components in the approximate ratio of 4:1 in addition to traces of **3** (starting material) and a third (minor) component. Fractional crystallization of the crude solid from acetone afforded 4.1 g of **4**: mp 214–218° (lit.[6a] mp 218–220°); ir spectrum (KBr pellet) intense bands at 1525 and 1350 cm^{-1} (NO_2).

Anal. Calcd for $C_6H_2BrN_3O_2S$: Br, 30.8; S, 12.3. Found: Br, 30.7; S, 12.6.

The combined mother liquors were concentrated to dryness. Fractional crystallization of the residual solid from ethanol gave 0.7 g of **5**, mp 155–157° (lit.[6b] mp 152–154°).

Anal. Calcd for $C_6HBr_3N_2S$: Br, 64.3; N, 7.5. Found: Br, 64.0; N, 7.7.

The combined mother liquors were concentrated to dryness. The residual solid (8.9 g) was resolved into its components by preparative tlc.[5] The first fraction, 120 mg (0.5%), consisted of **6**, a white crystalline solid melting at 144–145° (from methanol).

Anal. Calcd for $C_6Br_4N_2S$: C, 16.0; H, 0.0; Br, 70.8; N, 6.2; S, 7.1. Found: C, 16.0; H, 0.2; Br, 71.0; N, 6.2; S, 7.4.

The second fraction consisted of **3** (starting material) and was discarded. Fraction no. 3 consisted of 1.2 g of **5**; fraction 4 consisted of 5.1 g of **4**. The total yield of **4** was 35.3%; the total yield of **5** was 7.6%.

Reaction of 2,1,3-Benzothiadiazole (1) with Bromine in Refluxing 70% Nitric Acid.—A mixture of 27.2 g (0.2 mol) of **1** in 300 ml of 70% nitric acid was heated under reflux with stirring while 144 g (0.9 mol) of bromine was added within 30 min. After about 1 hr, a white crystalline solid precipitated from the refluxing solution; it was shown to be 4,7-dibromo-2,1,3-benzothiadiazole (**3**) (by glc), mp 188–189° (lit.[9] 184–185°). However, the precipitate redissolved gradually. After 6 hr, glc indicated that starting material **1** and intermediate **3** had disappeared. The cooled reaction mixture was poured into water and the product was filtered, washed well with water, and dried to yield 28.8 g (51.5%) of a light yellow crystalline solid consisting of a mixture of **4**, **5**, and **6** in the ratio of 84:14:2 (by glc).

Registry No.—**3**, 15155-41-6; **4**, 26460-78-6; **5**, 26460-79-7; **6**, 26460-80-0.

(9) V. G. Pesin, A. M. Khaletskii, and C. Chzhi-Chzhun, *J. Gen. Chem. (USSR)*, **27**, 1648 (1957).

Photolytic Studies on 4-Hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl, a Stable Nitroxide Free Radical

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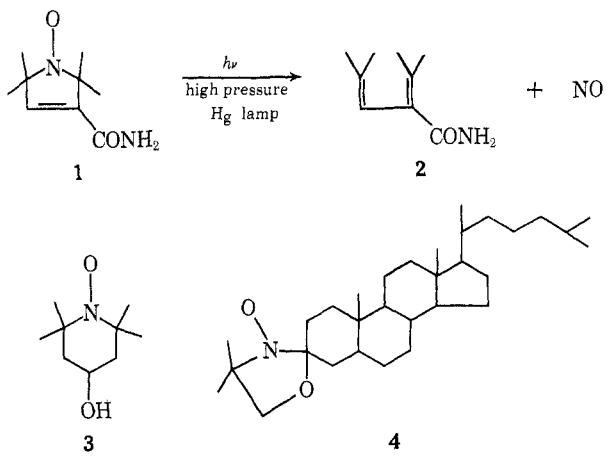
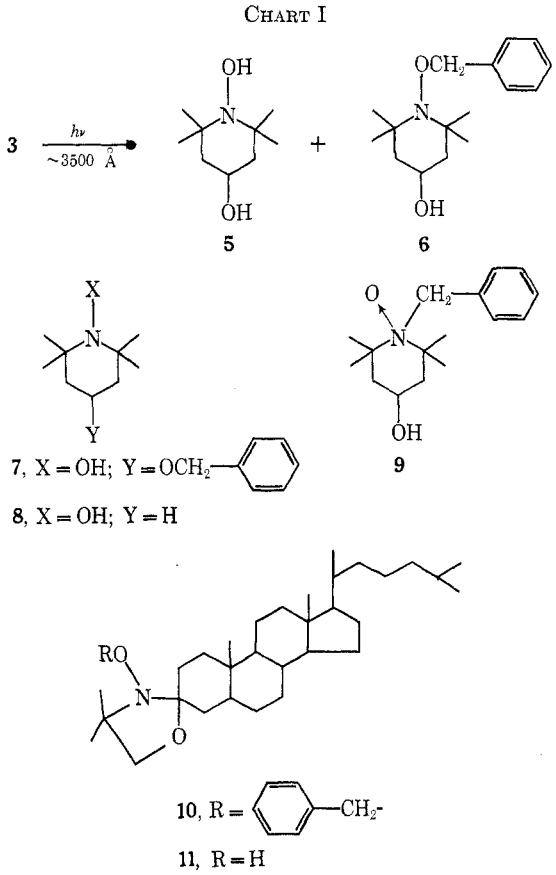
Recently,[3] we reported on the photolysis of the stable nitroxide, 3-carbamoyl-2,2,5,5-tetramethylpyrroline-1-oxyl (**1**), a process which afforded diene **2** in high yield. Under the same conditions the alcohol nitroxide **3** and the steroid nitroxide **4** underwent reaction at a much slower rate. We have now examined the photolysis of nitroxides **3** and **4** under somewhat different conditions. The products are in marked contrast to those derived from nitroxide **1** and are reported herewith.

Irradiation of a vacuum-degassed toluene solution



which was ~0.02 *M* in 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (**3**)[4] for 96 hr in sealed Pyrex tubes with ~3500 Å light resulted in almost complete (>98%) disappearance of starting material as estimated by esr spectroscopy. Removal of the solvent, followed by trituration of the resulting solid with benzene afforded a crystalline residue of 1,4-dihydroxy-2,2,6,6-tetramethylpiperidine (**5**)[5] (Chart I) (~50% crude yield).

CHART I



A recrystallized sample was shown to be identical with authentic **5**[5] by mixture melting point and spectral comparisons. Chromatography of the benzene-soluble

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(1) NDEA Graduate Fellow, 1966–1969; PRF Graduate Fellow, 1969–1970.

(2) Undergraduate Research Participant, 1966–1968.

(3) J. F. W. Keana and F. Baitis, *Tetrahedron Lett.*, 365 (1968).

(4) E. G. Rozantsev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **12**, 2187 (1964); *Chem. Abstr.*, **62**, 7721e (1965).

(5) E. G. Rosantsev and V. A. Golubev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **5**, 891 (1966); *Chem. Abstr.*, **65**, 10559e (1966).

fraction afforded 1-benzyloxy-4-hydroxy-2,2,6,6-tetramethylpiperidine (**6**) (50% crude yield), identified on the basis of analytical and spectral data (see Experimental Section) and the following observations.

That the substance was not 1-hydroxy-4-benzyloxy-2,2,6,6-tetramethylpiperidine (**7**) was shown by the failure of **6** to undergo oxidation to the corresponding nitroxide free radical upon treatment with air or *m*-chloroperoxybenzoic acid, oxidizing agents which readily oxidize, *inter alia*, *N*-hydroxy derivative **5** and 1-hydroxy-2,2,6,6-tetramethylpiperidine (**8**) to the corresponding nitroxides. The unlikely alternative *N*-oxide structure **9** for substance **6** was ruled out when it was demonstrated that substance **6** was thermally stable in dimethylacetamide at 170°. Compound **9** would have been expected to suffer a Meisenheimer rearrangement to structure **6** under these conditions.[6]

In a similar series of experiments a pale yellow toluene solution of steroid nitroxide **4**[7] was irradiated for 144 hr, affording a near colorless solution containing almost no (<2%) starting nitroxide (by esr). Since *N*-hydroxy derivative **11** appeared to suffer hydrolysis upon chromatography, a stream of dry oxygen was bubbled through the photolyzed solution prior to analysis in order to oxidize (see above) **11** back to stable nitroxide **4**. Chromatography at this point led to *N*-benzyloxy derivative **10** in 39% yield, identified on the basis of analytical and spectral data, and nitroxide **4** in 57% yield.

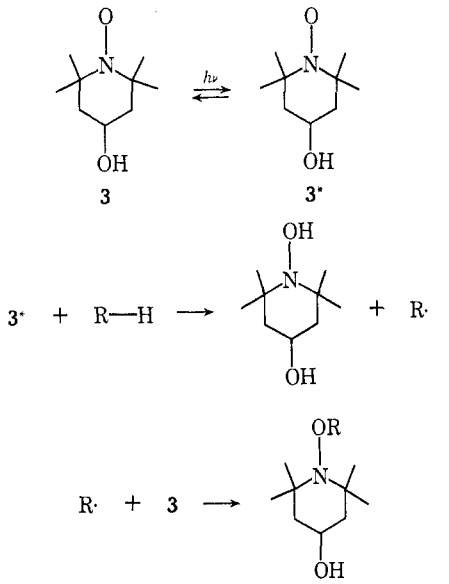
The nature of the photo products derived from nitroxides **3** and **4** suggests that the excited nitroxide is an effective hydrogen atom abstractor. Table I summarizes the results of a study of the effect of solvent on the rate of disappearance of nitroxide **3** upon irradiation of a $\sim 10^{-4}$ *M* solution while inside the cavity of an esr spectrometer. The light was from a PEK high pressure mercury lamp, filtered through Pyrex. The photolysis proceeded most rapidly in cumene and became progressively slower as the solvent was changed from cumene to toluene to cyclohexane to benzene, in qualitative accord with the respective hydrogen atom donor abilities of those solvents.[8] When the light was filtered so as to approximate the output of the Rayonet 3500-Å range lamps employed in the preparative experiments, the rate of disappearance of esr signal intensity in the solvents other than cumene proved too slow for convenient measurement.

TABLE I
RELATIVE RATES OF PHOTOLYSIS OF **3** IN VARIOUS SOLVENTS

Solvent	Relative rate
Cumene	420
Toluene	1.1
Cyclohexane	1.0
Benzene	0.52

A reaction sequence consistent with the above data and analogous to that proposed by Pitts[9] for the photoreduction of 2,2-diphenyl-1-picrylhydrazyl (DPPH) in hydrocarbons is shown in Scheme I. While no 1,2-diphenylethane was detected when irradiations were carried out in toluene, small amounts (~5%, based on starting **3**) of biphenyl could be isolated from the photolysis mixture by chromatography when benzene was the solvent, suggesting that excited nitroxide **3** is capable of abstracting a hydrogen atom from benzene to produce a phenyl radical.[10] Attack of phenyl radical on another benzene molecule followed by a disproportionation or oxidation step would afford biphenyl.[11] Benzyl radical, on the other hand, would not be expected to attack the aromatic ring of another toluene molecule and thus benzyl radical survives long enough to be scavenged by a molecule of nitroxide **3** to produce **6**.

SCHEME I



The ability of an excited nitroxide grouping to abstract a hydrogen atom could provide a novel method of functionalization at a site remote from the grouping in a large molecule, a possibility which we are presently investigating.

Experimental Section

Infrared spectra were recorded with a Beckman IR-5 spectrometer. The small letters in parentheses found after infrared maxima refer to the relative intensities of the peaks. Weak, moderate, and strong are referred to as w, m, and s, respectively.

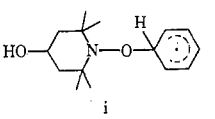
(6) See, *inter alia*, L. D. Quin, and L. A. Shelburne, *J. Org. Chem.*, **30**, 3135 (1965).

(7) J. F. W. Keana, S. B. Keana, and D. Beetham, *J. Amer. Chem. Soc.*, **89**, 3055 (1967).

(8) W. A. Pryor, "Free Radicals," McGraw-Hill, New York, N. Y., 1966, p 170.

(9) J. N. Pitts, Jr., E. A. Schuck, and J. K. S. Wan, *J. Amer. Chem. Soc.*, **86**, 296 (1964).

(10) Alternatively, the process leading to biphenyl might be initiated by attack of an excited nitroxide on a benzene molecule to produce species i,



i

dimerization of which, followed by loss of two molecules of **5**, would afford biphenyl.

(11) D. F. DeTar, *J. Amer. Chem. Soc.*, **89**, 4058 (1967).

Nmr spectra were determined on a Varian Associates Model A-60 high-resolution spectrometer. Chemical shifts are recorded in parts per million (δ) downfield from internal TMS. Elemental analyses were performed by either Alfred Berhardt Laboratories, Mullheim, Germany, or Micro-Tech Laboratories, Skokie, Ill. Preparative scale irradiations were conducted in a RPR-100 Rayonet photochemical apparatus employing the 3500-Å range lamps and fitted with a merry-go-round attachment.

Preparative Irradiation of 4-Hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (3).—Three Pyrex tubes were each charged with 40 mg of nitroxide **3**[4] and 10 ml of toluene. The solutions were vacuum-degassed three times, sealed in the tubes, and then irradiated for 96 hr at 30–40°. Removal of the toluene under reduced pressure afforded a residue which was triturated with benzene. The crystalline solid which remained, 69 mg (~50% crude yield), mp 144–150°, was recrystallized from hexane–ether to give 40 mg (30% yield) of pure diol **5**, mp 156–158° (lit.[5] mp 158°), no melting point depression upon admixture with authentic **5**.[5]

Immediate chromatography of the benzene-soluble fraction over basic alumina and elution with pentane afforded 109 mg (~50% crude yield) of a colorless oil which crystallized upon scratching. Recrystallization from pentane afforded 16 mg (8% yield) of 1-benzyloxy-4-hydroxy-2,2,6,6-tetramethylpiperidine (**6**) as white needles: mp 87–87.5°; nmr (CCl_4) 1.21 (s, 6, pair of methyl groups), 1.28 (s, 6, pair of methyl groups), 1.7 (m, 4, ring protons), 3.9 (m, 1, H-4), 4.78 (s, 2, benzylic protons), 7.24 (s, 5, aromatic protons); ir (CCl_4) 3350 (m), 3000 (s), 1450 (m), 1380 (s), 1250 (s), 1190 (m), 1045 (s), 1025 cm^{-1} (s).

Anal. Calcd for $C_{16}H_{25}NO_2$: C, 73.00; H, 9.51; N, 5.32. Found: C, 72.78; H, 9.57; N, 5.40.

Irradiation of Steroid Nitroxide 4.—Six Pyrex tubes were each charged with 40 mg of nitroxide **4**[7] and 10 ml of toluene. The solutions were vacuum-degassed three times, sealed in the tubes, and then irradiated for 144 hr at 30–40°. It could be estimated by esr spectroscopy that less than 2% of starting nitroxide **4** remained after the photolysis. Dried oxygen was then bubbled through the near colorless solutions for 24 hr. Removal of the toluene under reduced pressure afforded a pale yellow solid which was chromatographed over silica gel. Elution with 5:1 hexane–benzene afforded 113 mg (39% yield) of a white solid, mp 55–62°. Recrystallization from ether–methanol gave *N*-benzyloxy derivative **10** as white needles: mp 74–76°; nmr (CCl_4) 0.6–2.1 (m, 52), 3.43 (s, 2, oxazolidine ring protons), 4.65 (s, 2, benzylic protons), 7.28 (s, 5, aromatic protons).

Anal. Calcd for $C_{38}H_{61}NO_2$: C, 80.99; H, 10.83; N, 2.48. Found: C, 80.94; H, 10.80; N, 2.79.

Elution with benzene afforded 133 mg (57% yield) of a pale yellow solid which was recrystallized from ether–methanol and shown to be identical with starting **4** by ir and melting point comparisons.

Determination of Relative Rates of Photolysis of 3 in Various Solvents.—Rates of photolysis were determined on a Varian 4502 esr spectrometer equipped with a 50% transmittance cavity. The light source was a 100-W PEK high-pressure mercury lamp mounted on an optical bench about 50 cm from the cavity. The light was focused with quartz optics and passed through a Pyrex filter. Reagent grade cumene, toluene, cyclohexane, and benzene were carefully purified prior to use. Irradiations were conducted in stoppered quartz tubes and nitrogen was passed through the solutions immediately prior to irradiation. The photolysis exhibited cleanly first-order kinetics in each instance.

Registry No.—**3**, 2226-96-2; **4**, 78353-76-9; **6**, 26460-91-3; **10**, 26460-92-4.

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α-Ketols from Hydride Reduction of a Steroidal Enamino Ketone and the Corresponding α Diketone[1]

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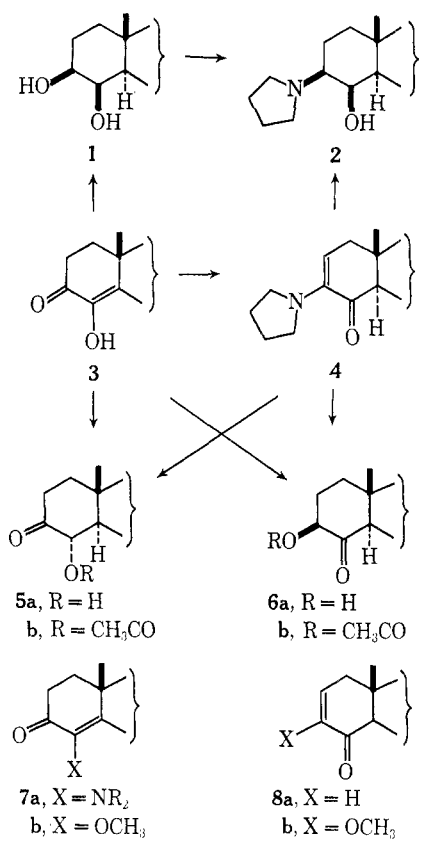
We describe here the reduction of the steroidal α diketone **3** and its derived enamine **4** with sodium borohydride, lithium aluminum hydride, and other reducing systems. Our interest in the reduction of the enamine **4** arose from the need to generate 3-amino-4-hydroxy steroids, both as precursors of steroidal heterocycles and as synthetic intermediates for naturally occurring steroid alkaloids. The pyrrolidyl enamine **4** seemed a convenient model compound for these studies, and the initial reduction results dictated additional experiments with the α diketone[2] **3**. The ultraviolet (λ_{max}^{MeOH} 277 nm, ϵ 12,500) and infrared ($\nu_{max}^{CHCl_3}$ 3484, 1672, and 1645 cm^{-1}) spectra of **3** testify to the enolized system and the nmr spectrum (no vinyl hydrogen) rules out the alternative 3-hydroxy-Δ^2-4-oxo system.[3] Reaction of **3** with pyrrolidine[4] gave, in high yield, the enamine-ketone **4**



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(1) This work was supported, in part, by U. S. Public Health Service Grant HE-08913 and GM 16492.

(2) A. Butenandt, G. Schramm, A. Wolff, and H. Kudszus, *Chem. Ber.*, **69**, 2779 (1936).

(3) *Cf.* D. P. Strike, D. Herbst, and H. Smith, *J. Med. Chem.*, **10**, 446 (1967).

(4) *Cf.* B. Camerino, D. Cattepan, U. Valcavi, and B. Patelli, *Gazz. Chim. Ital.*, **89**, 674 (1959).