acetate group from oxygen at 11 to the carbanion at carbon 1 which is formed in the initial stage of the Birch reduction.

Treatment of 3-methoxy-11,21-diacetoxy-19-nor-1,3,5(10),17(20)-pregnatetraene with osmium tetroxide and hydrogen peroxide yielded 11β,21-diacetoxy-17α-hydroxy-3-methoxy-19-nor-1,3,5(10)-pregnatrien-20-one (IV), m.p. 127–133° dec., $[\alpha]_D + 104°$ (acetone); (*Anal.* Calcd. for $C_{25}H_{32}O_7.H_2O$: C, 64.91; H, 7.41. Found: C, 65.18; H, 7.38). After the 21-acetate group of IV was selectively saponified with sodium bicarbonate, the 20-ketal, m.p. 220–223°, $[\alpha]_D + 61°$ (acetone); (*Anal.* Calcd. for $C_{25}H_{34}O_7$: C, 67.24; H, 7.67. Found: C, 67.15; H, 7.50), was prepared by reaction with ethylene glycol and *p*-toluenesulfonic acid in benzene solution. Reduction of the ketal first with lithium aluminum hydride and then with lithium-ammonia and alcohol followed by acidic hydrolysis completed the chemical synthesis of 19-norhydrocortisone V; m.p. 256–259°; $[\alpha]_D + 112°$ (MeOH); λ_{max}^{EtOH} 241 mμ, *a* 4.21.[7]

Acylation of I with two moles of acetic anhydride and pyridine forms the 3,21-diacetate which when treated with osmium tetroxide and hydrogen peroxide gives 3,21-diacetoxy-11β,17α-dihydroxy-19-nor-1,3,5(10)-pregnatrien-20-one, m.p. 167–168°. (*Anal.* Calcd. for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 67.24; H, 6.99). 3,11β,17α,21-Tetrahydroxy-19-nor-1,3,5(10)-pregnatrien-20-one (VI), m.p. 256–258°; (*Anal.* Calcd. for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57. Found: C, 69.20; H, 7.77), was obtained by mild saponification.

Acylation of I with excess acetic anhydride–pyridine followed by ozonization and lithium aluminum hydride reduction yielded 11β-hydroxyestradiol (VII), m.p. 285–288°; $[\alpha]_D + 129°$ (dioxane); (*Anal.* Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 75.18; H, 8.50).

Using similar techniques 11α-hydroxyestradiol VIII, m.p. 250–251°, $[\alpha]_D -63°$ (acetone); (*Anal.* Found: C, 75.29; H, 8.23) was prepared.

3,11β,17α,21-Tetrahydroxy-19-nor-1,3,5(10)-pregnatrien-20-one (VI) is as potent as hydrocortisone in the granuloma pouch assay, but lacks the glycogen deposition activity of hydrocortisone.

11β-Hydroxyestradiol possesses 0.6 the estrogenic activity of estradiol in stimulating the uterine weight of castrated female rats, whereas the 11α-hydroxy analog is less active.[8]

Acknowledgment.—The authors are indebted to V. R. Shellman for technical assistance; to Dr. J. L. Johnson, Mrs. G. S. Fonken and J. E. Stafford for infrared and ultraviolet absorption studies; to W. A. Struck and associates for microanalyses; and to L. M. Reineke and associates for paper-gram studies.

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[7] A. Zaffaroni, H. F. Ringold, G. Rosenkranz, F. Sondheimer, G. H. Thomas and C. Djerassi, THIS JOURNAL, **76**, 6210 (1954).

[8] The biological activity of the compounds described in this communication will be published in detail elsewhere by Drs. R. O. Stafford and W. W. Byrnes and associates of the Department of Endocrinology of the Upjohn Company.

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RECEIVED JANUARY 4, 1957

COPPER(II) BROMIDE COMPLEXES

Sir:

We wish to report the results of a study of the complexing of bromide ion with copper(II) ion in alcoholic solvents. Organic solvents effect a substantial increase in association of ions, allowing spectrophotometric observations at much lower concentrations of associating species than possible in water, and avoiding occultation of shorter wave-length ranges.[1]

Recent studies of halide complexing with copper(II) in water[2] allowed determination of the band maximum for only one species, $CuBr^+$.[2b] Otherwise, the end absorptions seemed in agreement with the idea that absorption maxima moved to longer wave lengths with increasing number of complexed halide ions.[2a]

We have found that, as increasing amounts of lithium bromide are added to alcoholic solutions of copper(II) perchlorate, new absorption bands successively appear (Fig. 1 illustrates a typical series). On the basis of measurements with other copper(II) concentrations, we have confirmed that each of the bands varies independently of the

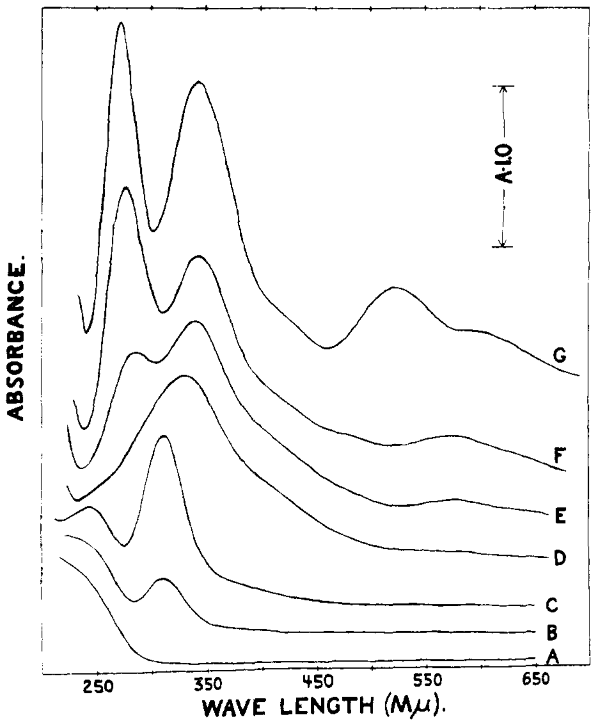

Fig. 1.—$Cu(ClO_4)_2$ concentration in ethanol was 4.00 × 10^{-3} *M*; varying amounts of LiBr were added: A, no LiBr; B, 1.00 × 10^{-3} *M*; C, 4.00 × 10^{-3} *M*; D, 25.0 × 10^{-3} *M*; E, 75.0 × 10^{-3} *M*; F, 720 × 10^{-3} *M*; G, 2800 × 10^{-3} *M* (path length, 0.1 cm.).

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[1] Organic solvents were used previously for cobaltous and nickelous complexes by A. v. Kiss, *et al.*, *Z. physik. Chem.*, **A187**, 211 (1940); **A188**, 27 (1940); L. I. Katzin and E. Gebert, THIS JOURNAL, **72**, 5659 (1950); *Nature*, **175**, 425 (1955); L. I. Katzin, *J. Chem. Phys.*, **20**, 1165 (1952); C. K. Jorgensen and J. Bjerrum, *Nature*, **175**, 425 (1955); *Acta Chem. Scand.*, **7**, 951 (1953); C. K. Jorgensen, *ibid.*, **8**, 175 (1954); H. L. Friedman, THIS JOURNAL, **74**, 5 (1952).

[2] (a) H. M. McConnell and N. Davidson, *ibid.*, **72**, 3164, 3168 (1950); (b) P. S. Farrington, *ibid.*, **74**, 966 (1952); (c) R. Kruh, *ibid.*, **76**, 4865 (1954).

others. The simplest interpretation of the data is that each maximum represents the major absorption band (but not necessarily the only one) for successive complexes of copper(II) ion with bromide ion. Since there are six such bands in methanol, ethanol, *n*-butanol, and isopropyl alcohol,[3] we ascribe the bands to $CuBr^+$, $CuBr_2$, $CuBr_3^-$, $CuBr_4^{--}$, $CuBr_5^{---}$, and $CuBr_6^{----}$. The band positions are given in Table I.

TABLE I[a]

Species	HOH[b]	MeOH	Solvent EtOH	*n*-BuOH	*i*-PrOH
$CuBr^+$	283	306	310	314	310
$CuBr_2$	[c]	238 ± 4	245 ± 4	252 ± 4	248 ± 8[d]
$CuBr_3^-$	338	339 ± 3	344	346	350 ± 3
$CuBr_4^{=}$	271	275	277	279	277
$CuBr_5^{\equiv}$	[d]	573	576	578	575 ± 5[d] (638)[e]
$CuBr_6^{\equiv -}$	514	522	524	525	521

[a] Band positions are considered accurate to 1–2 mμ, unless otherwise noted, and have not been corrected to equivalent ionic strengths [*e.g.*, $CuBr^+$ maximum: μ 0.5×10^{-3}, 310 mμ; μ 50×10^{-3}, 308 mμ, EtOH]. [b] Bands overlap considerably. [c] Presumably obscured by Cu^{++} and Br^- absorptions. [d] Was observed only as a shoulder at the concentrations used. [e] See footnote 3.

The startling result in Table I is the clear alternation in excitation energies for successive odd and even complexes. Equilibrium data[2a] signify that most of the differences must be at the level of the excited states. An oversimplified picture for the transition, presumably one of charge-transfer,[4] *e.g.*, $CuBr_3^- \rightarrow CuBr_2^- \cdot Br^0$, suggests that excited states with *even numbers of halide ions* are more stable than those with odd numbers. A similar situation exists for copper(II) chloride complexes[5] and may be true for ferric complexes with two, three, and four chloride ions.[6]

The relationship of the transition associated with $CuBr^+$ in alcohols to that in water can be shown approximately by plotting the transition energies against the transition energies for the charge-transfer band of 1-methyl-4-carbomethoxypyridinium iodide complex in the same solvents.[7]

Acknowledgment.—The authors wish to express their appreciation to Dr. Edward L. King of this Department for many helpful discussions.

[3] In this solvent a seventh band, apparently linear in copper(II) concentration, appears with certain copper(II)-bromide combinations.

[4] R. S. Mulliken, *J. Phys. Chem.*, **56**, 801 (1952); THIS JOURNAL, **74**, 811 (1952).

[5] R. L. Martin, unpublished.

[6] G. A. Gamlen and D. O. Jordan, *J. Chem. Soc.*, 1435 (1953).

[7] E. M. Kosower, THIS JOURNAL, **78**, 5700 (1956).

[8] Dow Chemical Company Fellow 1956–1957.

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RECEIVED JANUARY 26, 1957

OXIDATION OF *cis*- AND *trans*-1-AMINO-2,6-DIPHENYLPIPERIDINE. A NEW TYPE OF RING CLOSURE

Sir:

We wish to report a new type of stereospecific ring closure. Some examples of anomalous oxidations of 1,1-disubstituted hydrazines have been reported previously.[1,2,3,4,5] For example, the oxidation of 1-amino-2,6-dicyano-2,6-dimethylpiperidine with bromine in aqueous ethanol gave a theoretical yield of nitrogen, *cis*- and *trans*-1,2-dicyano-1,2-dimethylcyclopentane and 2,6-dicyanoheptene-2.[1] Busch and Weiss[3] reported bibenzyl as the principal product when 1,1-dibenzylhydrazine was treated in ethanolic solution with mercuric oxide. We have confirmed this interesting result and obtained an 82.5% yield of bibenzyl and 98% evolution of nitrogen in ethanol at 57°.

The *cis* and *trans* isomers of 1-amino-2,6-diphenylpiperidine were prepared via the N-nitroso compounds (*cis* nitroso, m.p. 66.5–67.5°, *Anal.* Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.65; H, 6.77; N, 10.31. *trans*, m.p. 87–88°. Found: C, 76.44; H, 6.86; N, 10.30) and oxidized with mercuric oxide at 58° in ethanol. The *cis*-1-amino-2,6-diphenylpiperidine (m.p. 133–134°, *Anal.* Calcd. for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.74; H, 8.09; N, 11.37) on oxidation gave a 64.5% yield of *cis*-1,2-diphenylcyclopentane, m.p. 45.8–47°, a 25% yield of 1,5-diphenyl-1-pentene,[6] with a 100% evolution of nitrogen. An infrared spectrum of the mixture of products indicated the presence of only the two aforementioned products. The infrared spectrum of the *cis*-1,2-diphenylcyclopentane was identical with an authentic sample,[7] m.p. 46–47° prepared according to Jappe and Lander,[8] mixture melting point 45.5–47°. The presence of 1,5-diphenyl-1-pentene was established by preparing the 2,4-dinitrobenzenesulfenyl chloride derivative, m.p. 114–115.5°, from the mixture of products. A mixture melting point with the derivative prepared from an authentic sample of 1,5-diphenyl-1-pentene, m.p. 113.5–115° (*Anal.* Calcd. for $C_{23}H_{21}O_4N_2SCl$: C, 60.46; H, 4.63; N, 6.13. Found: C, 60.52; H, 4.46; N, 6.32) melted at 113–115°. Oxidation of the *cis*-1-amino-2,6-diphenylpiperidine with potassium permanganate in acetone solution gave a 35% yield of *cis*-1,2-diphenylcyclopentane and an 88% evolution of nitrogen.

Oxidation of *trans*-1-amino-2,6-diphenylpiperidine, m.p. 80–81° (*Anal.* Calcd. for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.71; H, 7.89; N, 10.93) with mercuric oxide at 58° in ethanol gave a 59% yield of *trans*-1,2-diphenylcyclopentane, m.p. 64–65°[7], a 12% yield of *cis*-1,2-diphenylcyclopentane, a 14% yield of 1,5-diphenyl-1-pentene and 100% of the theoretical evolution of nitrogen. An infrared spectrum of the mixture of products indicated the presence of only the above mentioned products. A 2,4-dinitrobenzenesulfenyl chloride derivative of the olefin from the reaction

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[1] C. G. Overberger, P. Huang and T. B. Gibbs, THIS JOURNAL, **75**, 2082 (1953).

[2] C. G. Overberger and B. S. Marks, *ibid.*, **77**, 4097 (1955); **77**, 4104 (1955).

[3] M. Busch and B. Weiss, *Ber.*, **33**, 2701 (1900).

[4] R. L. Hinman and K. L. Hamm, Abs. of Papers, 130th Meeting, Am. Chem. Soc., 1956, p. 17-O.

[5] L. A. Carpino, *ibid.*, p. 18-O.

[6] W. Borsche and J. Wolleman, *Ber.*, **45**, 3713 (1912); C. G. Overberger and J. J. Monagle, THIS JOURNAL, **78**, 4470 (1956).

[7] H. A. Weidlich, *Ber.*, **71B**, 1601 (1938).

[8] F. Jappe and G. Lander, *J. Chem. Soc.*, **71**, 131 (1897).