

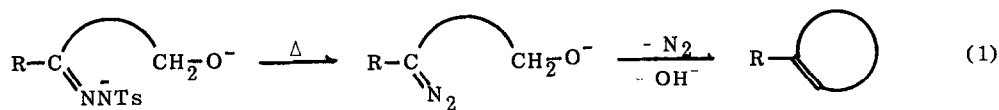
A NOVEL CYCLIZATION REACTION OF OXIDO DIAZOALKANES:
FORMATION OF 1-SUBSTITUTED CYCLOALKENES

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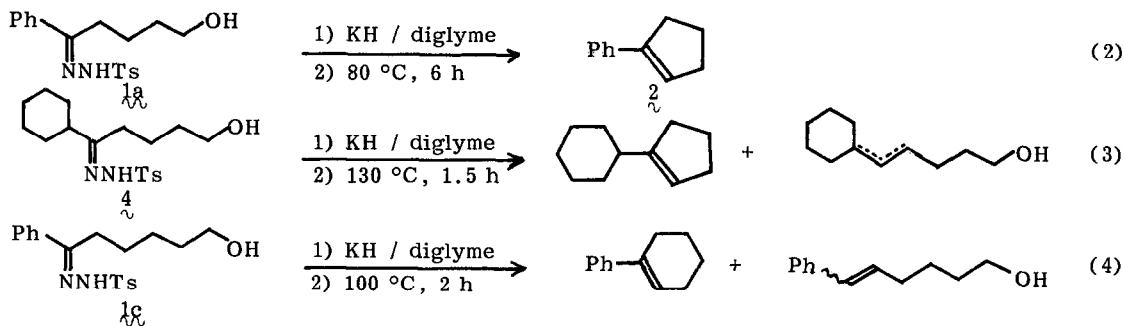
Abstract: The thermal decomposition of dialkali metal salts of δ -hydroxybutyl ketone and ϵ -hydroxypentyl ketone tosylhydrazones in diglyme at 80-120 °C produced the 1-substituted cyclopentene and cyclohexene, respectively.

There have been shown considerable interests in the intramolecular reaction of carbenes or carbenoids bearing heteroatom substituents at β or remoter positions from the carbenic carbon.¹ In those studies, the aprotic Bamford-Stevens reaction² of alkali metal salts of appropriate tosylhydrazones has frequently been utilized and has provided us with valuable information on the intramolecular interaction of carbenes with remote oxygen,³ nitrogen,^{3c,d} and sulfur functions.⁴ In the course of studying our recent finding of a novel oxyanionic substituent effect that greatly facilitates the insertion by carbenes into α C-H bond of alkoxides,⁵ we performed the Bamford-Stevens reaction of dialkali metal salts of ω -hydroxyketone tosylhydrazones in order to investigate the reaction of carbenes bearing a remote oxido substituent.⁶ Herein, we report a novel carbocycle formation reaction of ω -oxidodiazoalkanes that proceeds not via the intervention of carbenes but directly from diazoalkanes (eq 1).



Dipotassium salt of 5-hydroxyvalerophenone tosylhydrazone **1a** (mp 117-119 °C),⁷ prepared by the reaction of **1a** with KH (2.2 equiv), was decomposed in diglyme at 80 °C. The heterogeneous reaction mixture developed a dark red color, which gradually faded out in 6 h with an evolution of nitrogen. After aqueous workup followed by column chromatography, 1-phenylcyclopentene (**2**) was isolated in 74% yield (eq 2). It should be noted that the formation of 5-phenyl-4-pentenol (**3a**, see Table I), a normally expected product of the Bamford-Stevens reaction, was not observed.

In contrast to the potassium alkoxide, the sodium salt of the corresponding THP ether **1b** yielded the 5-phenyl-4-pentenyl tetrahydropyranyl ether (**3b**) as a major product and the cycliza-



tion did not occur. Moreover, a remarkable effect of alkali metal was observed: As shown in Table I, only a trace amount of $\underline{2}$ was produced from the dilithium salt of $\underline{1a}$, and a comparable amount of $\underline{3a}$ to that of $\underline{2}$ was obtained from the disodium salt. These results indicate that the reaction leading to $\underline{2}$ is facilitated as the charge density on the oxygen atom increases in the order of K^+ , Na^+ , Li^+ , and THP.

Similar cyclization also proceeded in the reaction of dipotassium salt of cyclohexyl 4-hydroxybutyl ketone tosylhydrazone ($\underline{4}$). The expected cyclohexylcyclopentene was obtained in 41% yield together with a mixture of byproduct olefinic alcohols (19% yield)(eq 3). The present reaction is also applicable to 6-membered ring formation: The thermolysis of dipotassium salt of 6-hydroxyhexanophenone tosylhydrazone ($\underline{1c}$) gave 1-phenylcyclohexene (26% yield) together with 6-phenyl-5-hexenol (11% yield)(eq 4). However, attempted 7-membered ring formation starting from dipotassium salt of 7-hydroxyheptanophenone tosylhydrazone ($\underline{1d}$) was unsuccessful, and 7-phenyl-6-heptenol was obtained (35% yield) instead.

It has been known that the photolysis of phenyldiazomethane in the presence of potassium benzyloxide gives the C-H insertion product 1,2-diphenylethanol,⁸ and that (4-oxidobutyl)-(phenylthio)carbenes can be inserted intramolecularly into the α C-H bond of alkoxide to give 2-phenylthiocyclopentanol.^{6b,8} If the present annelation reactions (eq 2, 3, and 4) take place analogously via the intervention of carbenic species, then the intramolecular insertion product 2-substituted cycloalkanols must undergo the elimination of metal hydroxides (Scheme I, path a). To examine this mechanistic plausibility, we independently prepared 2-phenyl- and 2-cyclohexylcyclopentanol,⁹ and treated their potassium salts under the same reaction conditions as in the thermolysis. While 2-phenylcyclopentoxide gave $\underline{2}$ in a low yield (16%) together with the recovery of the starting alcohol (57%), 2-cyclohexylcyclopentoxide did not afford any elimination product even after heating at 130 °C for 4 h in diglyme and the starting alcohol (86%) was recovered. Therefore, cycloalkanols which are rationally anticipated as carbene insertion products can not be involved in the present reaction and the possibility of path a was excluded.

When a reddish purple solution of (4-hydroxybutyl)(phenyl)diazomethane, which was prepared by the oxidation of the corresponding hydrazone with Ag_2O in benzene, was treated first with KH in THF-benzene and then heated at 70 °C for 0.5 h, $\underline{2}$ was detected by the VPC analysis of the reaction mixture and was isolated in 8% yield. In contrast, when the corresponding carbene intermediate was generated by the photolysis of dipotassium salt of $\underline{1a}$,¹⁰ neither 2-phenylcyclopentanol nor cyclopentene $\underline{2}$ was produced, but the major product was the H-migration product $\underline{3a}$ (38% yield). Thus, it is evident that the present reaction proceeds via oxidodiazalkanes without an intervention of a carbene intermediate.

Table I. Thermal Decomposition of Alkali Metal Salts of 4-Oxy-substituted Valerophenone Tosylhydrazones^a

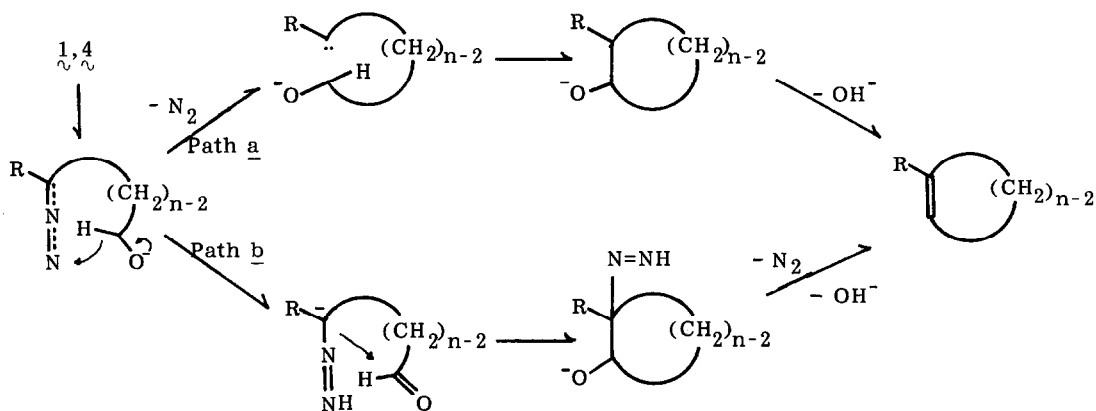
entry	Tosylhydrazone	Base (equiv)	Reaction Conditions		Products (Isolated Yield)
			Temp.,	Time	
1	1a; R = H	KH (2.2)	80 °C,	6 h	2 (74%), 3a ----
2	1a; R = H	NaH (2.2)	120 °C,	2 h	2 (37%), 3a (35%)
3	1a; R = H	BuLi (2.0)	100 °C,	2 h	2 (trace), 3a (19%)
4	1b; R = THP	NaH (1.1)	120 °C,	1 h	2 ----, 3b (54%)

a) Reactions were performed employing ca. 10 mL of diglyme per 1 mmol of **1** under a nitrogen atmosphere.

As the most plausible mechanism that is accountable for all of the above observations, we propose a novel annelation reaction (path **b**, Scheme I) that proceeds through an intramolecular hydride transfer from α position of alkoxide to the nitrogen terminus of the diazo group, followed by cyclization and olefin formation. The rationale of this mechanism lies on the fact that alkoxides have been well documented in literatures as the hydride donor,¹¹ and moreover, an electrophilic nature of the terminal nitrogen atom of diazoalkanes has been clearly demonstrated recently by a nitrene-type intramolecular 1,1-cycloaddition reaction.¹²

As a supporting evidence for the proposed mechanism, we observed the formation of 3-phenylpyridazine in the thermolysis of dipotassium salt of 4-hydroxybutyrophenone tosylhydrazone. The formation of the pyridazine can also be explained reasonably by a mechanism similar to path **b** in Scheme I, in which the reaction is initiated first by the intramolecular hydride migration from the α position of alkoxide to the nitrogen terminus of a diazo group. Details of this reaction will be reported separately.

Scheme I



References and Notes

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- (7) ω -Hydroxyketone tosylhydrazones, (1a-d, and 4) were prepared in 30-60 % overall yield starting from appropriate aldehydes according to the following reaction sequences:
 1) $\text{ClMgCH}_2(\text{CH}_2)_{2n-2}\text{OTHP} / \text{THF}$, 2) $\text{PCC} / \text{CH}_2\text{Cl}_2$, 3) aq AcOH-THF, 4) $\text{TsNHNH}_2 / \text{MeOH}$; structures were characterized by ^1H NMR, IR spectroscopy, and for 1a, 1c, and 1d by elemental analysis.
- (8) Harada, T.; Akiba, E.; Oku, A. unpublished results.
- (9) Mixtures of trans and cis isomers.
- (10) The reaction mixture in diglyme was irradiated with a high pressure mercury lamp through a Pyrex filter. For the generation of carbene by the photolysis of alkali metal salts of tosylhydrazones, see Dauben, W. G.; Willey, F. G. J. Am. Chem. Soc. 1962, 94, 1947.
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