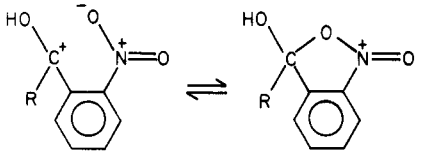
oleum are probably due to the formation of water-soluble sulfonation products, which are too reactive to be isolated.

Treatment of isomeric dinitrobenzophenone isomers with Sulfan (B) in ethylene dichloro led to the preferential reaction of *o*-nitro isomers. This indicates that concentration of sulfur trioxide, rather than acidity, is the controlling factor in the degradation reaction. The preferential nature of the reaction is attributed to the *o*-nitro group activation of the benzene ring toward the electrophilic substitution, owing to the nucleophilic character of the oxygen atom of the nitro group under protonating reaction conditions.[12]



R = *m*-O_2NPh, *m*-O_2NPhCO, CH_3

Experimental Section

Nitration in Fuming Nitric Acid. A total of 1200 g of 90% nitric acid was heated to 70 °C in a 2-L resin pot, and 200 g of benzophenone was added with stirring in increments over 1 h, while the temperature was maintained at 70 °C. After the addition was completed, the temperature was raised to 90 °C for 3 h. The reaction mixture was cooled, poured over 2 kg of cracked ice–water mixture, and filtered. The solids were washed with water (500 g) and digested in a Waring blender with 1 L of 10% sodium hydroxide solution. The solids were collected by filtration, washed four times with 500-g portions of water, and dried in a vacuum oven (100 °C, 16 h) to give 298 g (100%) of white product. The isomeric distribution of dinitrobenzophenones was determined by HPLC with a Varian Model 5000 liquid chromatograph. Analysis was carried out by using an alkylnitrile-bonded phase packing (10 μm particle size) in a 25 × 0.25 cm column. Isocratic elution with a *n*-hexane–methylene chloride–2-propanol mixture (15:82.5:2.5 by volume) at 1 mL/min gave separation of all six isomers at 30 °C, although the *o,p'* isomer was absent in our product. The order of elution followed the following sequence: *p,p'*-, *m,p'*-, *o,p'*-, *m,m'*-, *o,m'*-, and *o,o'*-dinitrobenzophenones. The analysis is reported in Table I.

Nitration in Fuming Sulfuric Acid. Preparation of Nitrating Mixture. A total of 165 g of 90% nitric acid was added dropwise with stirring and cooling to 573 g of oleum (22.5% SO_3), maintaining a temperature during addition below 20 °C.

Nitration. Benzophenone (200 g) was dissolved in 1910 g of oleum (22.5% SO_3), maintaining a temperature during addition around 20 °C. To this stirred mixture was added dropwise the nitrating mixture over 2 h at 15–20 °C. The reaction was then stirred for 0.5 h at room temperature and then heated to 70 °C for 1 h. After cooling, the reaction mixture was worked up as before. A total of 252 g (84%) of tan product was obtained containing 93.7% of the *m,m'*-dinitrobenzophenone. The final concentration of sulfur trioxide was estimated at 12%.

The above procedure was repeated with using 200 g of benzophenone, 165 g of 90% nitric acid, and 2500 g of oleum (33% SO_3). After the reaction mixture was heated to 70 °C for 0.2 h, 179 g (60%) of product was recovered containing 93.5% of the *m,m'*-dinitrobenzophenone.

In the final experiment, 200 g of benzophenone, 1260 g of oleum (33% SO_3), and 165 g of 90% nitric acid were reacted as above. With the reduced amount of oleum, however, it required 2 h at 80 °C for the *o,m'*-dinitro isomer to degrade. On workup, 232 g (77%) of product was isolated, containing 93.5% of desired isomer.

Nitration of 1,1-Diphenylethane. Into a 3-L, three-necked, round-bottomed flask, equipped with a mechanical stirrer, thermowell, and an addition funnel, was added 2550 g of 85% nitric acid (1610 mL of 90% HNO_3 and 140 mL of water), which was then cooled to 5–10 °C. To the stirred acid solution was added 280 g of 1,1-diphenylethane over 2.5 h, maintaining the temperature during addition below 10 °C. After the addition was completed, the product was allowed to warm to room temperature and was stirred for 30 min. It was then poured over ice–water and extracted with toluene. The organic layer was then washed with water, with 5% sodium hydroxide solution, and again with water. After being dried (anhydrous $MgSO_4$), the product was taken to dryness in a rotary evaporator to give a partially crystallized dark red oil, 389 g (93%).

Oxidation of Nitrated 1,1-Diphenylethane. A total of 135 g of nitrated diphenylethane was charged into a 1-L, 316 stainless-steel autoclave, followed by 200 g of water. The autoclave was heated to 170 °C and maintained at that temperature while 170 mL of 70% nitric acid was added over 1.5 h. When the addition of acid was complete, the reaction was allowed to proceed at 170 °C for 30 min, developing a final pressure of 450 psig. After the reaction mixture was cooled a total of 111 g of yellow solids was obtained by filtration (82%). Analysis by HPLC showed the following composition of dinitrobenzophenone isomers: *p,p'*, 57.9%; *m,p'*, 13.3%; *o,p'*, 25.0%; *o,m'*, 3.0%; *o,o'*, 0.8%.

Reaction of Nitro Aromatic Ketones with Oleum. A total of 50 g of the dinitrobenzophenones prepared above was added to 200 mL of oleum (15% SO_3), and the solution was heated with stirring to 70 °C. A sample was taken, and heating was continued for 1 h. The product was poured over ice–water, filtered, and washed two times with 10% sodium hydroxide solution (200 mL) and two times with water. After the product was dried in a vacuum oven (90 °C, 16 h), a total of 31.1 g (62%) of tan product was recovered. Analysis by HPLC showed only two dinitrobenzophenone isomers: *m,p'*, 18.3%; *p,p'*, 81.7%.

Registry No. *o,o'*-Dinitrobenzophenone, 51727-42-5; *o,m'*-dinitrobenzophenone, 60191-42-6; *m,m'*-dinitrobenzophenone, 21222-05-9; *m,p'*-dinitrobenzophenone, 1469-74-5; *p,p'*-dinitrobenzophenone, 1033-26-7; *o,p'*-dinitrobenzophenone, 79172-41-1; benzophenone, 119-61-9; 1,1-diphenylethane, 612-00-0.

(12) Szmant, H. H.; Harmuth, C. M. *J. Am. Chem. Soc.* **1959**, *81*, 962.

Electrochemical Reduction of Epoxy Ketones

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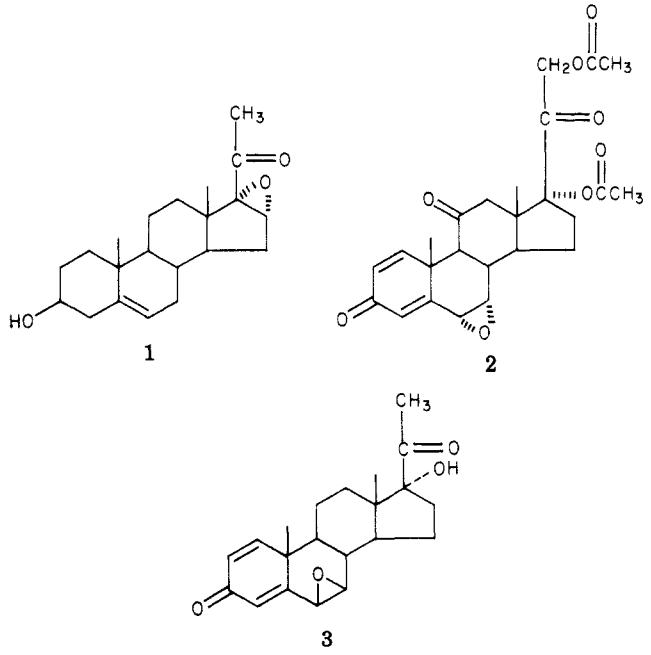
Hitherto, particularly in steroids, reductions of epoxy-keto systems for generation of a hydroxy ketone have been effected with reducing agents such as chromous ions,[1] or aluminum amalgam,[2] or palladium on barium sulfate with cyclohexene.[3] Our experiences with chemical reductive processes, particularly those with chromous salts and palladium, prompted us to investigate an alternative process.

To our knowledge electrochemistry has not previously been utilized for the transformation of epoxy ketones to hydroxy-keto systems. We report the successful application of the concept of electrochemical reduction for these systems. As will be noted, yields are relatively low, but we consider this point to be of secondary consideration for the purpose of this report.

(1) C. H. Robinson and R. Henderson, *J. Org. Chem.*, **37**, 565 (1972), and references therein cited.
(2) (a) A. M. M. Hossain, D. N. Kirk, and G. Mitra, *Steroids*, **27**, 603 (1976); (b) D. N. Kirk and M. L. Sae Melo, *ibid.*, **34**, 683 (1979).
(3) (a) Von R. Imhof, E. Gossinger, W. Graf, W. Schnuriger, and H. Wehrli, *Helv. Chim. Acta*, **54**, 2775 (1971); (b) E. Gossinger, W. Graf, R. Imhof, and H. Wehrli, *ibid.*, **54**, 2785 (1971).

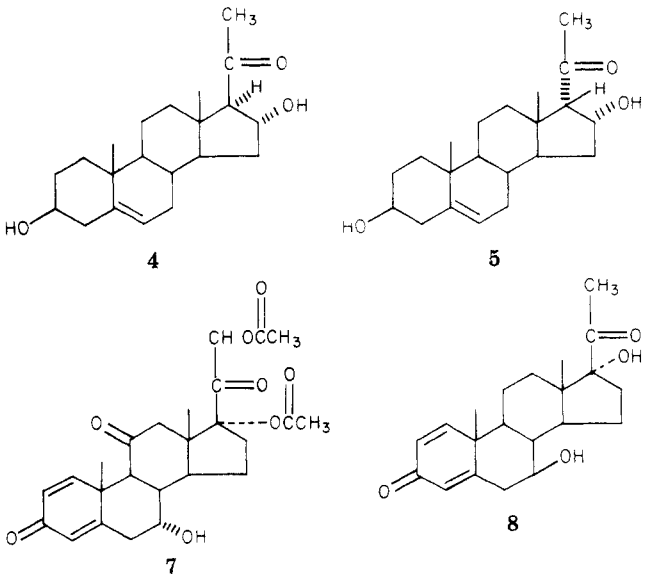
0022-3263/81/1946-5017$01.25/0

The substrates that we have studied in this conversion are 16α,17α-oxypregnenolone (1),[4] 17α,21-dihydroxy-6α,7α-oxy-1,4-pregnadiene-3,11,20-trione 17,21-diacetate (2), and 17α-hydroxy-6β,7β-oxy-1,4-pregnadiene-3,20-dione (3).



1 2 3

Oxide 1 was transformed electrochemically to the 16α-hydroxy 4[5] in 29% yield, as well as in 6% yield to the 16α-hydroxy-17-iso 5.[5c] The conjugated 6α,7α-oxide 2 was converted electrochemically to the 7α-hydroxy 7 in 26% yield,[9] and the conjugated 6β,7β-oxide 3 was similarly transformed to the 7β-hydroxy 8 in 36% yield. To our knowledge conversion of a 6β,7β-oxy-keto system by any of the reductive media referred to above has hitherto not been reported.



4 5 7 8

It is our consideration that electrochemical reduction of the type herein reported may have general applicability beyond its utility in steroids.

Experimental Section[6]

16α-Hydroxy-5-pregnenolone (4) and 16α-Hydroxy-17-iso-5-pregnenolone (5). A 20-mL solution consisting of 75% 3A ethanol (denatured with approximately 5% commercial methanol) and tetrabutylammonium bromide (0.2 M) and containing 50 mg of 1[4] was deaerated with high-purity argon (previously saturated with the solvent) for at least 30 min prior to reduction under argon at −2.10 V (SCE). Controlled-potential electrolyses[7] were continued until the current decreased to that of a blank.

The reaction solution was diluted with water and extracted with ethyl acetate. The EtOAc evaporated residue of 45 mg was chromatographed on 1000 μm silica gel plates, with successive passes of 4:1 $CHCl_3$/EtOAc and then 2:1 $CHCl_3$/EtOAc. Extraction of two areas with EtOAc afforded 14 mg of 16α-hydroxypregnenolone (4)[5] [$[\alpha]^{26}_D$ −10.2° (EtOH); CD, $[\theta]_{286}$ +12557 (MeOH); IR (Nujol) λ_{max} 3350, 1720, 1047 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.54 (13-CH_3), 0.93 (10-CH_3), 2.04 (20-CH_3), 3.20 (approximately, 3α-H), 4.5 (m, 16β-H, 3β-OH, and 16α-OH, with D_2O, only 16-βH), 5.32 (br d, 6 H); mass spectrum, m/z 332, 314, 299 (mol wt found 332.2344, calcd for $C_{21}H_{32}O_3$ 332.2351)], and 3 mg of the 17-iso analogue 5[5c] [^1H NMR (Me_2SO-d_6) δ 0.90 (13-CH_3), 1.04 (10-CH_3), 2.10 (20-CH_3), 4.28 (br, 16β-H), 4.58 (d, J = 2 Hz, 3β-OH), 4.84 (d, J = 2 Hz, 16-OH), 5.26 (br, 6 H); CD, $[\theta]_{282}$ sign is negative, qualitative measurement (MeOH); mass spectrum, m/z 332, 314, 299 (mol wt found 332.2341, calcd for $C_{21}H_{32}O_3$ 332.2351)].

7α,17α,21-Trihydroxy-1,4-pregnadiene-3,11,20-trione 17,21-Diacetate (7). A 30-mL solution consisting of 50% aqueous methanol, trimethylamine–HCl buffer (pH 9, 0.1 M) and containing 49.3 mg of the 6α,7α-oxy 2[8] was reduced[9] at −0.90 V (SCE) with controlled-potential electrolyses[7] continued until the current decreased to that of a blank.

The reaction was diluted with water and extracted with ethyl acetate. Evaporation afforded a residue of 46.5 mg, which was chromatographed on 1000-μm silica plates, using 2:1 $CHCl_3$/EtOAc to obtain 13 mg of 7: $[\alpha]^{26}_D$ +74.3 (dioxane); UV (MeOH) λ_{max} 238 nm (ε 14 200); ^1H NMR (Me_2SO-d_6) δ 0.616 (13-CH_3),

(4) P. L. Julian, E. W. Meyer, and I. Ryden, *J. Am. Chem. Soc.*, **72**, 367 (1950); P. L. Julian, E. W. Meyer, W. J. Karpel, and I. R. Waller, *ibid.*, **72**, 5145 (1950).

(5) (a) S. Bernstein, M. Heller, and S. M. Stolar [*J. Am. Chem. Soc.*, **76**, 5674 (1954)] report 4 by an alternate route: $[\alpha]^{24}_D$ −20 (EtOH); IR λ_{max} (Nujol) 3350, 1705, 1045 cm^{-1}. (b) Reference 2b reports aluminum amalgan conversion of 1 to 4, in "virtually a quantitative conversion". References therein cite low yield with chromous acetate. (c) Because the pH of the reaction medium changes from neutral to alkaline, we consider that 5 may arise from 4 via alkaline epimerization of the acetyl side chain.

(6) Mass spectra were obtained on a single-focusing Varian-MAT CH-5 (resolution 1000, source temperature 250 °C); accurate mass determinations of molecular ions were obtained by peak matching with a Varian-MAT 312 double-focusing mass spectrometer (resolution 5000, source temperature 150 °C). NMR spectra were obtained with a CFT-20 spectrometer, using Me_4Si as an internal standard; UV spectra were obtained on a Cary 118; rotations were determined on a Rudolph automatic polarimeter; infrared spectra were obtained with a Perkin-Elmer Model 180 spectrophotometer; and circular dichroism analyses were performed with a JASCO J-500A spectropolarimeter.

(7) Controlled-potential electrolyses were carried out with a Princeton Applied Research (Princeton, NJ) Model 170 electrochemistry system with an X-Y recorder display of the electrolyses current and a 10-cm^2 mercury pool cell [J. E. Harrar and C. L. Pomernacki, *Anal. Chem.*, **45**, 57 (1973), Figure 3, p 62] with 0.1 M tetramethylammonium chloride solution in both the salt bridge and the anode compartment.

(8) Prepared from the 1,4,6-triene essentially in the manner of A. L. Nussbaum, G. Brabazon, T. L. Popper, and E. P. Oliveto [*J. Am. Chem. Soc.*, **80**, 2722 (1958)], using metachloroperbenzoic acid in *tert*-butyl alcohol and methylene chloride: UV (MeOH) λ_{max} 240 nm (ε 15 000); $[\alpha]^{25}_D$ +63.5° (dioxane); ^1H NMR (Me_2SO-d_6) δ 0.654 (13-CH_3), 1.31 (10-CH_3), 3.50 (J = 4 Hz), and 3.82 (J = 4 Hz) (6-βH and 7-βH), 4.73 (21-$OCOCH_3$), 6.09 (d of d, J = 10, 1.6 Hz, 2 H), 6.43 (d, J = 1.6 Hz, 4 H), 7.67 (d, J = 10 Hz, 1 H); mass spectrum, m/z 456 (mol wt found 456.1767, calcd for $C_{25}H_{28}O_8$ 456.1784).

(9) (a) The $\Delta^{1,4}$-3-oxo-6α,7α-oxy system has been converted with palladium in the manner of ref 3 to the $\Delta^{1,4}$-3-oxo-7α-hydroxy system in these laboratories: unpublished work of E. Smith, G. Swiss, M. J. Gentles, and E. L. Shapiro. Complex mixtures were obtained. The yield of related substrate was in the order of 35%. (b) With chromous acetate a related substrate bearing the 3-oxo-$\Delta^{1,4}$-6α,7α-epoxy system was converted in our laboratories to its 7α-hydroxy product in approximately 40% yield. (c) Reference 1 cites chromous acetate conversion of the monoene 3-oxo-Δ^4-6α,7α-epoxy system in approximately 50% yield. Abu M. M. Hossain, D. N. Kirk, and G. Mitra [*Steroids*, **27**, 603 (1976)] report the conversion of a monoene 3-oxo-Δ^4-6α,7α-epoxy system with aluminum amalgam in 62% yield.

1.37 (10-CH_3), 2.06 and 2.08 (21-$OCOCH_3$ and 17-$OCOCH_3$), 3.94 (br, 7β-H), 4.77 (21-CH_2), 4.92 (d, J = 3 Hz, 7β-OH), 5.93 (4 H), 6.06 (d of d, J = 10, 2 Hz, 2 H), 7.59 (d, J = 10 Hz, 1 H); mass spectrum, m/z 458 (mol wt found 458.1950, calcd for $C_{25}H_{30}O_8$ 458.1940).

7β,17α-Hydroxy-1,4-pregnadiene-3,20-dione (8). In the manner of the electrochemical conversion of **2** to **7**, 6β,7β-oxy-17α-hydroxy-1,4-pregnadiene-3,20-dione (**3**;[10] 50.7 mg) was converted to a residue of 36.5 mg. Chromatography on 1000-μm silica gel plates (2:1 $CHCl_3$/EtOAc) afforded 17 mg of **8**: UV (MeOH) λ_{max} 243 nm (ε 14 400); ^1H NMR (Me_2SO-d_6) δ 0.566 (13-CH_3), 1.19 (10-CH_3), 2.09 (20-CH_3), 3.12 (br, 7-αH), 4.65 (d, J = 7 Hz, 7β-OH), 5.07 (17α-OH), 5.94 (4 H), 6.08 (d of d, J = 10, 2 Hz, 2 H), 7.16 (J = 10 Hz, 1 H); mass spectrum, m/z 344 (mol wt found 344.1979, calcd for $C_{21}H_{28}O_4$ 344.1987).

Acknowledgment. We thank Mr. P. Bartner, Mr. C. Eckhart, and Dr. M. Puar of the Physical and Analytical Chemistry Department for helpful discussions respectively with mass spectra, circular dichroism, and NMR data.

Registry No. 1, 974-23-2; 2, 79172-19-3; 3, 79172-20-6; 4, 520-88-7; 5, 79253-97-7; 7, 79172-21-7; 8, 79172-22-8.

(10) Prepared by L. Weber of these laboratories from the 1,4,6-triene essentially in the manner of H. Laurent, G. Schulz, and R. Wiechert [*Chem. Ber.*, **102**, 2570 (1969)], using *N*-bromosuccinimide, $HClO_4$, H_2O, dioxane, followed by K_2CO_3 in EtOH, acetone, water, on the 6-hydroxy-7-bromo intermediate; for **3**: UV (MeOH) λ_{max} 246 nm (ε 15 760); $[\alpha]^{26}_D$ −93.6° (dioxane); ^1H NMR (Me_2SO-d_6) δ 3.42 (J = 4 Hz) and 3.71 (J = 4 Hz, 6-αH and 7-αH), 6.13 (d of d, J = 10, 2 Hz, 2 H), 6.5 (d, J = 2 Hz, 4 H), 7.09 (d, J = 10 Hz, 1 H); mass spectrum, m/z 342 (mol wt found 342.1852, calcd for $C_{21}H_{26}O_4$ 342.1831).

N-[(4-Nitro-1*H*-inden-1-ylidene)methyl]dialkylamines by an Unexpected Reaction

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We have recently prepared 4-substituted indoles from 2-methyl-3-nitrobenzaldehyde by elaboration of the carboxaldehyde function prior to indole-nucleus formation by the Batcho–Leimgruber process.[1] To further assess the scope of this sequence, we investigated the fate of the 2-methoxyethenyl side chain in the reaction of 1-(2-methoxyethenyl)-2-methyl-3-nitrobenzene (**1**) with *N*,*N*-dimethylformamide dimethyl acetal and pyrrolidine in *N*,*N*-dimethylformamide. Of particular interest was the possibility of generating enamine **2** and the preparation of 4-(2-methoxyethenyl)-1*H*-indole by subsequent reductive cyclization. Enamine **2**, however, could not be isolated; instead, a dark magenta, crystalline product with the elemental composition $C_{14}H_{14}N_2O_2$ was the major reaction product. In view of the elevated reaction temperature required for the N,N-disubstituted aminomethylenation, a possible electrocyclic ring closure of the incipient product **2**, yielding a naphthalenoid system, had to be considered. 1-(8-Nitro-2-naphthalenyl)pyrrolidine (**3**), therefore, appeared to be a plausible structural proposal at first. The ^1H NMR spectrum revealed the pyrrolidine moiety, three contiguous benzenoid protons, a singlet at δ 7.78, and an AB pattern at δ 7.28 and 7.58, but J_{AB} was only 5 Hz. As an alternative, 1-[(7-nitro-1*H*-inden-1-ylidene)methyl]-pyrrolidine (**4**), featuring the formally unaltered carbon skeleton of **2** and the AB protons on a five-membered ring, appeared compatible with all spectral data although its genesis was difficult to explain. Roentgen crystallographic analysis revealed yet another isomer as the correct structure; the stereoscopic drawing is shown in Figure 1 and is represented by the two extreme canonical forms **9a** and **9b** (Scheme I). Bond lengths and bond angles of the two independent molecules present in the crystal are listed in Tables I and II, respectively. The pyrrolidine ring approaches planarity and is also nearly coplanar with the indene ring system which, in turn, is nearly coplanar with the nitro group. In the molecule shown in Figure 1 (upper portion, unprimed notation), the nitro group is twisted about 8° out of the indene plane, but deviates only 4° from coplanarity in the molecule shown on the bottom (primed notation).

The bright red color of a solution of **9** points to significant electron delocalization from the pyrrolidine nitrogen

Table I. Bond Lengths (Å) in 9 with Standard Deviations in Parentheses

atoms	unprimed	primed
O1-N2	1.214 (3)	1.220 (3)
O2-N2	1.231 (5)	1.229 (4)
N1-C10	1.316 (3)	1.331 (3)
N1-C12	1.467 (5)	1.472 (3)
N1-C15	1.457 (4)	1.458 (4)
N2-C4	1.456 (5)	1.455 (3)
C1-C2	1.436 (5)	1.439 (4)
C1-C7a	1.450 (3)	1.458 (3)
C1-C10	1.375 (5)	1.366 (3)
C2-C3	1.356 (4)	1.355 (3)
C3-C3a	1.434 (4)	1.436 (4)
C3a-C4	1.394 (3)	1.390 (3)
C3a-C7a	1.424 (5)	1.424 (3)
C4-C5	1.390 (5)	1.386 (4)
C5-C6	1.378 (6)	1.384 (4)
C6-C7	1.384 (4)	1.380 (4)
C7-C7a	1.392 (5)	1.386 (4)
C12-C13	1.457 (5)	1.450 (5)
C13-C14	1.499 (6)	1.440 (5)
C14-C15	1.515 (4)	1.508 (4)

Table II. Bond Angles (Degrees) in 9 with Standard Deviations in Parentheses

atoms	unprimed	primed
C10-N1-C12	122.5 (3)	122.5 (2)
C10-N1-C15	126.1 (3)	125.5 (2)
C12-N1-C15	111.4 (2)	112.0 (2)
O1-N2-O2	121.6 (3)	121.6 (2)
O1-N2-C4	119.8 (3)	120.0 (3)
O2-N2-C4	118.6 (2)	118.3 (2)
C2-C1-C7a	105.2 (3)	105.0 (2)
C2-C1-C10	132.1 (2)	132.8 (2)
C7a-C1-C10	122.7 (3)	122.2 (2)
C1-C2-C3	110.6 (3)	110.7 (2)
C2-C3-C3a	108.9 (3)	109.1 (2)
C3-C3a-C4	135.5 (3)	135.5 (2)
C3-C3a-C7a	107.0 (2)	107.0 (2)
C4-C3a-C7a	117.4 (3)	117.4 (2)
N2-C4-C3a	120.4 (3)	121.4 (2)
N2-C4-C5	117.6 (3)	116.9 (2)
C3a-C4-C5	122.0 (3)	121.7 (2)
C4-C5-C6	119.1 (3)	119.6 (2)
C5-C6-C7	121.2 (3)	120.8 (3)
C6-C7-C7a	119.7 (3)	119.7 (2)
C1-C7a-C3a	108.2 (3)	108.2 (2)
C1-C7a-C7	131.3 (3)	131.0 (2)
C3-C7a-C7	120.5 (2)	120.8 (2)
N1-C10-C1	130.9 (3)	130.6 (3)
N1-C12-C13	105.2 (3)	103.8 (3)
C12-C13-C14	107.3 (3)	111.0 (3)
C13-C14-C15	106.0 (3)	107.0 (3)
N1-C15-C14	104.8 (3)	104.2 (2)

(1) Maehr, H.; Smallheer, J. *J. Org. Chem.* **1981**, *46*, 1752.

0022-3263/81/1946-5019$01.25/0