CH₃), after recrystallization from ethanol, melted at 110–112°:[7] $\lambda_{max}^{CHCl_3}$ 6.24 (w), 6.32, 6.85, 6.95 μ; λ_{max}^{MeOH} 272 (log ϵ 3.34), 279 mμ (3.33). The nmr (CDCl₃) showed absorption at δ 3.76 ppm for the methoxyl group and an aromatic proton pattern consistent with the presence of three vicinal protons.[11]

The monotrimethylsilyl (TMS) derivative 6 (R = TMS), prepared by selective silylation of 6 (R = H) at 0° with bis(trimethylsilyl)trifluoroacetamide, gave, under the preferred cyclization conditions (see above), a very satisfactory para–ortho ratio of about 20:1, in essentially quantitative yield. The crude product was hydrolyzed with methanol and benzoylated (C₆H₅COCl, C₅H₅N) to yield 7 (R = C₆H₅CO), mp 114–116°, after recrystallization from methanol.[7]

Direct peracid epoxidation of the methoxy olefin 7 (R = CH₃) led to a 5:1 mixture of β and α epoxides[12] as judged by vpc analysis; however, stereoselective formation of the desired α epoxide could be accomplished via the chlorohydrin 9. The benzoate chlorohydrin 9 (R = C₆H₅CO), after preparative tlc (40% yield, not optimized, based on 5 (R = H)) and recrystallization from acetone, melted at 183–189°.[7] The 17-methyl nmr signal occurred at δ 1.50 ppm; however, no decision could be made between the two possible α-hydroxy β-chloro isomers. The phenolic epoxide 10 (R = H), after chromatography and recrystallization from methanol, melted at 196–202°.[7]

Scheme III

9

10   11
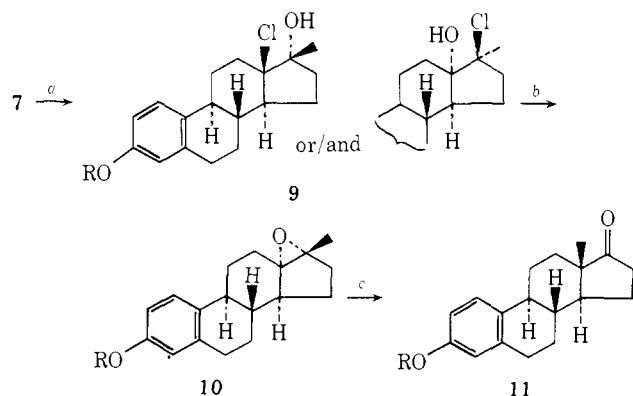
^{a} p-TsNCl₂, 1:9 H₂O–CH₃OCH₂CH₂OCH₃, 10 min, 0°. ^{b} (CH₃)₄-NOH, aqueous acetone, 2 hr, 25°. ^{c} BF₃·Et₂O, benzene, 1 min, 25°.

The crude phenolic epoxide 10 (R = H), upon treatment with boron trifluoride,[13] followed by chromatography, afforded dl-estrone 11 (R = H) (Scheme III), mp 243–252°, in 22% overall yield (eight steps) from 5 (R = H). Recrystallization from acetone gave material, mp 251–255°, which was identical with authentic dl-estrone by mixture melting point, vpc, and ir (KBr).

In the course of studying the cyclization of derivatives of 6 we observed that the para–ortho ratio (7/8) was strikingly dependent upon modification of the leaving (allylic) group of the substrate 6. This result suggested that the cyclization might be a concerted process; hence the matter has been studied in some detail.[14]

(12) Cf. J. Bascoul, C. Reliaud, A. Guinot, and A. Crastes de Paulet, Bull. Soc. Chim. Fr., 4074 (1968); S. K. Pradhan and V. M. Girijavallabhan, Steroids, 13, 11 (1969).

(13) Cf. J. Bascoul and A. Crastes de Paulet, Bull. Soc. Chim. Fr., 189 (1969).

(14) P. A. Bartlett, J. I. Brauman, W. S. Johnson, and R. A. Volkmann, J. Amer. Chem. Soc., 95, 7502 (1973).

For more than 25 years, the synthesis of estrone has held the special interest of chemists,[15] partly because it not only is an important intermediate in the production of 19-nor steroids[16] but it is one of few steroids produced commercially by total synthesis. Although in its present unrefined state[17] our synthesis is not as practical as the Torgov–Smith route,[16] it represents a fundamentally new approach based on a highly efficient, stereospecific olefinic cyclization, and it has versatile potential for development.

(15) For a partial review and bibliography see N. Anand, J. Bindra, and S. Ranganathan, "Art in Organic Synthesis," Holden-Day, San Francisco, Calif., 1970, pp 177–181.

(16) See R. Pappo in "The Chemistry and Biochemistry of Steroids," Vol. 3, No. 1, N. Kharasch, Ed., Intra-Science Research Foundation, Santa Monica, Calif., 1969, pp 123–130.

(17) Pertaining to one of various possible improvements, mechanistic studies[14] suggest the possibility that the resolved form of substrate 6 may cyclize with retention of optical activity, a matter which is currently under investigation.

(18) National Science Foundation Predoctoral Fellow, 1969–1972.

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Concerning the Mechanism of a Nonenzymic Biogenetic-Like Olefinic Cyclization

Sir:

The question of the mechanism of nonenzymic polyolefinic cyclizations, involving the formation of more than one ring, has been open to debate, and up until now there has been no direct evidence on this point. On the one hand, the intermediacy of partially cyclized cations has been shown to be consistent with the observed stereospecificity of such cyclizations.[1] The present communication, on the other hand, presents evidence which supports a process involving concerted formation of two rings in the cyclization of compounds 1 → 2 and 3.

1

2   3
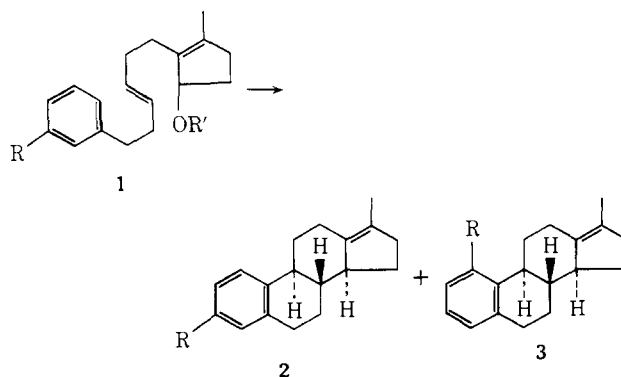
The major synthetic transformation in a total synthesis of estrone,[2] namely the Lewis acid catalyzed cyclizations of allylic alcohols 1, to the corresponding

(1) See inter alia W. S. Johnson, Trans. N. Y. Acad. Sci., 29, 1001 (1967); K. E. Harding, R. C. Ligon, T.-C. Wu, and L. Rodé, J. Amer. Chem. Soc., 94, 6245 (1972); K. E. Harding, J. Biorg. Chem., 2 (3), 248 (1973).

(2) P. A. Bartlett and W. S. Johnson, J. Amer. Chem. Soc., 95, 7501 (1973).

tetracyclic substances **2** and **3** was studied in detail. Several derivatives of the cyclization substrate **1** were prepared from the phenolic cyclopentenol **1** (R = OH; R' = H),[2] and the ratios of products **2** to **3** (para–ortho ratios) were obtained upon cyclization by the addition of the substrate to 3 mol equiv of stannic chloride in methylene chloride at −75°. For R = TMSO (trimethylsilyloxy) and R' = H the ratio of **2** to **3** was 8.4; for R = TMSO and R' = TMS, 2.6; for R = TMSO and R' = C_6H_5CO, 3.1; for R = $C_6H_5CO_2$ and R' = H, 2.4; for R = $C_6H_5CO_2$ and R' = C_6H_5CO, 1.3; for R = CH_3O and R' = H, 3.0.

The dependence of the para–ortho ratio on the nature of the leaving group is most strikingly shown by comparison of the first two cases. That this dependence is probably not a medium effect was suggested by the fact that these ratios were unaffected by a 3.3-fold increase in the amount of stannic chloride or by the prior addition of 1 mol equiv of water to the cyclization mixture. It is important to note that all of these cyclization reaction mixtures were homogeneous and the yields were essentially quantitative. The most obvious rationalization of these results is that the dependence of the para–ortho ratio on the nature of the leaving group requires some degree of bond formation between the aromatic ring and C-9 (as well as between C-8 and C-14) before the interaction of the leaving group with the cation has ceased.

Additional details of the mechanism were probed by varying substituents in the aromatic ring of the cyclization substrates and measuring relative rates of reaction. Cyclopentenols **1** (R = R' = H), **1** (R = CH_3; R' = H), **1** (R = Cl; R' = H), and **1** (R = CF_3; R' = H) were synthesized from the appropriate β-arylpropionaldehydes by a scheme similar to that employed for the preparation[2] of **1** (R = OCH_3; R' = H). Specimens of the various cyclization substrates were obtained as colorless oils.[3,4] Treatment of these new cyclopentenols with stannic chloride in methylene chloride at −95° resulted in extremely rapid, complete cyclization.[5]

Nitroethane with zinc bromide catalyst was found to be a convenient medium for measuring rates. Relative rates were determined for equimolar mixtures of pairs of substrates[6] by determining the relative amounts of cyclization products and starting material by vpc analysis[7] after reaction periods of 5–90 min. Reactions were first order in cyclization substrate. The relative rates are summarized in Table I; various pairwise comparisons gave internally consistent results.

Table I. Relative Cyclization Rates[6] of Substrate **1** (R' = H)

R	σ^a	k_{rel}
CF_3	0.54	1
Cl	0.23	3.12
H	0.00	5.90
CH_3	−0.17	6.50
OCH_3	−0.27	6.70

^{a} Hammett σ values taken from C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 323 (1964).

The relative rates increase with increasing nucleophilicity of the aromatic nucleus, indicating second-order anchimeric assistance by the aryl group in the heterolysis of the allyl–O bond, but a Hammett plot shows pronounced curvature. The data can be accommodated, however, by the formal two-step process,[8] eq 1, for

$$\text{substrate } 1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\text{intermediate A}] \xrightarrow{k_2} \text{products } 2 + 3 \quad (1)$$

which the rate = $k_{obsd}[1]$, where $k_{obsd} = k_1k_2/(k_{-1} + k_2)$. If k_2 is the only step involving participation of the aromatic nucleus, both k_1 and k_{-1} will be independent of the aryl substituents and thus essentially identical for each of the cases in Table I. According to this scheme then, for those cases (Table I) with the more electron-rich substituents (R = CH_3 and OCH_3), k_1 should be rate determining, while for those with the more electronegative substituents (R = Cl and CF_3), k_2 is becoming rate determining. Since a satisfactory Hammett plot can be made only with k_2, it is possible to estimate a minimum ρ for step 2 from the slower cases. Such a plot from the first three examples (Table I) gives a ρ of −1.4.

More rigorously, given that k_1 and k_{-1} are identical for all substrates and that k_1 is indeed rate determining with R = OCH_3,[9] then $k_{obsd}^{OCH_3}/k_{obsd}^R = 1 + (k_{-1}/k_2^R)$. Relative values of k_2^R thus obtained for R = CF_3, Cl, and H give a Hammett plot[10] with ρ = −3. This value, as compared with those[11] for typical electrophilic aromatic substitution reactions (−4.5 to −12), suggests considerable aromatic participation in the present cyclization reactions, but less than might have been expected from alkylation with a fully charged, reactive electrophile.

The nature of the aforementioned intermediate A is not known but could be one (or more) of several possibilities, e.g., the reversibly formed complex of zinc bromide with the oxygen of the hydroxyl group of the substrate, i.e., **1** (R' = H·$ZnBr_2$). Alternatively, a reasonable possibility is an ion pair of the allylic cation resulting from heterolysis of the allylic–O bond of **1** (R' = H·$ZnBr_2$). The tricyclic cation **4** ion paired with the leaving group also could serve as intermediate A, provided it could return cleanly to **1**. However, since **1**, **2**, and **3** represented the sole constituents of the reaction mixture, and no products corresponding to partially cyclized material (derived from **4**) could be

(3) Products were submitted to bulb-to-bulb distillation using a Büchi kugelrohrofen.

(4) The nmr and ir spectra were entirely consistent with the assigned structures, and satisfactory elemental analysis were obtained for all new compounds.

(5) Substrate **1** (R = R' = H) yielded **2** (R = H),[3,4] mp 59–62°, after crystallization from methanol. Similarly, **1** (R = Cl; R' = H) afforded a mixture of **2** (R = Cl)[3,4] and **3** (R = Cl),[3,4] mp 75–76°, after crystallization from methanol. The substrates **1** (R = CH_3; R' = H) and **1** (R = CF_3; R' = H) were cyclized by the zinc bromide method (see below). The tetracyclic products were characterized only as the mixtures of isomers: **2** and **3** (R = CH_3)[3,4] and **2** and **3** (R = CF_3),[3,4] mp 37–40°.

(6) Conditions involved the addition of 1 mol equiv of cyclopentenol to a solution containing 4.3 mol equiv of zinc bromide and 22 mol equiv of water at −23°. The excess water served to obviate any effects of adventitious water as well as that formed as a product of the reaction.
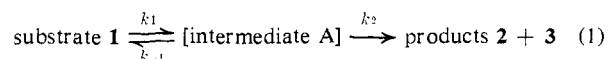
(7) In all cases the reaction mixtures consisted of only starting material and tetracyclic products. Relative vpc detector responses were obtained with pure materials.

(8) Some catalyst, e.g., $ZnBr_2$, is obviously required, but as the kinetics are pseudo first order, and the detailed nature of the catalyst is not known, the catalyst is not included explicitly here.

(9) Consistent with essentially identical rates for R = CH_3 and OCH_3.

(10) Relative k_2 values of 1, 5, 41, 99, and 194 can be obtained for R = CF_3, Cl, H, CH_3, and OCH_3, respectively. The last two values were obtained by extrapolation from the Hammett plot.

(11) See, *inter alia*, H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958).

4
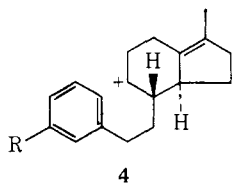
detected [12] we consider **4** an unlikely candidate. Furthermore, there appears to be no precedent for ring opening of such a bicyclic to a monocyclic cation. Finally, if **4** were the intermediate, the value of ρ for the cyclization might be expected to be larger than -3. Thus, the dependence of para:ortho ratios on the leaving group,[13] the second-order anchimeric assistance in a two-step scheme, the relatively low value of ρ, and the absence of products derived from an intermediate bicyclic cation are most easily accommodated by a mechanism involving the concerted formation of two rings.

Acknowledgments. We are indebted to the National Institutes of Health and the National Science Foundation for support of this research.

(12) For example, treatment of 0.40 mmol of substrate **1** (R = R' = H) with 3.45 mmol of zinc bromide in 100 ml of nitromethane for 16 min at $-23°$ afforded, after chromatography, 0.12 mmol of starting cyclopentenol and 0.28 mmol of tetracyclic product **2** (R = H), accounting for 100% of the material. When the reaction period was extended to 23 min the yield of **2** (R = H) was essentially quantitative.

(13) The dependence of para–ortho ratios on the leaving group of **1** was also observed in the case of the zinc bromide catalyzed cyclization, although the effect was less pronounced than with stannic chloride.

(14) National Science Foundation Predoctoral Fellow, 1969–1972.

(15) National Institutes of Health Postdoctoral Fellow, 1972–1973.

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Trigonal Prismatic and Antiprismatic Coordination in an Isoelectronic Series of Tris(benzenedithiolato) Complexes
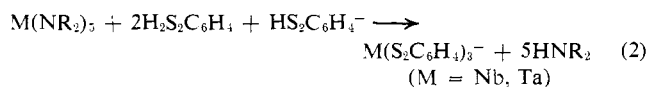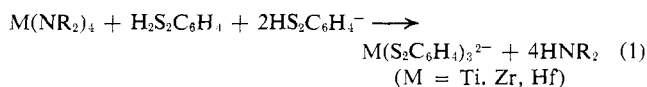
Sir:

The relative stabilities of the trigonal prismatic and antiprismatic coordination in tris(dithiolene) complexes of the transition metals have been the subject of considerable study.[1] The molecular orbital treatment of Gray, *et al.*,[2] has been particularly successful in explaining the physical properties of several trigonal prismatic complexes. In this energy level scheme, two types of molecular orbitals are important in stabilizing the trigonal prism. The first, $2a_1'$ using the notation of Gray, *et al.*, is the bonding combination of the ligand π_h orbitals with the metal d_{z^2} orbital. The second, $4e'$, is the bonding combinations of ligand π_v orbitals with the metal d_{xy} and $d_{x^2-y^2}$ orbitals. Information on the first of these factors has been investigated by studies of species where the antibonding combination $3a_1'$) is populated; *e.g.*, $ReS_6C_6(C_6H_5)_6$ with one electron in this orbital retains the trigonal prismatic structure[3] while $MoS_6C_6(CN)_6^{2-}$ with two electrons in this level has a structure intermediate between the prism and

(1) R. Eisenberg, *Progr. Inorg. Chem.*, **12**, 295 (1970).

(2) E. I. Stiefel, R. Eisenberg, R. C. Rosenberg, and H. B. Gray, *J. Amer. Chem. Soc.*, **88**, 2956 (1966).

(3) R. Eisenberg and J. A. Ibers, *Inorg. Chem.*, **5**, 411 (1966).

antiprism.[4] The irregular distortion[5] of $VS_6C_6(CN)_6^{2-}$ is not expected by the simple scheme, and reversals in the energy level ordering have been considered.[6]

The $4e'$ molecular orbitals are derived from metal and ligand orbitals which are close in energy and should be relatively sensitive to changes in the d orbital energies. We describe here the results of a crystallographic investigation of the structures of the isoelectronic series ZrL_3^{2-}, NbL_3^-, and MoL_3 (where L is the benzenedithiolate ligand) in which no changes may be ascribed to occupancy of the $3a_1'$ antibonding orbital. The observed changes should correspond to the changing d orbital energies and overall charge on the species. These two effects are linked and may not be separable.

The neutral molybdenum tris complex was prepared by the reaction of the pentachloride with the dithiol.[2] This type of reaction does not yield the corresponding zirconium and niobium anionic complexes. Therefore a new synthetic method was sought for these derivatives. Reaction of the transition metal amido complexes[7] with stoichiometric quantities of the dithiol and its mono anion readily produces the desired trischelate complexes (eq 1 and 2). These reactions

$$M(NR_2)_4 + H_2S_2C_6H_4 + 2HS_2C_6H_4^- \longrightarrow$$
$$M(S_2C_6H_4)_3^{2-} + 4HNR_2 \quad (1)$$
$$(M = Ti, Zr, Hf)$$

$$M(NR_2)_5 + 2H_2S_2C_6H_4 + HS_2C_6H_4^- \longrightarrow$$
$$M(S_2C_6H_4)_3^- + 5HNR_2 \quad (2)$$
$$(M = Nb, Ta)$$

afford all the advantages of an acid–base reaction: mild conditions, speed, absence of undesirable by-products, and consequentially good yield ($\sim 70\%$ after recrystallization). The complex anions were isolated and characterized as either their tetraalkylammonium (Ti, Zr, Hf) or tetraphenylarsonium (Nb, Ta) salts.

$Mo(S_2C_6H_4)_3$ crystallizes in the orthorhombic space group *Pnam* with the unit cell dimensions $a = 16.093$ (3), $b = 10.177$ (1), $c = 11.906$ (2) Å, and four molecules per unit cell ($\rho_{obsd} = 1.74$, $\rho_{calcd} = 1.752$ g ml^{-1}). The structure (Figure 1) has been solved by conventional heavy-atom techniques using 1047 statistically reliable reflections measured using Cu $K\alpha$ radiation on a Picker FACS I diffractometer (sin $\theta/\lambda_{max} = 0.575$) and has been refined by full-matrix least-squares techniques to give a conventional R value of 0.035. The molecules have the expected trigonal prismatic structure (approximate symmetry C_{3h}) with the crystallographic mirror plane being coincident with the molecular σ_h plane.

The tetraphenylarsonium salt of tris(benzenedithiolato)niobium crystallizes in the monoclinic system with space group $P2_1/n$, unit cell dimensions $a = 22.983$ (7) Å, $b = 12.747$ (4) Å, $c = 13.150$ (3) Å, $\beta = 92.09$ (2)°, and four formula units per unit cell ($\rho_{obsd} = 1.52$, $\rho_{calcd} = 1.540$ g ml^{-1}). The structure has been solved using 3604 statistically reliable reflections and has been refined to a value of 0.049. Experimental conditions and procedures were essentially as for the molybdenum complex. The structure of the anion is trigonal prismatic with the longest yet observed sulfur–sulfur con-

(4) G. F. Brown and E. I. Stiefel, *Chem. Commun.*, 728 (1970).

(5) F. I. Steifel, Z. Dori, and H. B. Gray, *J. Amer. Chem. Soc.*, **89**, 3353 (1967).

(6) R. Eisenberg and H. B. Gray, *Inorg. Chem.*, **6**, 1844 (1967).

(7) (a) D. C. Bradley and I. M. Thomas, *J. Chem. Soc.*, 3857 (1960); (b) D. C. Bradley and I. M. Thomas, *Can. J. Chem.*, **40**, 449, 1355 (1962).