol, 4.185 g, 28.619 mmol) and 30 mL of diphenyl ether were placed in a 50 mL, round-bottomed flask. NIS (6.352 g, 28.232 mmol) was weighed in another flask. Both flasks were placed on a vacuum rack and the system was evacuated. The chemicals were mixed, stirred, and irradiated for 1 h 22 min. Analysis gave an 80% yield of ethene with a molecular weight of 29.0 g/mol. Mass spectrometer analysis of the gas collected indicated 82–83% ethene and 17–18% acetone.

Collection of Ethene in the Oxidation of 2,5-Diphenyl-2,5-hexanediol with NIS and Irradiation. The diol (2,5-diphenyl-2,5-hexanediol, 7.336 g, 32.61 mmol) and 75-mL of diphenyl ether were placed in a 100-mL, round-bottomed flask. NIS (7.336 g, 32.61 mmol) was weighed in another flask. Both flasks were placed on a vacuum rack and the system was evacuated. The chemicals were mixed, stirred, and irradiated for 1 h 20 min. Analyses gave a 57% yield of ethene with a molecular weight of 29.2 g/mol. Mass spectrometer analysis of the ethene indicated a purity of 97–99%.

Iodine Determination. The iodine produced in the oxidation of the 1,4-diols with NIS was determined by adding reaction mixtures to 25 mL of a 1:1 mixture of acetic acid and water. Several drops of concentrated HCl were added, and the iodine was titrated with a standardized solution of thiosulfate. The iodine percentage yield was determined by assuming that 1 mol of iodine is produced from 2 mol of NIS.

Succinimide Determination. Succinimide was recovered from the completed reactions by pouring the reaction mixture into diethyl ether and extracting the ether solution with water. The combined water extracts were washed with fresh ether, and the water solution was evaporated.

On the Stereospecifity of Intrinsic ^{2}H/^{1}H NMR Isotope Effects on ^{13}C Chemical Shifts in Cyclohexanes

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The structural dependence of intrinsic ^{2}H/^{1}H NMR isotope effects on ^{13}C chemical shifts, $^n\Delta(^{13}C)$, where n is the number of intervening bonds, in organic compounds is of current interest[1] because the determination of these parameters profits from the increasing number of high-field NMR instruments. Another reason is the use of $^n\Delta(^{13}C)$ values for assignment purposes in ^{13}C NMR spectra[2] and in this context stereospecific isotope effects are of practical importance. For adamantane, we found $^n\Delta_{anti} > {^n\Delta_{syn}}$ for $n = 3$ and 4.[3] More recently, Jurlina and Stothers[4] have shown that in bicyclic systems $^3\Delta$ has its maximum value for an eclipsed arrangement between the respective C–D and C–^{13}C bonds. The authors concluded that these shifts arise from spacial proximity and supporting evidence for such a mechanism was seen in the results of Anet and Dekmezian,[5] who had found large ^{2}H/^{1}H isotope effects on ^{1}H chemical shifts in situations where van der Waals interactions are involved. However, ^{2}H/^{1}H isotope effects on ^{19}F chemical shifts violate this principle, displaying maxima for maximum distances,[6] and further studies of the relationship between stereochemistry and NMR isotope effects are indicated.

Results and Discussion

In the present note we report data on the geometrical dependence of $^n\Delta(^{13}C)$ values in cyclohexane derivatives. From low-temperature measurements for cyclohexane-d_1[7] (7), we were able to measure $^1\Delta_{ax}$ and $^1\Delta_{eq}$ separately, but long-range isotope effects could not be resolved. Only the corresponding ^{1}H/^{2}H data for cyclohexane-d_{11}[8] (8) are available. Therefore, we decided to study derivatives substituted in the 4-position by a *tert*-butyl group, known to stabilize the conformation with the alkyl group in the

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