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(23) Using the bond dissociation energies of T. L. Cottrell ("The Strengths of Chemical Bonds", 2nd ed, Butterworths, London, 1958)—D(-O—O-), 35 kcal/mol; D($>$C—H, formaldehyde or benzyl), ~80; D($>$C—N$<$, average), 73; D(H$_2$N—H, average), 93; D($>$C=O, ketone) − D($>$C—O-), 93—it is calculated that 91 kcal/mol is liberated from the fragmentation of 4a-FIROOCHR$_1$R$_2$ (eq 4).

(24) The reasonable assumption is made that the nonflavin carbonyl fragment (which would be an aliphatic acid in the reaction of Fl$^+$$_{ox}$R + CH$_3$-(CH$_2$)$_8$CH(OH)OOH and benzaldehyde in the reaction of Fl$^+$$_{ox}$R + C$_6H_5CH_2$OOH) will not be generated in an excited state since the energy difference between its lowest excited state and ground state would be expected to be considerably higher than that for the flavin fragment.

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(28) These chemiluminescent reactions result on addition of hydroperoxides to 1,3,10-trimethylisoalloxazinium perchlorate (A) at the 10a position. The 10a-flavin peroxides cannot be alternative models for the luciferase bound oxygenated FMN intermediate as claimed, because the spectral characteristics of the latter are distinctly different from that of 10a adducts of A.

(29) This study will be submitted by C.K. in partial fulfillment of the requirements for the Ph.D. in Chemistry.

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Five- and Six-Membered-Ring Formation from Olefinic α,β-Epoxy Ketones and Hydrazine

Sir:

A few years ago, Ohloff reported[1] that treatment of the conjugated epoxide **1** with hydrazine in methanol gave the expected allylic alcohols **2** from the Wharton reaction,[2] together with an equal amount of an unexpected product, the cyclopentenol **3**.
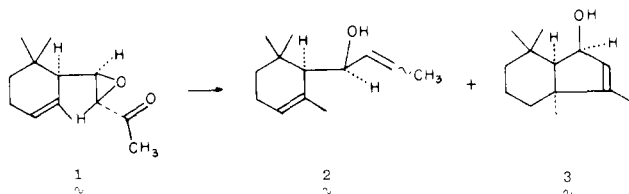

We now report studies which were initiated because the mechanism which was suggested[1] for the formation of **3** seemed very unlikely to us, and because we hoped to develop Ohloff's observation into a cyclization method of some generality.

In the search for systems which might cyclize we finally discovered that epoxy ketone **4** was[3] cyclized with hydrazine in methanol to the hydrindenol **5** in 85% yield.

The structure of **5** (mixture of diastereoisomers) was strongly suggested by its NMR: δ 0.98 (2 d, *J* = 6 Hz, 3 H), 1.19 (2 s, 3 H), 1.21–2.90 (complex m, 10 H). In particular, the absence of vinyl hydrogen absorptions showed that essentially none of the "normal" Wharton product was formed. There also appeared to be no six-membered ring formed in the reaction.[4]

Conclusive evidence for the structure of **5** was obtained by independent synthesis via 3-(4-iodo-2-butyl)-2-cyclohexenone (**6**), which was readily obtained by Birch reduction of 3-(*m*-methoxyphenyl)-1-butanol,[5] followed by tosylation of the resulting dihydroanisole and exchange with iodide (sodium iodide
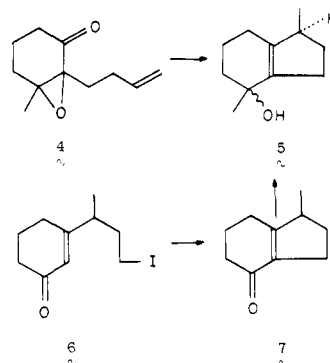

in refluxing acetone to form **6** directly). Cyclization (potassium *tert*-butoxide in refluxing *tert*-butyl alcohol), followed by isolation by preparative VPC (20% SE-30), gave the pure indenone **7**:[6] IR 1680, 1640 cm⁻¹; NMR δ 0.83 (d, *J* = 8 Hz, 3 H); *m/e* 150.1044. Addition of lithium methyl gave a mixture of tertiary alcohols **5**, essentially indistinguishable (NMR, VPC) from the product of the hydrazine cyclization.

The type of substitution around the side-chain double bond does not appear to be crucial. The dimethyl homologue **8**[7] of **4** was similarly cyclized to **9** (~60% yield after Kugelrohr distillation): NMR δ 0.60 (d, *J* = 4 Hz), 0.68 (d, *J* = 4 Hz), 0.85 (s), 0.90 (s), 1.25 (s), 1.4–2.8 (m), 5.2 (br s, OH).
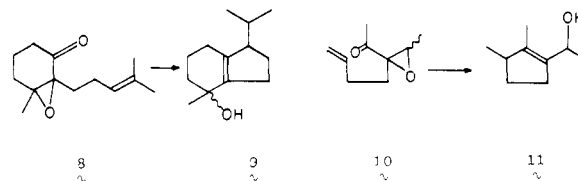

The cyclization is also successful with acyclic systems. This was established with the epoxide **10** derived from 3-ethylidene-6-hepten-2-one. The latter was made in excellent overall yield by titanium tetrachloride mediated aldol condensation[8] of acetaldehyde with 2-trimethylsilyloxy-2,6-heptatriene (from the oxy-Cope rearrangement of the trimethylsilyl ether[9] of 3-methyl-1,5-hexadien-3-ol[10]), followed by dehydration (toluenesulfonic acid–benzene, reflux). Cyclization with hydrazine gave the cyclopentenecarbinol **11** in 70% yield as a mixture of the two possible diastereoisomers, identified by direct comparison with authentic material made by reduction (lithium aluminum hydride) of 2,3-dimethyl-1-acetylcyclopentene.[11]

Finally, although there is a clear preference for five- rather than six-membered-ring formation (**4** → **5**), six-membered rings can nevertheless be made. This was demonstrated by cyclization of the epoxide **12** derived from the related conjugated ketone.[12] Hydrazine cyclization gave a 1:1 mixture of the two epimers of **13** in 60% yield. Identification was made by comparison with the mixture of epimers from lithium methyl and 3-methyl-4-isopropyl-2-cyclohexenone.[13] No simple Wharton elimination product (independently synthesized) could be found.[14,15]
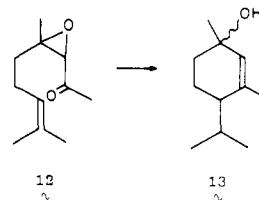

Very subtle (geometric?) factors affect the cyclization reactions. We were, for instance, unable to find any evidence of cyclization with the epoxy ketone **14**.[16] Only the normal Wharton product could be found.[17] This was also the case with

the related epoxyketones **15**[18] and **16**.[19] The lack of cyclization here is presumably due to the geometric difficulty of achieving the proper superposition of the necessary centers (cf. **17**), so that only the normal Wharton product is formed. More surprising is the lack of cyclization observed with the unsaturated epoxy ketone **18**, in which the carbonyl function is in a 1,5 relationship to the double bond, as it is in **4**: it has been reported to give the normal Wharton product in 70% yield.[20] No cyclization was observed.
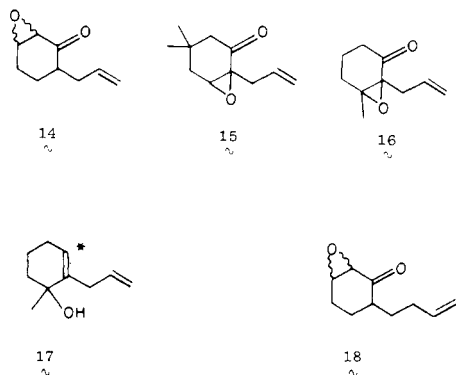
We now offer a few comments on possible mechanisms. The suggestion originally made that the cyclizations might involve addition of a vinyl carbanion[1] must be rejected because such a species could not survive in the methanolic medium, and would not be expected to add to an unactivated trisubstituted olefin (**8 → 9; 12 → 13**). We have observed that formation of the cyclized products is not markedly affected by changing the medium from trifluoroethanol to *tert*-butyl alcohol, except that the overall rate of the reaction is faster, as a reflection of the faster rate of hydrazone formation in the more polar media. An intense yellow color is observed several minutes after the reactants are first mixed and fades progressively until the end of the reaction. This color is observed whether or not the reaction results in cyclization and strongly suggests a common intermediate, the vinyldiazene **19**. Indeed, the reaction mixtures exhibited a strong absorption maximum at 232 nm and a very weak one at 409 nm, as reported for simple vinyldiazenes.[21]

We believe that two possibilities may be considered seriously. One is that there is a concerted collapse of the vinyldiazene, as illustrated in **19**.[22] The other is that decomposition of the diazene gives a radical[21] which then adds to the double bond, as shown in **20**. The concerted diazene decomposition may be deceptively attractive because of the difficulty of achieving the proper arrangement of the relevant centers. With either mechanism, the difference between **18** and **4** is difficult to explain and may have to be ascribed to conformational problems in the transition state which are too subtle to interpret at this stage.
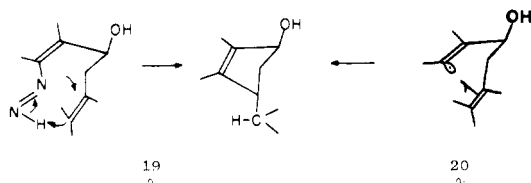
We finally point out that there is an operational difference between the two mechanisms: the new carbon–carbon and carbon–hydrogen bonds resulting from cyclization would be cis via the "concerted" diazene, but not via the radical path. We are attempting to elucidate this point.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their support of this work.

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(15) The reactions with hydrazine were conducted with ca. sixfold excess of hydrazine hydrate in methanol under nitrogen, and kept at 0 °C until VPC showed disappearance of starting material. The reactions which led to **5**, **9**, **11**, and **13** were thus kept for 80, 68, 12, and 24 h, respectively.
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Remarkable Reversibility in Aromatic Friedel–Crafts Acylations. Para ⇌ Ortho Acyl Rearrangements of Fluorofluorenones in Polyphosphoric Acid

Sir:

"Acylation differs from alkylation in being virtually irreversible",[1] free of rearrangements and isomerizations.[2-5] This authoritative exposition of the state of the art of Friedel–Crafts chemistry[1] has been long recognized and not without reason. The difference in behavior between Friedel–Crafts acylation and Friedel–Crafts alkylation was attributed to the resonance stabilization existing between the acyl group and the aromatic nucleus.[2] It may serve as a barrier against rearrangements and reversible processes. However, if the acyl group is tilted out of the plane of the aromatic nucleus by neighboring bulky substituents, the resonance stabilization is reduced and the pattern of irreversibility of Friedel–Crafts acylation may be challenged.[2,6] The phenomenon of *reversibility* of Friedel–Crafts