

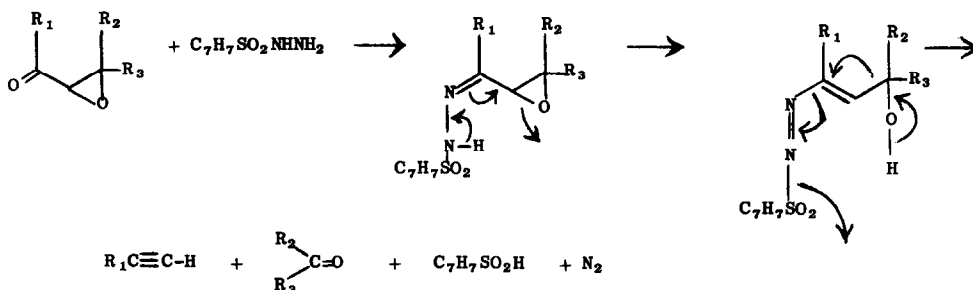
A NOVEL FRAGMENTATION REACTION OF α,β -EPOXYKETONES
 THE SYNTHESIS OF ACETYLENIC KETONES¹

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We wish to report that p-toluenesulfonylhydrazones of certain α,β -epoxyketones undergo a novel fragmentation reaction to yield an acetylene and a ketone as shown in Scheme 1.

Scheme 1



The application of this fragmentation method for the formation of medium-sized rings is exemplified by the reaction of 9,10-epoxy-1-decalone² (I) with 1 equivalent of p-toluenesulfonylhydrazine in ethanol at 50°. After 2 hours nitrogen evolution ceased and none of the intermediate p-toluenesulfonylhydrazine was detected by thin-layer chromatography on silica G plates. From the reaction a 50% yield of distilled cyclodecyn-6-one (II), 75-80°/2 mm; $\lambda_{\text{max}}^{\text{film}}$ 5.85 μ ; was isolated. The structure of II was confirmed by the catalytic absorption of 2 mole equivalents of hydrogen to yield cyclodecanone. This reaction thus affords a convenient method for the formation of medium sized rings^{3a-h} and internal acetylenes via α,β -unsaturated ketones.

The utility of the reaction for the preparation of terminal acetylenic ketones from α,β -unsaturated ketones is exemplified by the conversion of 10-methyl- $\Delta^{1,9}$ -octal-2-one (VI)

to the cyclohexanone derivative IV. The preparation of the epoxydecalone III from VI was accomplished with alkaline hydrogen peroxide. Reaction of III with 1.17 equivalents of p-toluenesulfonylhydrazine in ethanol at 25° proceeded with the evolution of nitrogen. After 1/2 hour the fragmented terminal acetylenic ketone IV was isolated by distillation in 35% yield, 76-80°/1.0 mm; n_D^{23} 1.4829; $\lambda_{\max}^{\text{film}}$ 3.0 μ ($\text{C}\equiv\text{C}-\text{H}$); 4.5 μ ($\text{C}\equiv\text{C}$); 5.85 μ ($\text{C}=\text{O}$)

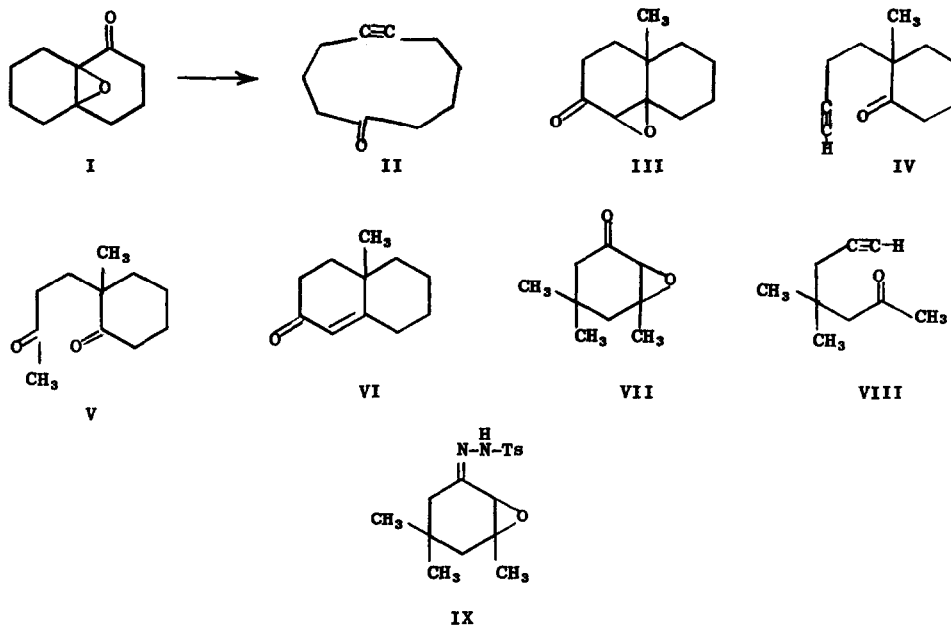
Confirmation of structure IV was achieved by hydration of the triple bond in IV, catalyzed by mercuric oxide in the presence of sulfuric acid. The intermediate methyl ketone V was converted under these conditions back to the octalone derivative VI.

A further illustration of this reaction is the conversion of isophorone oxide VII to 4,4-dimethylheptyn-6-one VIII. A solution of 15.4 g (0.1 M) VII in 1100 ml of ethanol and 18.6 g (0.1 M) of p-toluenesulfonylhydrazine was heated at 55° for 2 hours. Isolation of the product by extraction into chloroform, followed by distillation yielded 5.5 g of VIII, 40%, 75-80°/14 mm; $\lambda_{\max}^{\text{film}}$ 3.0 μ and 4.72 μ ($\text{C}\equiv\text{C}-\text{H}$); 5.85 ($\text{C}=\text{O}$); $\tau_{\text{TMS}}^{\text{CCl}_4}$ 7.85 ($-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{CH}_3$), 7.93 (quartet, $\equiv\text{C}-\text{H}$).

In an alternate procedure the reaction of isophorone oxide with 1.1 equivalents of p-toluenesulfonylhydrazine in ethanol at 20° for 20 minutes yielded the unstable p-toluenesulfonylhydrazone derivative IX; $\lambda_{\max}^{\text{Nujol}}$ 3.15 (NH); 6.23, 7.5 and 8.6 μ ($\text{C}_7\text{H}_7\text{SO}_2-$); $\lambda_{\max}^{\text{MeOH}}$ 227 $m\mu$ ($\epsilon = 21,000$). Decomposition of IX occurred readily at 50° in ethanol with brisk nitrogen evolution to afford the acetylenic ketone VIII in 80-85% yield.

We have observed that 2,3-epoxycyclohexanone does not yield the expected fragmentation product 1-hexyn-6-ol. This result appears to indicate that the presence of a β -hydrogen alters the course of the reaction.

Our initial studies of this new reaction have been limited to cyclic α,β -epoxyketones. These cyclic p-toluenesulfonylhydrazones meet the necessary geometric requirements for facile concerted fragmentation since the ketonic carbon-nitrogen bond and the $\text{C}_\alpha-\text{C}_\beta$ bond maintain a trans co-planar alignment⁴ in the N-p-toluenesulfonylazo intermediate (Scheme 1). This reaction is formally related to the reaction of an



α,β -epoxyketone with hydrazine described by Wharton,⁵ where the intermediate hydrazone decomposes to the allylic alcohol and nitrogen.

Padwa⁶ reports that an acyclic α,β -epoxyketone, trans-chalcone oxide, reacts with p-toluenesulfonylhydrazine in acidic ethanol to yield a cyclic product, 1-p-toluenesulfonyl-3,5-diphenyl-4-hydroxypyrazoline. Thus it appears that an alternate mode of reaction other than the fragmentation process is available to acyclic α,β -epoxyketones.⁷

Further studies on the application of this reaction with other α,β -unsaturated ketones will be reported.⁸

References

1. Since the completion of this work A. Eschenmoser, D. Felix, and G. Ohloff, Helv. Chim. Acta **50**, 708 (1967) have described the fragmentation of bicyclo [10.3.0]-1,12-epoxy-13-pentadecanone with p-toluenesulfonylhydrazine to the large ring ketone 4-cyclopentadecyn-1-one.

2. All new compounds reported herein gave satisfactory analytical data. The epoxy-decalone I was prepared from $\Delta^{9,10}$ -1-octalone \xrightarrow{a} 1-hydroxy- $\Delta^{9,10}$ octalin \xrightarrow{b} 1-hydroxy-9,10-epoxy-octalin \xrightarrow{c} I; a = LAH, b = M-chloroperbenzoic acid, c = CrO_3 + pyridine, with isolation of the intermediates in an over-all yield of 25%.
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