aromatic); MS m/e calculated for $C_{12}H_8N_2F_2$ 218.0653, observed 218.0660, difference 0.0007. Anal. Calcd for $C_{12}H_8N_2F_2$: C, 66.03; H, 3.69; N, 12.84; F, 17.42. Found: C, 66.00; H, 3.85; N, 12.73; F, 17.73.

4,4'-Difluoroazobenzene (18c): 30%; mp 98–99 °C; ^{1}H NMR (acetone-d_6) δ 7.96 (q, 4 H, aromatic), 7.34 (t, 4 H, aromatic); ^{19}F NMR (acetone, ppm) −109.05 (s, 2 F, aromatic); MS m/e calculated for $C_{12}H_8N_2F_2$ 218.0653, observed 218.0662, difference 0.0009. Anal. Calcd for $C_{12}H_8N_2F_2$: C, 66.03; H, 3.69; N, 12.84; F, 17.42. Found: C, 65.98; H, 3.66; N, 12.90; F, 17.27.

2,2',3,3'-Tetrafluoroazobenzene (18d): 20%; mp 140–142 °C; ^{1}H NMR (acetone-d_6) δ 7.64–7.53 (m, 4 H, aromatic), 7.42–7.32 (m, 2 H, aromatic); ^{19}F NMR (acetone, ppm) −148.68 (d, J = 20.7 Hz, 2 F, aromatic), −137.30 (d, J = 20.7 Hz, 2 F, aromatic); MS m/e calculated for $C_{12}H_6N_2F_4$ 254.0466, observed 254.0476, difference 0.001. Anal. Calcd for $C_{12}H_6N_2F_4$: C, 56.68; H, 2.38; N, 11.02; F, 29.91. Found: C, 56.68; H, 2.42; N, 10.80; F, 29.89.

2,2',4,4'-Tetrafluoroazobenzene (18e): 20%; mp 115–117 °C; ^{1}H NMR (acetone-d_6) δ 7.54–7.43 (m, 6 H, aromatic); ^{19}F NMR (acetone, ppm) −127.69 (d, J = 17.5 Hz, 2 F, aromatic), −116.51 (d, J = 17.5 Hz, 2 F, aromatic); MS m/e calculated for $C_{12}H_6N_2F_4$ 254.0466, observed 254.0473, difference 0.0007. Anal. Calcd for $C_{12}H_6N_2F_4$: C, 56.68; H, 2.38; N, 11.02; F, 29.91. Found: C, 56.97; H, 2.56; N, 10.71; F, 29.71.

2,2',5,5'-Tetrafluoroazobenzene (18f): 39%; mp 138–140 °C; ^{1}H NMR (acetone-d_6) δ 8.0–7.82 (m, 2 H, aromatic), 7.36–7.25 (m, 2 H, aromatic), 7.21–7.12 (m, 2 H, aromatic), ^{19}F NMR (acetone, ppm) −118.81 (d, J = 10.1 Hz, 2 F, aromatic), −103.81 (d, J = 10.1 Hz, 2 F, aromatic); MS m/e calculated for $C_{12}H_6N_2F_4$ 254.0466, observed 254.0477, difference 0.0011. Anal. Calcd for $C_{12}H_6N_2F_4$: C, 56.58; H, 2.38; N, 11.02; F, 29.91. Found: C, 57.04; H, 2.56; N, 10.64; F, 29.76.

3,3',4,4'-Tetrafluoroazobenzene (18g): 39%; mp 65–67 °C; ^{1}H NMR (acetone-d_6) δ 7.89–7.76 (m, 4 H, aromatic), 7.56 (q, 2 H, aromatic); ^{19}F NMR (acetone, ppm) −135.75 (d, J = 22.2 Hz, 2 F, aromatic), −132.84 (d, J = 22.2 Hz, 2 F, aromatic), MS m/e calculated for $C_{12}H_6N_2F_4$ 254.0466, observed 254.0472, difference 0.0006. Anal. Calcd for $C_{12}H_6N_2F_4$: C, 56.68; H, 2.38; N, 11.02; F, 29.91. Found: C, 56.60; H, 2.32; N, 10.97; F, 29.87.

EPR Experiments. All EPR measurements were obtained on a Varian E-112 X-Band Century Series EPR spectrometer equipped with a modified microwave cavity which admitted light through a series of louvres on one side. Samples were sealed in 4-mm suprasil quartz tubes under vacuum after three freeze–pump–thaw cycles to remove oxygen. Samples were irradiated with filtered light (λ > 295 nm) from a Schoeffel Universal 1000-W Hg–Xe arc lamp. Triplet nitrene spectra were recorded at 10 mW of microwave power while triplet radical pair spectra were recorded at 1 mW of microwave power.

Product Studies. Samples were prepared by putting 0.5 mL of the solution of interest in 6-mm Pyrex tubes which were prewashed with ammonium hydroxide and oven-dried. The solutions were then degassed using three freeze–pump–thaw cycles and then sealed under vacuum. Samples were photolyzed with 350-nm light using Southern New England RPR 3500-Å lamps. The product mixtures were analyzed by gas chromatography. The yields and identities of the products were determined by co-injection of authentic samples and by GC–mass spectroscopy.

Acknowledgment. Support of this work by the NIH (GM 34823-04) is gratefully acknowledged.

Registry No. **12a**, 3296-04-6; **12b**, 3296-03-5; **12c**, 3296-02-4; **12d**, 123330-49-4; **12e**, 91229-55-9; **12f**, 123330-50-7; **12g**, 123330-51-8; **12h**, 102284-85-5; **12i**, 1423-15-0; **15a**, 123330-52-9; **15b**, 123330-53-0; **15c**, 370-77-4; **15d**, 123330-54-1; **15e**, 123330-55-2; **15f**, 123330-56-3; **15g**, 123330-57-4; **15h**, 115910-96-8; **15i**, 36375-86-7; **16h**, 123330-60-9; **16i**, 123330-61-0; **17a**, 348-54-9; **17b**, 372-19-0; **17c**, 371-40-4; **17d**, 4519-40-8; **17e**, 367-25-9; **17f**, 367-30-6; **17g**, 3863-11-4; **17h**, 5509-65-9; **17i**, 771-60-8; **18a**, 401-44-5; **18b**, 331-21-5; **18c**, 332-07-0; **18d**, 123330-58-5; **18e**, 326-17-0; **18f**, 325-84-8; **18g**, 123330-59-6; **18h**, 42808-62-8; **18i**, 2285-06-5; imidogen, 13774-92-0; hydrogen, 1333-74-0; toluene, 108-88-3; benzyl radical, 2154-56-5; 2,4-difluorophenylamanyl radical, 51460-59-4.

Photoinduced Molecular Transformations. 104.[1] Pathways of the Photorearrangements of Five-Membered Cyclic Steroidal α-Nitro Ketones to *N*-Hydroxy Cyclic Imides, Cyclic Hydroxamic Acid, and Cyclic Imide

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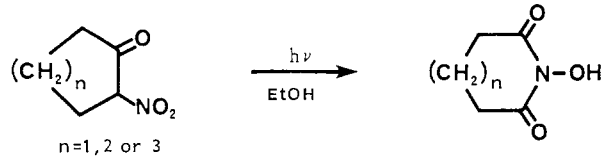
We report on the photolysis of three five-membered and two seven-membered cyclic α-nitro ketones with a steroidal skeleton. The photoreaction in ethanol of two five-membered cyclic steroidal α-nitro ketones that exist largely as the enol forms in ethanol gave the corresponding cyclic *N*-hydroxy imides (57–61%) which arose from photorearrangements. A similar photolysis of a five-membered cyclic steroidal α-nitro ketone that exists exclusively as the keto form in ethanol led to an unprecedented formation of the corresponding cyclic imide (12%) instead of a cyclic *N*-hydroxy imide. The corresponding cyclic α-hydroxyimino ketones (5–18%) are accompanying products in all three photoreactions, while a cyclic hydroxamic acid (11%) is the accompanying product of the cyclic *N*-hydroxy imide in one of the photoreactions. In contrast, photoreactions of the two seven-membered α-nitro steroidal ketones in ethanol gave only the corresponding α-hydroxyimino ketones. The photochemical nitrogen insertions in the photoreactions of cyclic steroidal α-nitro ketones thus depend on their ring size. On the basis of the independent photolysis of 16α- and 16β-hydroxy-5α-androstan-17-one nitrites, as well as quenching experiments with oxygen, we suggest the formation of cyclic hydroxamic acid and cyclic *N*-hydroxy imides is from the enols of the five-membered cyclic steroidal α-nitro ketones. The cyclic imide is formed when 5α-androstane-15,16-dione monooxime is irradiated in ethanol. This first example of a photo-Beckmann rearrangement of a cyclic α-diketone monooxime established the genesis of the cyclic imide.

The photochemistry of α-nitro carbonyl compounds as bichromophoric molecules is of considerable interest since the diverse photochemical behavior of nitroalkanes and nitroolefins has become reasonably well understood.[2]

0022-3263/89/1954-5945$01.50/0

Scheme I



There had been only a brief report on the photochemistry of α-nitrocarbonyl compounds before we initiated our systematic exploration using steroids as the substrates;[3-5] Reid and Tucker reported[6] that the irradiation of 2-nitrocyclohexanone, 2-nitrocycloheptanone, and α-nitrocamphor in ethanol gave the corresponding cyclic *N*-hydroxy imides and α-hydroxyimino ketones (Scheme I).

In contrast to their results, obtained on the *monocyclic* six-membered α-nitro ketones,[6] our study[3] has shown that none of the cyclic *N*-hydroxy imides are formed when fused cyclic 6-membered α-nitro ketones, which are partly or wholly enolized, are irradiated in ethanol. Our study disclosed that three classes of products (the corresponding α-diketones, α-diketone monooxime, and the rearranged α-diketone monooxime) are formed in these photolysis processes.[3] We also found that when six-membered cyclic steroidal α-nitro ketones, which exist exclusively as their keto forms, are irradiated in ethanol, the corresponding α-diketone monooximes are still the product, but without the accompanying formation of α-diketones.[3]

The most typical results of the photoreaction of six-membered cyclic steroidal α-nitro ketone together with the pathways to the products are outlined in Scheme II; the photoreaction of 3-nitro-5α-cholestan-2-one (**1**), which is highly enolized in ethanol, gives 5α-cholestane-2,3-dione (**2a** and **2b**) and 5α-cholestane-2,3-dione 3-oxime (**3**). As outlined, the diosphenols **2a** and **2b** are formed from the n,π* excited enol **1a** through oxaziridine intermediate A and nitrite B, whereas the dione monooxime **3** is formed from the n,π* excited carbonyl form **1b** through intermediates E and F.[3]

We now wish to report on the results of investigations into the photolysis of three five-membered cyclic steroidal α-nitro ketones and two seven-membered cyclic steroidal α-nitro ketones in ethanol.

We have found that (in contrast to the results on the above-mentioned six-membered ring) the formation of nitrogen heterocycles, arising from the insertion of a nitrogen atom, is the major photoreaction of the five-membered cyclic steroidal α-nitro ketones. We also found that the results on seven-membered cyclic steroidal α-nitro ketones are nearly parallel with those on the above-mentioned six-membered ring. These results, which may shed further light on the photochemistry of these classes of nitro ketones, are described in this paper.

Results

Preparations and Structures of the Cyclic α-Nitro Ketones. The three new five-membered cyclic α-nitro ketones [3α-nitro-*A*-nor-5α-cholestan-2-one (**5**), 15α-nitro-5α-androstan-16-one (**9**), and 16-nitro-5α-androstan-17-one (**14**)] used as substrates were prepared by mononitration of the corresponding steroidal ketones with an alkyl nitrate and a base by the modified standard method.[4,7,8]

Table I. Spectral Data of Five- and Seven-Membered Cyclic α-Nitro Ketones

	λ_{max} nm (ε)		
	EtOH	hexane	EtOH–NaOEt
5	336 (1360)	270–330 (ca. 80)	337 (9400)
	231 (2200)	226 (2200)	227 (3700)
9	280–340 (ca. 100)	270–330 (ca. 100)	336 (50)
	239 (1900)	228 (2100)	235.5 (11 000)
14	329 (6100)	300 (460)	330 (14 700)
	230 (2800)	231 (2400)	226.5 (3800)
			339 (1100)
21	338 (90)	284 (100)	234 (5900)
			335 (10 000)
22	332 (1200)	321 (760)	232 (2800)

Thus, the treatment of *A*-nor-5α-cholestan-2-one[9] and 5α-androstan-16-one[10] in THF with propyl nitrate and potassium *tert*-butoxide resulted in a regioselective introduction of a nitro group to C-3 and to C-15 and gave 3α-nitro ketones **5** (77%) and **9** (78%), respectively. No regioisomers were formed in these nitrations. Ketone **14** was similarly prepared in 79% yield by nitration of 5α-androstan-17-one (**13**).

On the other hand, the two seven-membered α-nitro ketones (4aα-nitro-*A*-homo-5α-cholestan-4-one (**21**) and 3-nitro-*A*-homo-5α-cholestan-4-one (**22**)) were prepared through nitration of the isomeric enol acetates **19**[11] and **20**, derived from *A*-homo-5α-cholestan-4-one (**18**).[12] The reaction of ketone **18** with isopropenyl acetate in the presence of *p*-toluenesulfonic acid gave the reported enol acetate **19**[11] together with its unreported isomer **20** in 50 and 36% yields. Nitrations of the enol acetates **19** and **20** with ammonium nitrate and trifluoroacetic anhydride[13] in chloroform gave α-nitro ketones **21** and **22** in 86 and 73% yields. The IR spectra of these nitro ketones in Nujol exhibited no absorption bands assignable to the conjugated nitro group, indicating that all of the α-nitro ketones exist as their keto form in the mulls. On the other hand, the UV spectra of these α-nitro ketones in ethanol (Table I) indicated that some are strongly enolized in the solvent. The aliphatic nitro group exhibits two absorption maxima, one in the 210-nm region (π → π* transition) and another in the 270–280-nm region with a low intensity (n → π* transition).[2,14-17]

The α,β-unsaturated nitro group, on the other hand, appeared in the 220–250-nm region with high intensity (π → π* transition). As reported in our previous paper,[3]

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(2) For reviews see: (a) Morrison H. A. in *The Chemistry of the Nitro and Nitroso groups, Part 1*; Feuer, H., Ed.; Interscience: New York, 1969; pp 167–168; (b) Chow, Y. L. In *The Chemistry of Amino, Nitroso, Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; pp 181–290.
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(8) For a recent review on preparation of cyclic α-nitro ketones, see: Fischer, R. H.; Weitz, H. M. *Synthesis* **1980**, 261.
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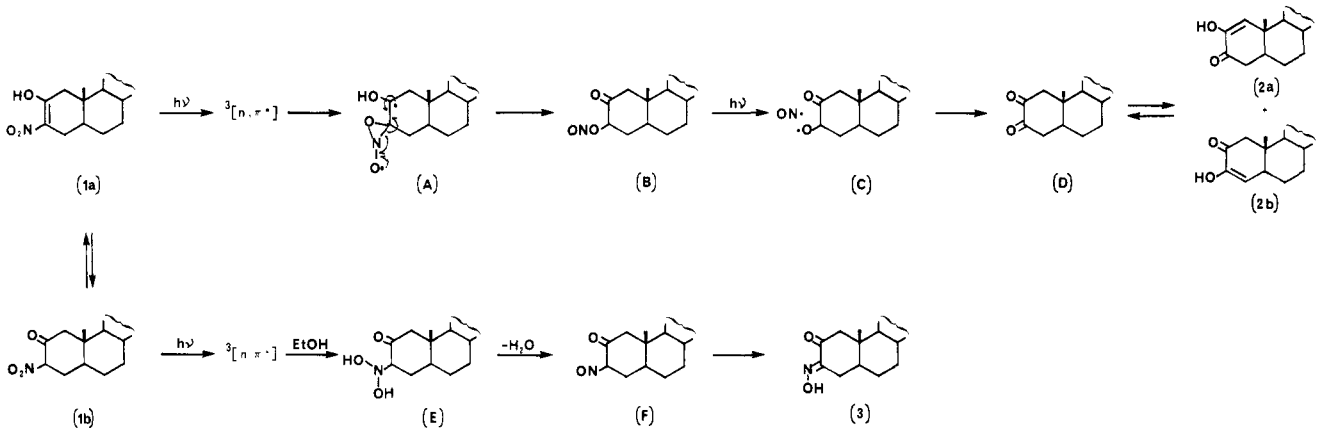
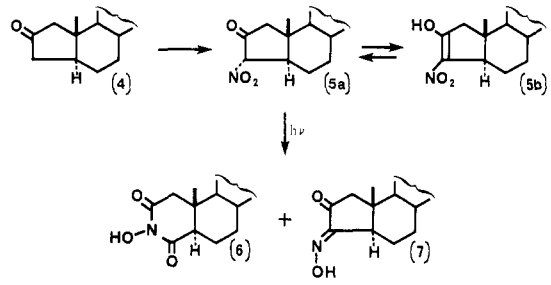
(13) Dampawan, P.; Zajac, Jr. W. W. *Synthesis* **1983**, 545.
(14) For a review of early literatures see: Gillam, A. E.; Stern, E. S.; Jones, E. R. H. *An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry*, 2nd ed.; Edward Arnold: London, 1958; pp 65–66.
(15) Nagakura, S. *Mol. Phys.* **1960**, *3*, 152.
(16) Jaffe, H. H.; Orchin, M. *Theory and Applications of Ultraviolet Spectroscopy*; Wiley: New York, 1962; p 182.
(17) For reviews see: Rao, C. N. R. In *The Chemistry of The Nitro and Nitroso groups, Part 1*; Feuer, H., Ed.; Interscience: New York, 1969; pp 92–106. (b) Morrison, H. A. *Ibid.*, pp 167–168.

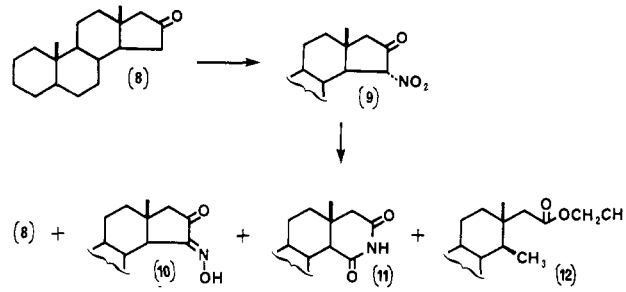
Scheme II



Scheme III



Scheme IV

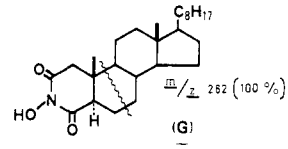


2-nitro-5α-cholestan-3-one, which exists as an enol form in ethanol, exhibited an intense absorption maximum at 343 nm. We assigned this absorption to the $\pi \rightarrow \pi^*$ transition of the conjugated nitro group. The displacement of the absorption maximum to a longer wavelength, when compared with the absorption maxima of the corresponding nitroolefins, was attributed to the effects of the additional hydroxyl group in the chromophore. Examination of the UV data in Table I indicates that nitro ketones **5**, **14**, and **22** are partly enolized in ethanol, as shown by the presence of intense absorption maxima at 239–336 nm, while nitro ketones **9** and **21** exist as their keto form in ethanol.

The ^{1}H NMR spectrum of nitro ketone **14** in CD_3OD exhibited two singlets at δ 0.86 and 0.98, assignable to 19-H and 18-H of nitro ketone **14a**, and two singlets at δ 0.87 and 1.1, assignable to 19-H and 18-H of the enol **14b**. The spectrum also exhibited a doublet of a doublet at δ 5.17 (J = 10 and 8.5 Hz) assignable to 16α-H of 16β-nitro isomer **14c** and a doublet of a doublet assignable to 16β-H of 16α-nitro isomer **14a**. The spectral results clearly show that the two isomeric keto forms and the enol are in equilibrium. On the basis of the integrals of each of the tautomers in CD_3OD (0.35 mL)–$CDCl_3$ (0.1 mL), the ratio of three tautomers (**14a–c**) was estimated to be 53:43:4. It is interesting to note that a pure 16α-nitro isomer **14a** crystallizes from the ethanolic solution.

Photochemistry of the α-Nitro Cyclic Ketones. (a) 3α-Nitro-*A*-nor-5α-cholestan-2-one (5, Scheme III). Photolysis of the nitro ketone **5** in ethanol with a Hanovia 450-W high-pressure Hg arc through a Pyrex filter for 15 h in an atmosphere of nitrogen gave a product mixture from which two crystalline products **6** and **7** were isolated by column chromatography (Sephadex LH 20). The elemental analysis and the mass spectrometry indicated that product **6** (61%) had the molecular formula $C_{26}H_{43}NO_3$. The IR spectrum exhibited a series of bands assignable to the *N*-hydroxy imide function. The ^{1}H NMR spectrum of **6** (13.5%) exhibited a doublet at δ 2.91 (J = 16.85 Hz).

These results suggest that the structure of **6** is 3-hydroxy-3-aza-5α-cholestane-2,4-dione (**6**). The EI mass spectrum exhibited an ion at m/z 262 as the base peak. This ion almost certainly arose from a cleavage across ring B, as indicated in formula G. The structure of the more



polar product **7**, $C_{26}H_{43}NO_3$, was deduced to be *A*-nor-5α-cholestane-2,3-dione 3-oxime (**7**) by means of its IR, ^{1}H NMR, and EI mass spectra; this was confirmed by a direct comparison with a specimen prepared by a regiospecific nitrosation of *A*-nor-5α-cholestan-2-one.

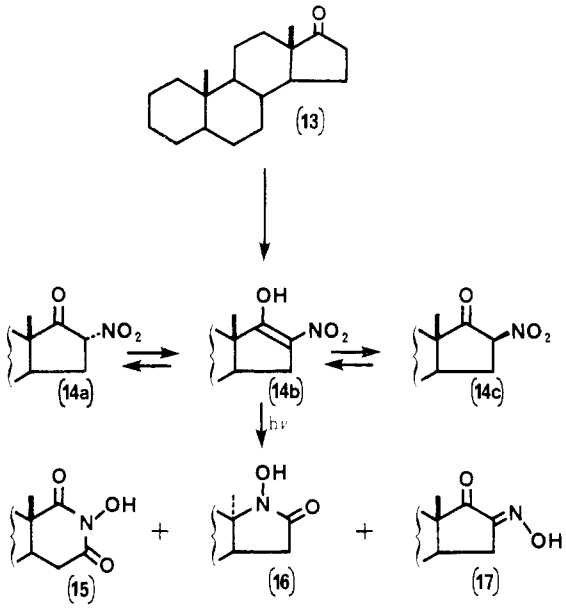
The photolysis of α-nitro ketone **5** in ethanol saturated with oxygen gave the *N*-hydroxy cyclic imide **6** exclusively (33% yield); none of the oxime **7** was obtained.

(b) 15α-Nitro-5α-androstan-16-one (9, Scheme IV). Nitro ketone **9** exists as the keto form in ethanol. It is, therefore, of considerable interest to compare the products of the photolyses with those of the photolysis of partly or wholly enolized nitro ketones, such as **5** and **14**.

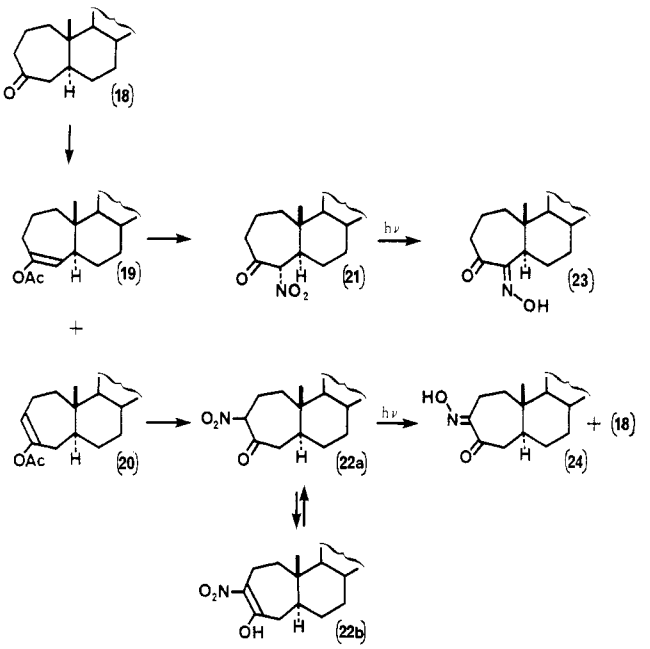
Irradiation of nitro ketone **9** under the conditions described above gave a product mixture from which four products were isolated by preparative TLC. The most polar products **10** (5%) had the molecular formula $C_{19}H_{29}NO_2$ (high-resolution mass spectrometry). The structure was deduced to be 5α-androstane-15,16-dione 15-oxime (**10**) on the basis of the spectroscopic results (see Experimental Section) and its independent synthesis.

The next polar product **11** (12.3%) had the molecular formula $C_{19}H_{29}NO_2$ (high-resolution mass spectrometry) and exhibited a series of bands assignable to a cyclic imide group (3212, 3088, 1720, and 1693 cm^{-1}). The mass spectrum exhibited a molecular ion at m/z 303 as the base peak. The ^{1}H NMR spectrum exhibited a doublet at δ 2.37

Scheme V



Scheme VI



(J = 17.4 Hz) and a doublet of a doublet at δ 2.48 (J = 17.58 and 1.1 Hz), assignable to a methylene group adjacent to a carbonyl. It also exhibited a doublet at δ 2.00 (J = 10.62 Hz) assignable to a methine proton adjacent to an imide carbonyl. These spectral results indicated that product **11** is 16-aza-*D*-homo-5α-androstane-15,17-dione (**11**). The third polar product (7.7%) was 5α-androstan-16-one (**8**). High-resolution mass spectrometry of the least polar product **12** (11%) indicated a molecular formula of $C_{21}H_{36}NO_2$. On the basis of IR, ^{1}H NMR, and mass spectra (see Experimental Section) the structure was established to be 15,16-seco-5α-androstan-16-oic acid ethyl ester.

(c) Photolysis of 16-Nitro-5α-androstan-17-one (14) in the Presence or Absence of Oxygen (Scheme V). Irradiation of an equilibrium mixture of 16-nitro-5α-androstan-17-one (**11a**:**11b**:**11c** = 53:43:4) in ethanol for 8 h with a Hanovia 450-W high-pressure Hg arc through a Pyrex filter in a nitrogen atmosphere gave a product mixture from which three crystalline products, **15**–**17**, were isolated by preparative TLC. The elemental analysis and the mass spectrometry of the major and most polar product **15** (56.8%) indicated that it had the molecular formula $C_{19}H_{29}NO_2$. The IR spectrum exhibited two signals at δ 2.41 (dd, J = 17.95 and 13.9 Hz) and 2.95 (dd, J = 17.95 and 4.4 Hz) assignable to a methylene proton adjacent to the imide function. These spectral results indicated that product **15** is 17-hydroxy-17-aza-*D*-homo-5α-androstane-16,18-dione (**15**). The next most polar product **16** (11.4%) was identified to be 17-hydroxy-17-aza-5α,13α-androstan-16-one (**16**)[18] by spectroscopy and by a direct comparison with an authentic specimen obtained by the photolysis of *D*-nor-5α-androstan-16-ol nitrite.[18] The least polar product **17** (18.4%) had the molecular formula $C_{19}H_{29}NO_2$ (elemental analysis and mass spectrometry). The structure was deduced to be the reported 5α-androstane-16,17-dione 16-oxime[10] on the basis of the spectra and a direct comparison with an authentic specimen.

When the photolysis of α-nitro ketone **14** was conducted in ethanol saturated with oxygen for 8 h, none of the products **16** and **17** was produced and only cyclic *N*-hydroxy imide **15** was obtained in 42.7% yield.

(d) Photolysis of 4aα-Nitro-*A*-homo-5α-cholestan-4-one (21) and 3-Nitro-*A*-homo-5α-cholestan-4-one (22, Scheme VI). The photolysis of an ethanolic solution of seven-membered cyclic α-nitro ketone **21**, which exists as a keto form in ethanol, under the above conditions for 1.5 h gave the parent ketone **18** (6.7%) and product **23** (27.6%). The structure of product **23**, $C_{28}H_{47}NO_2$, was deduced to be *A*-homo-5α-cholestane-4,4a-dione 4a-oxime (**23**, see Experimental Section). Its attempted synthesis by nitrosation of the parent ketone **18** led to the formation of two inseparable regioisomeric α-hydroxyimino ketones.

The photolysis for 1.5 h of an ethanolic solution of an isomer **22** that was an equilibrium mixture of the ketone **22a** and the enol **22b** resulted in a 32% coversion of the nitro ketone and gave product **24**. Spectroscopic analysis indicated that its structure was *A*-homo-5α-cholestan-3,4-dione 3-oxime (**24**), an isomer of the hydroxyimino ketone **23**. No product arising from the insertion of a nitrogen atom to the ring was formed.

(e) Photolysis of 16α- and 16β-Hydroxy-5α-androstan-17-one Nitrites (27 and 32, Scheme VII). As is discussed later in this paper, the path leads to the formation of cyclic *N*-hydroxy imide **12** and cyclic hydroxamic acid **13** very likely involves nitrite intermediates 16α- and 16β-hydroxy-5α-androstan-17-one nitrites **27** and/or **32**. To confirm the involvement of nitrites **27** and **32** as the intermediates, isomeric nitrites, **27** and **32** were prepared by nitrosation of 16α-**26** and 16β-hydroxy-5α-androstan-17-one (**31**), and their photolysis was undertaken.

The authentic 16α-hydroxy-5α-androstan-17-one (**26**) was prepared through the hydrolysis of 16α-bromo-5α-androstan-17-one (**25**) according to a published procedure.[19] The authentic 16β isomer **31** was prepared according to a method reported by Nambara and his colleagues.[20] The reaction of 16α-acetoxy-5α-androstan-17-one (**28**)[21] with mercaptoethanol–BF_3 etherate thus gave

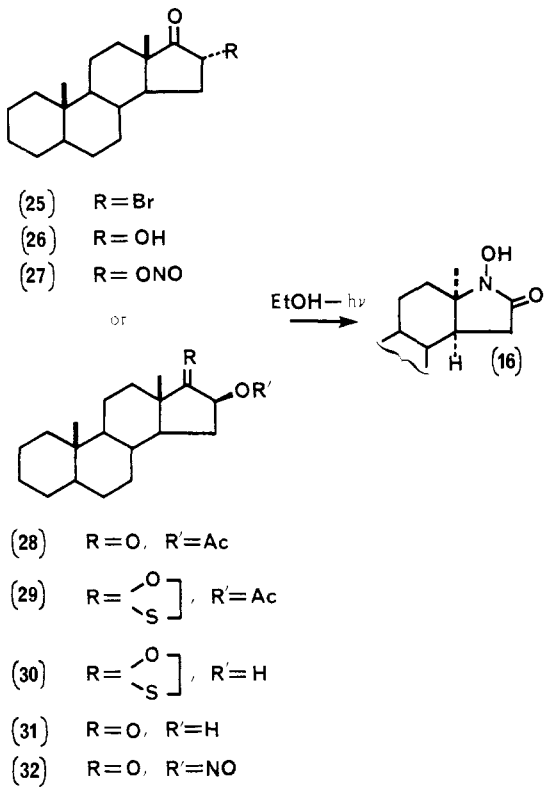
(18) Suginome, H.; Uchida, T. *J. Chem. Soc., Chem. Commun.* **1979**, 702, and references therein.

(19) Numazawa, M.; Nagaoka, M.; Osawa, Y. *J. Org. Chem.* **1982**, *47*, 4024.

(20) Hosoda, H.; Sato, Y.; Okamura, T.; Kamiya, K.; Miyaiti, S.; Nambara, T. *Chem. Pharm. Bull.* **1987**, *26*, 2209.

(21) Comb, M. G.; Denny, W. A.; Meakins, G. D.; Morisawa, Y.; Richard, E. E. *J. Chem. Soc. C* **1971**, 2300. Brutcher, F. V.; Bauer, W. *J. Am. Chem. Soc.* **1962**, *84*, 2236.

Scheme VII



the corresponding 17-(ethylene hemithioketal) **29**. The hydrolysis of the ketal **29** followed by deketalization with mercury(II) chloride gave 16β-hydroxy ketone **31** in 80% yield. Both 16α-**26** and 16β-hydroxy ketone **31** were transformed into their nitrites **27** and **32**, respectively, by the standard method.

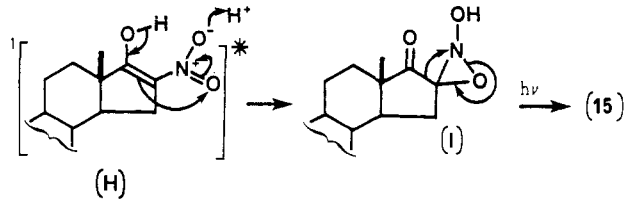
The photolysis of nitrite **27** in ethanol under conditions similar to those for the photolysis of α-nitro ketone **14** gave hydroxamic acid **16** in 28% yield. Similar photolysis of isomeric nitrite **32** gave the hydroxamic acid in 25% yield. In neither case was the expected *N*-hydroxy imide **15** formed.

Discussion

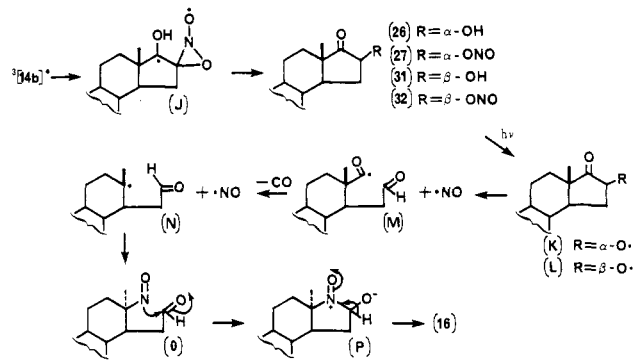
The above results show that in contrast to the photoreaction of six-membered α-nitro steroidal ketones,[3] the major products of the photoreaction of five-membered α-nitro steroidal cyclic ketones are *N*-hydroxy cyclic imides, cyclic hydroxamic acid, and cyclic imide arising from nitrogen insertion to the ring carrying the nitro group, while the products of the photoreaction of the seven-membered α-nitro steroidal ketones are the corresponding cyclic α-hydroxyimino ketones parallel to the case of six-membered α-nitro ketones.[3] The products of the photoreactions of steroidal α-nitro ketones thus depend on their ring size.

The above-mentioned experiments also show that the results of the photolysis of the six- and seven-membered α-nitro steroidal cyclic ketones are not parallel with those obtained on the *monocyclic* six- and seven-membered α-nitro ketones; in contrast to the photolysis of 2-nitrocyclohexanone and 2-nitrocycloheptanone,[6] none of the cyclic *N*-hydroxy imides is formed when cyclic steroidal six-[3] and seven-membered α-nitro ketones **21** and **22** are irradiated. The photoreactions of two highly enolized five-membered steroidal α-nitro ketones **5** and **14**, however, gave *N*-hydroxy imides **6** and **15** parallel to those in the photoreaction of the monocyclic substrates and α-nitrocamphor,[6] although non-enolized five-membered steroidal substrate **9** gave no *N*-hydroxy imide but gave cyclic imide **11**.

Scheme VIII



Scheme IX



In the following part, we discuss the pathways to each of the several types of the above-mentioned products.

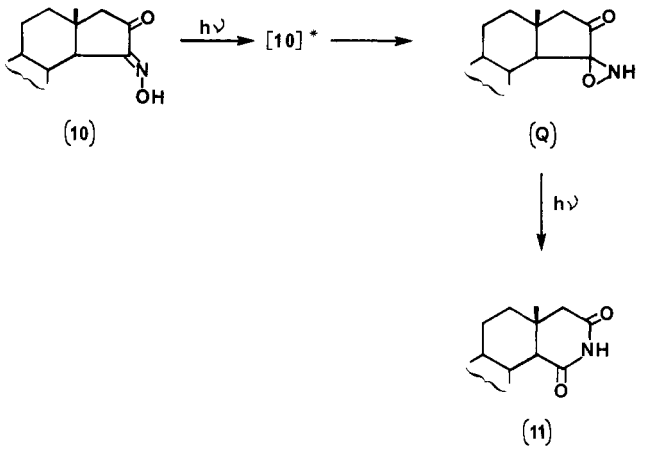
Cyclic Hydroxamic Acid 16 and Cyclic *N*-Hydroxy Imides 6 and 15 (Schemes III–V and VII–IX). *N*-Hydroxy imides **6** and **15** and hydroxamic acid **16** are formed when five-membered α-nitro ketones **6** and **15**, which are partly enolized in ethanol, are irradiated in the solvent, while five-membered α-nitro ketones **9**, which exist exclusively as the keto form, gave no *N*-hydroxy imide. It is therefore evident that the *N*-hydroxy imides and the hydroxamic acid are derived from the such excited enols as **5b** or **14b**. The formation of cyclic hydroxamic acid is unprecedented. The pathways that lead to the two types of products will be discussed together, taking the case of the photoreaction of 16-nitro-5α-cholestan-17-one as a representative example. Reid and Tucker[6] have suggested a plausible path involving a nitro–nitrite rearrangement[22] for the formation of *N*-hydroxy imides which they obtained when 2-nitrocycloheptanone and α-nitrocamphor were irradiated in ethanol.

As described in the foregoing part, the irradiation in ethanol of either nitrites **27** or **32**, probable intermediates to products **15** and **16**, under conditions similar to those for the photolysis of α-nitro ketone **14** gave the hydroxamic acid **16** in 28 and 25% yields, but none of the expected *N*-hydroxy cyclic imide **15** was formed. These results exclude the involvement of 16α- and/or 16β-hydroxy-5α-androstan-17-one nitrites **27** and **32** as the intermediate in the formation of imide **15**.

The results of the photolysis of α-nitro ketones **5** and **11** in the presence of oxygen also exclude the involvement of any radical intermediates in the pathway to *N*-hydroxy cyclic imides **6** or **15**. Thus, the products **6** and **7** or the products **16**–**17** are differentially scavenged with oxygen to give only *N*-hydroxy cyclic imides **6** or **15** in the photolysis of α-nitro ketones **2** or **11** in the presence of oxygen.

(22) Chapman, O. L.; Cleveland, P. G.; Hoganson, E. D. *Chem. Commun.* **1966**, 101. Pinhey, J. T.; Rizzardo, E. *Tetrahedron Lett.* **1973**, 4057. Saito, I.; Takami, M.; Matuura, T. *Tetrahedron Lett.* **1975**, 3155. Hunt, R. G.; Reid, S. T. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2462. Cridland, J. S.; Moles, P. J.; Reid, S. T.; Taylor, K. T. *Tetrahedron Lett.* **1976**, 447.

Scheme X



One of the probable paths leading to *N*-hydroxy cyclic imide **15** is outlined in Scheme VIII; imide **15** can be formed by the photorearrangement of an oxaziridine (I), an intermediate of the photo-Beckmann rearrangement of oximes,[23] generated from an excited enol **14b**. The nature of the excited state (H), which differs from the excited state to lead to cyclic hydroxamic acid **16** (Scheme IX), is uncertain at the present stage. The similarity with the photo-Beckmann rearrangement,[23] however, suggests that the rearrangement might be a singlet process. The similar regioselectivity found for the photorearrangement of the oxime **10** through the oxaziridine intermediate (Q, vide infra, Scheme X) might also support the proposed hypothesis.

We outline the most probable paths leading to cyclic hydroxamic acid **16** in Scheme IX, which accommodates all of the above-mentioned experimental results. Thus, a Chapman rearrangement of excited enol **14b** generates epimers **17** and/or **32**. A β-scission of alkoxyl radical (k) and/or (L) generated from nitrite **27** and/or **32** gives another intermediate (M). A decarbonylation of the radical (M) and a combination of nitric oxide with the resulting radical (N) gives hydroxamic acid **16**. An alternative pathway leading to hydroxamic acid **16**—a photochemical decarbonylation of *N*-hydroxy imide **15**—was excluded on the basis of the results of a separate photolysis of the *N*-hydroxy imide **15** (under the conditions carried out for the nitro ketone **14**) where none of hydroxamic acid **16** was formed.

Cyclic Imide 11 (Scheme X). This unprecedented formation of a cyclic imide intead of *N*-hydroxy cyclic imide has been observed only when five-membered cyclic α-nitroketone **9** was photolyzed. Since nitro ketone **9** exists exclusively as the keto form in ethanol and this type of aza steroid **11** is not formed in the photolysis of two other five-membered cyclic α-nitro ketones **5** and **14**, which are highly enolized, we assumed that imide **11** is a product from a keto form of the cyclic α-nitro ketone. This was then proved to be correct when we found that the irradiation of α-hydroxyimino ketone **10**, which is formed together with cyclic imide **11** in the photolysis of α-nitro ketone **9**, indeed gave cyclic imide **11** in 13% yield. It should be noted that this is the first example of a photo-Beckmann rearrangement[23] of a cyclic α-hydroxyimino ketone since the photoreactions of cyclic α-hydroxyimino ketones were reported to give only products that arise from the reaction of an excited carbonyl group (α-fission and an intramolecular hydrogen abstraction).[24] The path to cyclic imide **11** involves an oxaziridine intermediate (as outlined in Scheme X).

α-Hydroxyimino Ketones 7, 10, 17, 23, and 24. The formation of α-hydroxyimino ketones has been found throughout the current photolysis of α-nitro ketones in ethanol, with no exception.

The formation of these products in the photolysis of α-nitro ketones **9** and **21**, which exist exclusively in their keto form, indicates that these photoproducts are produced from the keto forms of α-nitro ketones. The genesis of these photoproducts discussed in our previous paper[3] may involve an abstraction of hydrogens from ethanol by the n,π^* excited nitro group,[25] followed by a loss of water to give nitroso compounds.

Parent Ketones 8 and 18 and Seco Ester 12. The formation of parent ketones **8** and **18** is found in the photolysis of α-nitro ketones **9** and **21**, while none of the parent ketones is formed in the photolysis of α-nitro ketones **5**, **14**, and **22**. The fact that α-nitro ketones **9** and **21** exist exclusively as their keto form in ethanol indicates that the parent ketones derive from the keto form of α-nitro ketones through the photochemical homolysis of their C–N bond to give carbon-centered radicals that abstract hydrogens from the solvent. The seco seter **12** should be formed through a photochemical α-fission[26] of the excited ketone **8**.

Experimental Section

Melting points were recorded with a Yanagimoto melting point apparatus. IR spectra were determined for Nujol mulls with JASCO IR 810 infrared spectrophotometer. The ^{1}H NMR spectra were determined with a JEOL JNM-FX 270 spectrometer (270 MHz; solvent $CDCl_3$; $SiMe_4$ as an internal standard; Faculty of Pharmaceutical Sciences of this university) unless otherwise indicated. TLC was carried out with Merck Kiesel gel 60-PF_{245}. The high- and low-resolution mass spectra were determined with a JEOL JMS-300 spectrometer (70 eV, Faculty of Pharmaceutical Sciences of this university). Elemental analyses were performed by the staff of the analytical laboratory of the Faculty of Pharmaceutical Sciences.

Preparation of 15α-Nitro-5α-androstan-16-one (9). To THF (14 mL) containing potassium *tert*-butoxide (0.5 g, 4 mmol) 5α-androstan-16-one[8] (0.7 g, 2.56 mmol) in THF (14 mL) was added over 0.5 h at −40 °C. Propyl nitrate (0.56 mL) was then added to the solution, and the temperature of the solution was raised to 0 °C over 45 min. The solution was then neutralized by the addition of glacial acetic acid (pH ca. 3) and poured into iced water; all of the solution was then extracted twice with diethyl ether. The combined ethereal layers were washed with water and dried over Na_2SO_4. Evaporation of the solvent gave a crude nitro ketone **9** (840 mg) which was recrystallized from methanol to yield pure nitro steroid **9** (635 g, 78%): mp 164.5–167.0 °C (Found: C, 71.24; H, 9.23; N, 4.22. Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.39); IR (Nujol) 1770 (C=O) and 1557 cm^{-1} (NO_2); ^{1}H NMR (270 MHz) δ 0.82 (3 H, s, 19-H), 0.94 (3 H, s, 18-H), 2.30 (1 H, d, J = 17.6 Hz, 17α-H), 2.39 (1 H, d, J = 17.6 Hz, 17β-H), 2.45 (1 H, dd, J = 12.5 and 10.99 Hz, 14α-H), and 4.89 (1 H, d, J = 12.5 Hz, 15β-H); MS, m/z (rel intensity) 319 (M^+, 9.0), 219 [($M - CO^+$), 6.7)], 271 (15.2), 257 (14.1), 229 (15.6), 215 (22.9), 175 (20.7), 163 (30.2), 147 (19.5), 121 (38.1), 109 (83.4), 95 (81.8), 81 (89.7), 67 (89.5), 55 (100), and 41 (75.0).

Preparation of *A*-Homo-5α-cholestan-4-one Enol Acetates 19 and 20. A solution of *A*-homo-5α-cholestan-4-one (**18**, 1 g, 2.5 mmol) in isopropenyl acetate (25 mL) containing *p*-toluenesulfonic acid (500 mg) was heated under reflux for 7.5 h in an atmosphere

(23) Suginome, H.; Yagihashi, F. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2488, and references therein.

(24) Stojiljkovic, A.; Tasovac, R. *Tetrahedron Lett.* **1970**, 1405. Yates, P.; Wong, J.; Mclean, S. *Tetrahedron* **1981**, *37*, 3357.

(25) Barltrop, J. A.; Bunce, N. J. *J. Chem. Soc. C* **1986**, 1467.

(26) For a review, see: Chapman, O. L.; Weiss, D. S. *Organic Photochemistry*; Chapman, O. L., Ed.; Marcel Dekker: New York, 1973; Vol. 3, Chapter 3, pp 197–288.

of nitrogen. Diethyl ether and aqueous saturated sodium hydrogen carbonate were then added to the solution. After the solution was shaken, the organic layer was dried over Na_2SO_4. The usual workup gave a brown oil (1.367 g) which was treated with diethyl ether–ethanol to give crystals of enol acetate **19** (302 mg, 27.3%), mp 110–112 °C. These crystals were recrystallized from ethanol to give pure crystals (238 mg), mp 112.5–114 °C. All of the mother liquors from the recrystallization were combined, and the solvent was evaporated from the combined solution. The residue was subjected to preparative TLC with a 1:1 benzene–hexane to give two fractions. The more mobile fraction (252 mg, 22.8%) was enol acetate **19**, and the less mobile fraction (533 mg) was isomeric enol acetate **20**. The enol acetate **19** was recrystallized from methanol to give pure material **19** (229 mg), mp 116–119 °C (lit.[10] mp 111–114 °C); IR (Nujol) 1748 (OAc), 1694 (C=C), and 1240 cm^{-1} (COC); ^1H NMR (270 MHz) δ 0.65 (3 H, s, 18-H), 0.85 (3 H, s, 19-H), 2.09 (3 H, s, OAc), 4.81 (1 H, dt, J = 4.4, 2.2 and 2.2 Hz, 4a-H), MS, m/z (rel intensity), 422 (M^+, 3.9), 400 [(M – $CH_2CO)^+$, 81.5], 382 (35.5), 367 (14.6), 287 (19.8), 269 (62.5), 245 (15.7), 111 (100), 95 (40.3), 81 (36.4), 69 (26.4), 55 (39.4), and 43 (53.8).

The enol acetate **20** was recrystallized from methanol to give pure material **20** (400 mg, 36.2%), mp 67–70 °C (Found: C, 81.31; H, 11.41. Calcd for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38); IR (Nujol) 1758 (OAc), 1687 (C=C), and 1225 (COC) cm^{-1}; ^1H NMR (270 MHz) δ 0.65 (3 H, s, 18-H), 0.83, (3 H, s, 19-H), 2.08 (3 H, s, OAc), and 5.39 (1 H, br t 3-H); MS, m/z (rel intensity), 442 (M^+, 3.8), 400 [M – CH_2=C=O)$^+$, 100], 328 (9.2), 357 (19.8), 269 (18.1), 245 (43.5), 217 (14.2), 203 (14.1), 95 (30.3), 81 (25.9), 69 (22.3), 55 (32.1), and 43 (42.6).

Photolysis of 3α-Nitro-*A*-nor-5α-cholestan-2-one (5). (a) In the Absence of Oxygen. 3α-Nitro-*A*-nor-5α-cholestan-2-one (**5** 100 mg, 0.24 mmol) in absolute ethanol (100 mL) was irradiated for 15 h with a Hanovia 450-W high-pressure mercury arc through a Pyrex filter in an atmosphere of dry nitrogen. Removal of the solvent under reduced pressure gave an oily residue (100 mg) which was subjected to column chromatography (Sephadex SH20, 10 g). Elution with dichloromethane first gave 3-hydroxy-3-aza-5α-cholestane-2,4-dione (**6**, 61 mg, 61%). It was recrystallized from hexane to give the specimen for analysis (44 mg, 43.7%), mp 189–196 °C (Found: C, 74.96; H, 10.45; N, 3.41. Calcd for $C_{26}H_{43}NO_3$: C, 74.78; H, 10.38; N, 3.35); IR (Nujol) 3217 (OH), 1738 (C=O), 1680 (C=O), 1655 (C=O), and 1243 cm^{-1}; ^1H NMR (270 MHz) δ 0.67 (3 H, s, 18-H), 0.96 (3 H, s, 19-H), 2.91 (1 H, d, J = 16.85 Hz, 1β-H), 7.93 (1 H, br s, OH); MS, m/z (rel intensity) 417 (M^+, 66.4), 401 (6.6), 304 (9.3), 278 (14.2), 262 (100), 248 (24.4), 234 (11.1), 175 (8.8), 161 (13.0), 142 (12.7), 105 (20.1), 95 (29.6), 81 (33.2), 69 (38.7), 55 (59.6), and 43 (60.7).

Further elution of the column gave *A*-nor-5α-cholestane-2,3-dione 3-oxime (**7**, 13 mg, 13.5%), which was recrystallized from hexane to yield the specimen for analysis (7 mg, 7.7%), mp 193–197 °C (Found: C, 77.62; H, 10.79; N, 3.60. Calcd for $C_{26}H_{43}NO_2$: C, 77.75; H, 10.79; N, 3.49); IR (Nujol) 3248 (OH), 1761 and 1722 (C=O), 1660 and 1627 (C=N), 964, and 934 cm^{-1}; IR ($CHCl_3$) 3212 (OH), 1744 (C=O), and 1649 (C=N); ^1H NMR (270 MHz), δ 0.68 (3 H, s, 18-H), 0.90 (3 H, s, 19-H), 2.07 (1 H, d, J = 16.86 Hz, 1α-H), 2.37 (1 H, d, J = 16.86 Hz, 1β-H), and 2.49 (1 H, dd, J = 12.09 and 3.3 Hz, 5α-H), 2.66 (1 H, m, 6α-H); MS, m/z (rel intensity) 401 (M^+, 29.5), 385 (28.4), 370 (13.1), 357 (100), 342 (18.7), 246 (30.8), 230 (18.8), 202 (23.0), 188 (16.7), 124 (31.0), 95 (53.1), 55 (80.5), and 43 (96.0).

(b) In the Presence of Oxygen. A solution of α-nitro ketone **5** (350 mg) in ethanol (350 mL) was saturated with oxygen by bubbling and then irradiated for 15 h, as mentioned above. The product (371 mg) was subjected to preparative TLC (silica gel–$CHCl_3$) to give the starting α-nitro ketone **5** (128 mg, 36.6%) and 3-hydroxy-3-aza-5α-cholestane-2,3-dione (**6**, 73 mg). The yield based on the converted nitro ketone **5** was 32.9%. None of 2,3-dione 3-oxime **7** was obtained.

Preparation of *A*-Nor-5α-androstane-2,3-dione 3-Oxime (7). To *A*-nor-5α-cholestan-2-one (**4**, 100 mg) in potassium *tert*-butoxide (42 mg), butyl nitrite (0.042 mL) was added. The solution was stirred for 1 h at room temperature and poured into iced water. After aqueous 2 N hydrochloric acid had been added, the aqueous solution was extracted with diethyl ether. The combined organic layers were washed with an aqueous 5% sodium hydrogen carbonate solution and with water and then dried over anhydrous sodium sulfate. The usual workup of the solution gave an oily product (185 mg) which was subjected to preparative TLC with a 1:1 benzene–ethyl acetate to give a crude oxime (85 mg, 78.8%). Recrystallization from ethanol gave pure oxime **7** (59 mg), mp 193–197 °C. This oxime was identical with oxime **7** obtained from the photolysis of nitro ketones **5**.

Photolysis of 15α-Nitro-5α-androstan-16-one (9). Nitro steroid **9** (300 mg, 0.94 mmol) in ethanol (350 mL) was irradiated for 6 h with an Eikosha 500-W high-pressure mercury arc through a Pyrex filter in an atmosphere of nitrogen. The removal of the solvent left a residue (352 mg) which was subjected to preparative TLC with dichloromethane to give seven fractions. The most mobile fraction (38 mg, 11%) was 15,16-seco-5α-androstane derivative **12** (found M^+ 320.2723, calcd for $C_{21}H_{36}O_2$ 320.2715); IR (Nujol) 1736 (ester C=O), 1209, and 1119 cm^{-1} (COC); ^1H NMR (270 MHz) δ 0.74 (3 H, s, 19-H), 0.81 (3 H, d, J = 6.6 Hz, 15-H), 0.88 (3 H, s, 19-H), 12.5 (3 H, t, J = 7.15 Hz, CH_3CH_2), and 4.11 (2 H, br q, J = 7.15 Hz, CH_3CH_2); MS, m/z (rel intensity) 320 (M^+, 1.4), 305 [(M – $CH_3)^+$, 1.1)], 275 [(M – $OC_2H_5)^+$, 2.7], 232 [(M – EtOC(OH)=$CH_2)^+$, 100], 217 (52.2), 122 (32.1), 109 (24.7), 95 (20.7), 81 (19.9), 67 (17.8), 55 (19.9), and (14.9).

The next mobile fraction (20 mg, 7.7%) was 5α-androstan-16-one (**8**), which was recrystallized from methanol–water to give crystals, mp 105–109 °C (lit.[8] mp 108–109.5 °C).

The third mobile fraction (35 mg, 12.3%) was 16-aza-*D*-homo-5α-androstane-15,17-dione (**11**). This fraction was recrystallized from methanol–water to give the specimen for analysis, mp 261–262.5 °C (found M^+ 303.2188, calcd for $C_{19}H_{29}NO_2$ 303.2197); IR (Nujol) 3212 and 3088 (NH), 1720, and 1693 cm^{-1} (imide C=O); ^1H NMR (270 MHz) δ 0.81 (3 H, s, 19-H), 0.96 (3 H, s, 18-H), 2.00 (1 H, J = 10.62 Hz, 14α-H), 2.37 (1 H, d, J = 17.58 Hz, 17aα-H), 2.66 (1 H, ddd, J = 12.45, 6.59, and 3.3 Hz, 12β-H), and 7.57 (1 H, br s, NH); MS, m/z (rel intensity) 303 (M^+, 100) 288 (29.7), 246 [(M – $CH_2CONH)^+$, 54.8], 218 [(M – $CH_2CONHCO)^+$, 13.8], 208 (38.6), 194 (28.7), 180 (28.2), 110 (40.4), 95 (36.9), 81 (35.0), 67 (30.5), 55 (30.7), and 41 (27.0).

The most polar fraction (14 mg, 5%) was 5α-androstane-15,16-dione 15-oxime (**10**) which was recrystallized from methanol–water to give the specimen for analysis, Mp 148–151.5 °C (found M^+ 303.2200, Calcd for $C_{19}H_{29}NO_2$ 303.2198); IR (Nujol) 3582, 3456 and 3304 (OH), 1743 (C=O), and 1638 cm^{-1} (C=N); ^1H NMR (270 MHz) δ 0.84 (3 H, s, 19-H), 0.91 (3 H, s, 18-H), 2.11 (1 H, d, J = 17.58 Hz, 17α-H), 2.51 (1 H, d, J = 11.0 Hz, 14α-H), 2.77 (1 H, d, J = 17.58 Hz, 17β-H), 2.77 (1 H, ddd, J = 12.83, 6.23, and 3.3 Hz, 12β-H); MS, m/z 303 (M^+, 16.8), 286 [(M – OH)$^+$, 37.2], 244 [(M – COC=NOH)$^+$, 100], 109 (61.1), 95 (47.6), 81 (29.2), 67 (29.1), 55 (35.9), and 41 (29.0).

Photolysis of 16α- and 16β-Nitro-5α-androstan-17-one (14). (a) In the Absence of Oxygen. Nitro steroid **14** (250 mg, 0.78 mmol) in ethanol (400 mL) was irradiated for 8 h with a Hanovia 450-W high-pressure mercury arc through a Pyrex filter in an atmosphere of nitrogen. The removal of the solvent left a residue (287 mg) which was subjected to preparative TLC with a 2:1 benzene–ethyl acetate to give three fractions. The most mobile fraction (44 mg, 18.4%) was 5α-androstane-16,17-dione 16-oxime (**17**) which was recrystallized from hexane to give the specimen for analysis, mp 200.0–203.5 °C (lit.[10] mp 173–177 °C); IR (Nujol) 3305 (OH), 1727 (C=O),. 1630 (C=N), 948, 875, and 761 cm^{-1}; ^1H NMR (270 MHz) δ 0.83 (3 H, s, 19-H), 0.95 (3 H, s, 18-H), 2.31 (1 H, dd, J = 17.4 and 4.4 Hz, 15β-H), 2.92 (1 H, dd, J = 17.4 and 6.6 Hz, 15α-H), and 7.79 (1 H, br s, OH); MS, m/z (rel intensity) 303 (M^+, 14.2), 288 (10.8), 258 (100), 247 (7.2), 218 (28.7), 203 (12.3), 175 (12.1), 162 (14.0), 148 (21.9), 135 (12.8), 121 (18.6), 109 (75.3), 95 (54.0), 81 (47.5), 67 (51.3), 55 (43.1), and 41 (38.8).

The next mobile fraction (26 mg, 11.4%) was 17-hydroxy-17-aza-5α,13α-androstan-16-one (**16**), which was recrystallized from hexane to give the specimen for analysis, mp 236–241 °C (lit.[18] mp 234–236 °C). The most polar fraction was a colorless solid which was dissolved in acetic acid. The solution was poured into ice water and the aqueous solution was extracted with diethyl ether. The organic layer was washed with water and dried over Na_2SO_4. The usual workup of the solution gave crude 17-hydroxy-17-aza-*D*-homo-5α-androstane-16,17a-dione (**15**, 142 mg, 56.8%), which was purified by passing it through a column of sephadex LH-20 (10 g). Elution with dichloromethane gave pure

dione **15** (102 mg, 40.7%). It was further recrystallized from hexane to give the specimen for analysis, mp 188.5–193 °C Found: C, 71.37; H, 9.29; N, 4.31. Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.39), IR (Nujol) 3190 cm^{-1} (OH), 1738 and 1658 (imide C=O), 1253, 1237, 1190, 1076, and 987 cm^{-1}; ^1H NMR (270 MHz) δ 0.78 (3 H, s, 19-H), 1.22 (3 H, s, 18-H), 2.41 (1 H, dd, J = 17.95 and 13.19 Hz, 15β-H), 2.95 (1 H, dd, J = 17.95 and 4.4 Hz, 15α-H); MS, m/z (rel intensity) 319 (M^+, 18.4), 303 (44.4), 288 (36.8), 276 (100), 246 (34.5), 216 (12.6), 109 (26.4), 95 (35.9), 81 (41.4), 67 (46.12), 55 (47.0), and 41 (50.1).

(b) In the Presence of Oxygen. Nitro steroid **14** (150 mg) in ethanol (240 mL) was saturated with oxygen by bubbling. The solution was irradiated for 8 h with a Hanovia 450-W high-pressure mercury arc through a Pyrex filter. The product was subjected to preparative TLC with 2:1 benzene–ethyl acetate to give *N*-hydroxy imide **15** (64 mg, 42.7%) which was recrystallized from hexane to give a pure specimen, mp 188.5–193 °C. No evidence of oxime **17** or cyclic hydroxamic acid **16** was found in the product.

Photolysis of 4aα-Nitro-*A*-homo-5α-cholestan-4-one (21). α-Nitro ketone **21** (350 mg, 0.79 mmol) in ethanol (350 mL) was flashed with nitrogen and irradiated with an Eikosha 500-W high-pressure mercury arc through a Pyrex filter for 1.5 h under an atmosphere of nitrogen. The removal of the solvent left an oily residue (363 mg) which was subjected to preparative TLC with dichloromethane to yield three fractions. The most mobile fraction (72 mg, 20.5%) was the starting nitro ketone **18**, which was recrystallized from ethanol (40 mg). The next most mobile fraction (17 mg, 6.7%) was *A*-homo-5α-cholestane-4,4a-dione 4a-oxime (**23**) which was recrystallized from methanol–water (36 mg), mp 192–197 °C (Found: C, 77.99; H, 10.90; N, 3.04. Calcd for $C_{28}H_{47}NO_2$: C, 78.27; H, 11.03; N, 3.26); IR (Nujol) 3360 (OH) and 1704 cm^{-1} (C=O); ^1H NMR (270 MHz) δ 0.66 (3 H, s, 18-H), 0.90 (3 H, s, 19-H), 2.21 (1 H, dd, J = 12.3 and 3.5 Hz, 5α-H), and 2.35–2.68 (2 H, m, 3-H), MS m/z (rel intensity) 429 (M^+, 20.2), 412 [$(M - OH)^+$, 52.1], 401 [$(M - CO)^+$, 9.0], 384 (14.9), 256 (15.6), 138 (100), 110 (68.8), 95 (43.8), 81 (44.6), 69 (44.3), 55 (60.8), and 43 (62.1).

Photolysis of 3-Nitro-*A*-homo-5α-cholestan-4-one (22). α-Nitro ketone **22** (300 mg, 0.67 mmol) in ethanol (1050 mL) was flashed with nitrogen and irradiated with an Eikosha 500-W high-pressure mercury arc through a Pyrex filter for 1.5 h in an atmosphere of nitrogen. Removal of the solvent under reduced pressure gave an oily product (332 mg) which was subjected to preparative TLC with 9:1 benzene–ethyl acetate to give two fractions. The more mobile fraction (203 mg, 67.7%) was recrystallized from ethanol–water to yield crystals of *A*-homo-5α-cholestane-3,4-dione 3-oxime (**24**, 19 mg), mp 180–185 °C (found M^+ 429.3585, calcd for $C_{28}H_{47}NO_2$ 429.3060); IR (Nujol) 3238 (OH), 1698 (C=O), and 1584 cm^{-1} (C=N); ^1H NMR (270 MHz) δ 0.66 (3 H, s, 18-H), 0.92 (3 H, s, 19-H), 2.88 (1 H, dd, J = 16 and 11.5 Hz, 4aβ-H), and 3.06 (1 H, dd, J = 16 and 10 Hz, 4aα-H); MS, m/z (rel intensity) 429 (M^+, 51.1), 412 [$(M - OH)^+$, 100], 401 [$(M - CO)^+$, 32], 384 (26.3), 274 (68.8), 167 (28.6), 121 (43.1), 107 (42.8), 95 (66.3), 81 (80.2), 69 (65.9), 57 (70.8), and 43 (92.1).

16α-Hydroxy-5α-androstan-17-one (26). This α-hydroxy ketone was prepared through hydrolysis of 16α-bromo-5α-androstan-17-one according to a published precedure,[19] mp 161–165 °C (Found: C, 78.55; H, 10.49. Calcd for $C_{19}H_{30}NO_2$: C, 78.57; H, 10.41); IR (Nujol) 3452 (OH) and 1742 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 0.80 (3 H, s, 19-H), 0.95 (3 H, s, 18-H), 4.36 (1 H, dd, J = 7.32 and 2.2 Hz, 16β-H); EI-MS, m/z (rel intensity) 290 (M^+, 15.5), 218 [$(M - D\text{-ring})^+$, 100], 203 (29.6), 175 (25.1), 148 (32.4), and 109 (48.0).

Preparation of 16α-Hydroxy-5α-androstan-17-one Nitrite (27). To a solution of the hydroxy ketone (250 mg) in dry pyridine (10 mL), a solution of nitrosyl chloride in pyridine was added dropwise at room temperature until the color of the solution turned reddish brown. The solution was stirred for 5 min and poured into iced water. The nitrite was collected by filtration, dried, and used immediately for next photolysis.

Photolysis of Nitrite 27. The nitrite obtained above was dissolved in ethanol (400 mL) and flashed with nitrogen. The solution was irradiated with a 450-W Hanovia high-pressure Hg arc through a Pyrex filter for 30 min at room temperature. Evaporation of the ethanol under reduced pressure gave an oily product mixture (256 mg). The mixture was subjected to preparative TLC with 2:1 benzene–ethyl acetate to give hydroxamic acid **16**[18] (71 mg, 28.3%), mp 238–242 °C (lit.[18] mp 234–236 °C); R_f 0.2–0.4.

16β-Acetoxy-5α-androstan-17-one 17-(Ethylene hemithioketal) (29). To 16β-acetoxy-5α-androstan-17-one (**28**, 2.7 g) in dry diethyl ether (62 mL) and dichloromethane (9.3 mL), 2-mercaptoethanol (12.4 mL) and BF_3 etherate (12.4 mL) were added. The solution was stirred for 4 h at room temperature. The solution was then diluted with ethyl acetate (400 mL), washed with aqueous 5% sodium hydroxide solution and with water, and dried over anhydrous sodium sulfate. The removal of the solvent gave a product (3.114 g) which was subjected to column chromatography (silica gel, benzene) to give a ketal (2.575 g, 80.7%). This ketal was recrystallized from methanol to give a specimen for analysis (2.477 g), mp 240–242 °C (Found: C, 70.22; H, 9.40; S, 8.03. Calcd for $C_{23}H_{36}SO_3$: C, 70.37; H, 9.24; S, 8.17); IR (Nujol) 1740 (OAc), 1236, 1071, and 1056 cm^{-1}; ^1H NMR (270 MHz) δ 0.79 (3 H, s, 19-H), 0.84 (3 H, s, 18-H), 2.08 (3 H, s, Ac), 0.79 (3 H, s, 19-H), 0.84 (3 H, s, 18-H), 2.08 (3 H, s, Ac), 4.03–4.2 (4 H, m, OCH_2CH_2S), 4.93 (1 H, dd, J = 8.43 and 5.5 Hz, 16α-H).

16β-Hydroxy-5α-androstan-17-one (31). To 16β-acetate **29** (2 g) in dioxane (36 mL), ethanol (130 mL), and dry THF (20 mL), aqueous 10% sodium hydroxide was added, and the solution was stirred for 5 h at room temperature. The solution was neutralized by adding acetic acid (2.6 mL) and diluted with ethyl acetate, washed with water, and dried over anhydrous sodium sulfate. The removal of the solvent gave 16β-hydroxy-5α-androstan-17-one 17-(ethylene hemithioketal) (**30**, 2.189 g), which was immediately subjected to deketalization. The ethylenehemithioketal **30** was dissolved in 80% acetonitrile (180 mL). To this solution, mercury(II) chloride (9 g) and calcium carbonate (3.5 g) were added, and the solution was stirred for 1 h at room temperature. The solution was then diluted with ethyl acetate, washed with 50% aqueous ammonium acetate and with water, and dried over anhydrous sodium sulfate. The removal of the solvent gave a crude 16β-hydroxy-5α-androstan-17-one (**31**, 1.53 g), which was recrystallized from methanol to give crystals of 16β-ol (1.184 g, 80.1%). The specimens for analysis were obtained by recrystallization from methanol, mp 156–160 °C (Found: C, 78.30; H, 10.61. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41); IR (Nujol) 3468 (OH) and 1743 cm^{-1} (C=O); ^1H NMR (270 MHz) δ 0.81 (3 H, s, 19-H), 0.93 (3 H, s, 18-H), and 3.39 (1 H, t, J = 8.61 Hz, 16α-H); EIMS, m/z (rel intensity) 290 (M^+, 59.13), 218 [$(M - D\text{-ring})^+$, 100], 203 (31.49), 175 (21.41), 148 (17.34), 135 (7.69), 121 (7.28), and 109 (25.14).

Preparation of 16β-Hydroxy-5α-androstan-17-one Nitrite (32). To a solution of the hydroxy ketone (250 mg) in dry pyridine (10 mL), a solution of nitrosyl chloride in pyridine was added dropwise at room temperature until the color of the solution turned reddish brown. The solution was stirred for 5 min. and poured into iced water. The nitrite was collected by filtration, dried, and used immediately for photolysis.

Photolysis of Nitrite 32. The nitrite obtained above was dissolved in ethanol (400 mL) and flashed with nitrogen. The solution was irradiated with a 450-W Hanovia high-pressure Hg arc through a Pyrex filter for 30 min at room temperature. Evaporation of the ethanol under reduced pressure gave an oily product mixture (240 mg) which was subjected to preparative TLC with 2:1 benzene–ethyl acetate to give 16β-hydroxy-5α-androstan-17-one (44 mg, 17.6%) and hydroxamic acid **16** (62 mg, 24.7%). Both products were in every respect identical with the authentic specimens.

Photolysis of 5α-Androstane-15,16-dione 15-Oxime (10). α-Oxo oxime **10** (134 mg) in ethanol (200 mL) was irradiated through a Pyrex filter with a 500-W high-pressure Hg arc in an atmosphere of nitrogen for 11 h. After the evaporation of the solvent, the oily product (135 mg) was subjected to preparative TLC with 9:1 dichloromethane–ethyl acetate to give imide **11** (13 mg, 12.9%) and the recovered starting material **10** (33 mg). The imide **11** was recrystyallized from methanol–water to give a specimen for analysis (6 mg), mp 261–262.5 °C. This imide was identical with the imide **11** obtained by the photolysis of 15α-nitro-5α-androstan-16-one.

Registry No. **4**, 2310-36-3; **5a**, 123239-81-6; **6**, 123263-93-4; **7**, 123239-82-7; **8**, 1032-16-2; **9**, 123239-83-8; **10**, 123239-84-9; **11**,

123239-85-0; **12**, 123239-86-1; **13**, 963-74-6; **14a**, 123239-87-2; **14c**, 123239-88-3; **15**, 123239-89-4; **16**, 72670-43-0; **17**, 1158-62-9; **18**, 5885-22-3; **19**, 31687-40-8; **20**, 14222-37-8; **21**, 123239-90-7; **22a**, 123239-91-8; **23**, 123239-92-9; **24**, 123239-93-0; **25**, 5987-29-1; **26**, 25846-17-7; **27**, 123239-94-1; **28**, 32694-25-0; **29**, 123239-95-2; **30**, 123239-96-3; **31**, 112925-02-7; **32**, 123239-97-4.

Supplementary Material Available: Experimental details for the synthesis of **5**, **10**, **14**, **21**, and **22** (4 pages). Ordering information is given on any current masthead page.

Reductive Cyclization of *o*-(3-Butenyl)fluorobenzene at Mercury and Lead Cathodes

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The cathodic behavior of *o*-(3-butenyl)fluorobenzene (**1**) at mercury and lead cathodes in DMF was investigated. Cyclic voltammograms were recorded, and the products of preparative electrolyses were isolated and identified. The reduction products at either cathode were 1-methylindane (**3**) and 3-butenylbenzene (**2**), the first predominating in all experiments with dry solvent. The effects of various reaction conditions on the product composition were studied, and the highest yield of **3** was obtained at a lead cathode at 22 °C (**3**/**2** = 3.8). Dimethylpyrrolidinium (DMP^+) was tested as a possible catalyst for the reduction of **1**. It catalyzed the reaction and increased the proportionate amount of the cyclic product. However the mediated process at lead was very inefficient. The mechanism for the reductive cyclization of **1** at mercury and lead and the mediation by DMP^+ are discussed. It is proposed that tetraalkylammonium–metals are involved in these processes.

Introduction

Reduction of halobenzenes can be accomplished with a variety of reagents, including a cathode. Electrochemical studies have been useful in investigating the mechanisms of reduction of halobenzenes.[2]

Cyclic voltammograms (CV) of halobenzenes at mercury, platinum, or carbon electrodes exhibit a single irreversible reduction peak. The CV peak potentials vary with the halogen and become more negative in the order PhI < PhBr < PhCl < PhF. The cathodic product of halobenzenes is benzene. The reaction is believed to proceed via the mechanism outlined in Scheme I,

Scheme I

$$PhX + 1e^- \rightarrow PhX^{\bullet -}$$

$$PhX^{\bullet -} \rightarrow Ph^{\bullet} + X^-$$

path A:

$$Ph^{\bullet} + 1e^- \rightarrow Ph^-$$

$$Ph^- + ZH \rightarrow PhH + Z^-$$

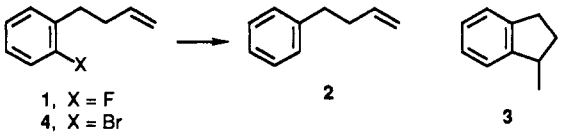
path B:

$$Ph^{\bullet} + ZH \rightarrow PhH + Z^{\bullet}$$

$$Z^{\bullet} + 1e^- \rightarrow Z^-$$

where ZH is the solvent, tetrabutylammonium ion (supporting electrolyte), or residual moisture. Following path A or path B, two electrons per molecule are consumed. Homogeneous catalysts have been used as mediators for the cathodic reduction of halobenzenes, and homogeneous redox catalysis studies[3] have provided thermodynamic and kinetic information about the mechanism in Scheme I. For example, using such techniques, Savéant and co-workers[4] determined that for PhF $E^\circ = -2.97$ V (SCE) and that the rate constant for the cleavage of $PhF^{\bullet -}$ is greater than 10^6 s^{-1}.

Beckwith and co-workers have reported that phenyl radicals with *o*-3-butenyl substituents cyclize, to form 1-methylindane derivatives[5] and have used such cyclizations to probe the mechanisms of reactions which were thought to involve the intermediacy of aryl radicals.[6] Such cyclization reactions have recently been used to investigate the intermediacy of aryl radicals, in the cathodic reduction[7] of **4** and in the reduction of **1**, **4**, and the analogous iodo and chloro compounds by solvated electrons in liquid ammonia.[8]



1, X = F
4, X = Br

2

3

Reduction of tetraalkylammonium ions (R_4N^+) at a variety of electrodes forms tetraalkylammonium–metals (R_4N–metals). R_4N–metals are insoluble composites that contain R_4N^+ cations, metal from the electrode, and electrons.[9] Of particular relevance here are the R_4N–metals derived from dimethylpyrrolidinium (DMP^+) and

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