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Novel Cyclization of Vinyl Nitrene into 1-Azaphenalene#

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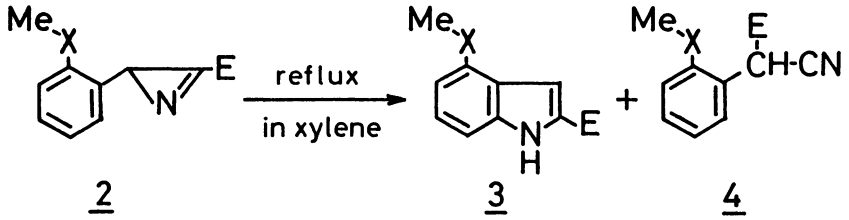
Thermal reaction of 2H-azirines, bearing a methoxy or methylthio group at the neighboring position to azirine ring, was studied. In thermolysis of ethyl 2-(2-methoxynaphth-1-yl)-2H-azirine-3-carboxylate, attack of the vinyl nitrene at the peri position to form a 1-azaphenalene ring was observed. In thermal reaction of its thio analogue, 1-azaphenalene was also formed, but a naphthothiazine formed by the attack of vinyl nitrene at the sulfur atom was the major product. Mechanisms and differences of the reactions depending on O and S are discussed.

Formation of 5-membered nitrogen containing heterocycles in thermal reaction of 2H-azirines has been well known.[1] Intermediacy of vinyl nitrenes is established by our study on thermal behavior of optically active 2H-azirines.[2] Our previous studies further revealed that 6- and 7-membered heterocycles are also formed by introducing an alkyl or unsaturated group at the position for nitrene to cyclize into 5-membered ring compounds.[3] As these transformations can be accomplished by only heating azirines in inert media, azirines are considered as versatile starting materials for the synthesis of nitrogen containing heterocycles.

Here, we wish to report the first example of 1-azaphenalene formation, which was found in our investigation to explore further extension of the synthetic utility of thermal rearrangement of 2H-azirines.

First, we examined thermal rearrangement of 2-phenyl-2H-azirine system bearing methoxy or methylthio group at the ortho position of the phenyl ring, expecting the participation of oxygen or sulfur in intramolecular cyclization of



2 3 4

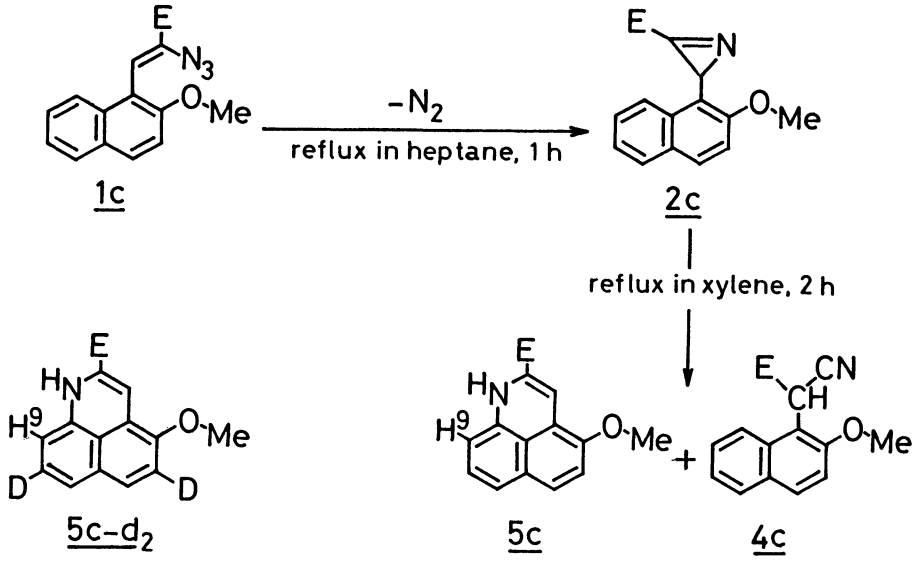
E=CO_2Et, a: X=O, b: X=S

This paper is dedicated to the late Professor Ryozo Goto, Kyoto University.

vinyl nitrene. When ethyl 2-(2-methoxyphenyl)- 2a and ethyl 2-(2-methylthiophenyl)-2H-azirine-3-carboxylate 2b, prepared by photolysis of the corresponding vinyl azides 1a and 1b,[4] were heated in xylene under reflux for 2 h, indoles, 3a and 3b, were obtained in more than 90% yields. Small amount of ethyl cyanoacetate derivative 4a was accompanied in the reaction of 1a. These two reactions were usually observed ones[5] and no evidence was obtained for the attack of vinyl nitrene to the methoxy or methylthio group.

Then, we chose 2-(naphth-1-yl)-2H-azirine system having a methoxy or methylthio group at 2-position of the naphthalene nucleus to prevent cyclization into 5-membered rings.

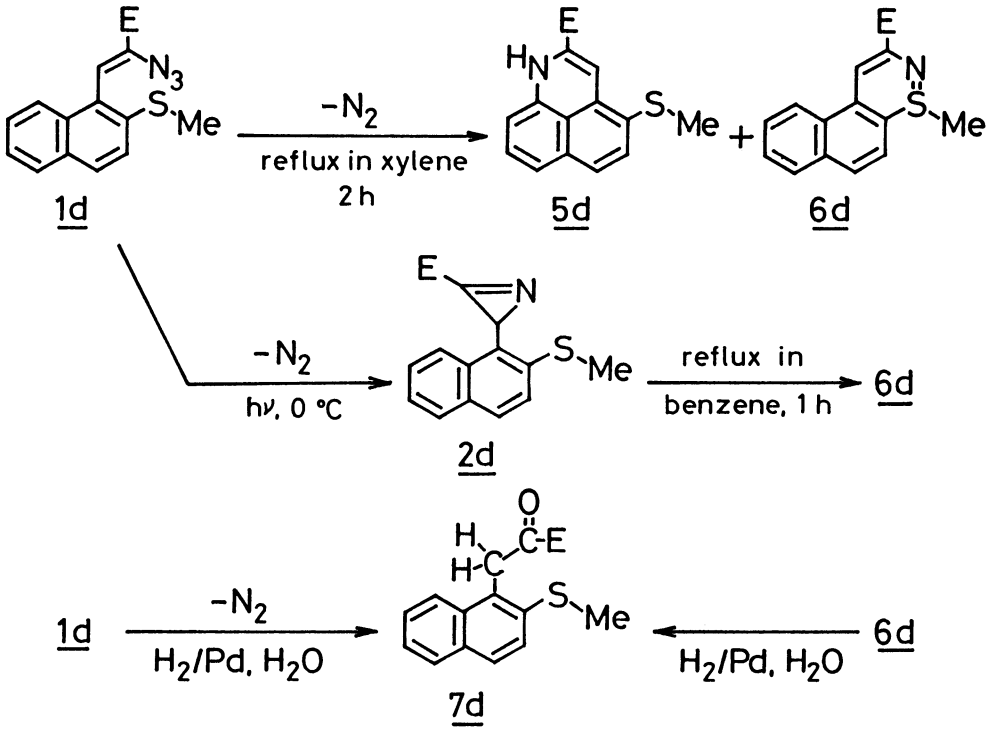
When ethyl α-azido-β-(2-methoxynaphth-1-yl)acrylate 1c[4] was heated in heptane under reflux for 1 h, ethyl 2-(2-methoxynaphth-1-yl)-2H-azirine-3-carboxylate 2c was obtained. Heating 2c in xylene under reflux for 2 h gave a red solution. Evaporation of the solvent followed by chromatography on silica gel gave a colorless oil and red crystalline in 15 and 60% yield, respectively. The colorless oil was assigned as ethyl α-cyano-(2-methoxynaphth-1-yl)acetate 4c, on the basis of spectral results and elemental analysis. Mass spectrum (M^+ m/e=269) and elemental analysis of the red compound 5c, mp 134.5-136 °C, revealed that this compound has a molecular formula of $C_{16}H_{15}NO_3$. On the basis of IR, NMR, and electronic spectra,[6] this compound was strongly suggested to be ethyl 4-methoxy-1-azaphenalene-2-carboxylate. Especially, the double doublet signal at δ 5.39 ($J_{7,9}$=2 Hz and $J_{8,9}$=6 Hz) coinsides with the reported signal assigned to the proton at the 9-position of 1-azaphenalene.[7] Formation of this compound requires intramolecular attack of nitrene at the peri position of naphthalene ring. As this type of cyclization has not been known in azirine chemistry so far,[5] we decided to identify this structure more decisively. The red compound 5c-d_2, obtained by thermal decomposition of 1c-d_2, having two deuterium atoms at the 3- and 6-position of the naphthalene ring, showed broad NMR signal centered at δ 5.36, by eliminating coupling with the proton at 8-position. This observation



1c 2c 5c-d_2 5c 4c

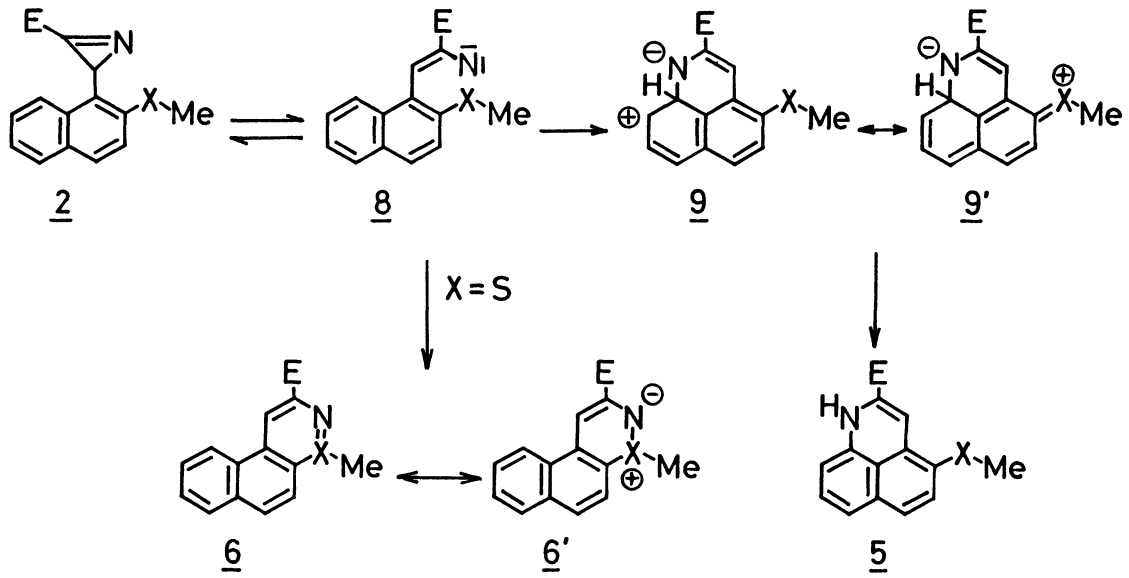
clearly substantiated the assigned azaphenalene structure of 5c, which is the new type of reaction product from 2H-azirine.

Thermolysis of ethyl α-azido-β-(2-methylthionaphth-1-yl)acrylate 1d[4] in xylene under reflux for 2 h also gave a red solution. Same work-up as in the case of 1c gave also 1-azaphenalene derivative 5d, mp 80 °C(dec.), however, only in 20% yield. The major product, obtained in 40% yield in this reaction, was pale yellow oil 6d. The naphthothiazine structure of 6d was easily assigned on the basis of spectral results. Its transformation into ethyl (2-methylthionaphth-1-yl)pyruvate 7d on catalytic hydrogenation on Pd-black further substantiated the structural assignment. The pyruvate derivative 7d was identical with the authentic sample prepared from 1d.



The marked difference of methylthio substituted system is not only in the formation of thiazine but also in the reactivity of the azirine 2d. Thermal decomposition of 1d in refluxing heptane for 1 h did not afford the corresponding 2H-azirine 2d but gave the mixture of 5d and 6d. However, the 2H-azirine 2d was isolated by irradiating the solution of 1d in ether-acetone (1 : 1) with a 100W high pressure mercury lamp equipped with a Pyrex filter at 0 °C. Heating this azirine in benzene for 2 h gave 6d as the exclusive product.

The results obtained in this paper may be rationalized by the reaction pathways as shown in Scheme 1, in which the vinyl nitrene is the key intermediates. Formation of thiazine ring would be made possible by the availability of d-orbital of sulfur atom, as had been reported in similar system.[8] Higher reactivity of 2d to give 6d can be recognized by participation of d-orbital of sulfur. Lacking of d-orbital on oxygen would prevent the same type of reaction. Inhibition of the 5-membered ring formation by the methoxy or methylthio group blocking the 2-



Scheme 1.

position of the naphthalene ring, would compelled the formation of azaphenalene ring by intramolecular cyclization via 9. Higher temperatures required for the formation of 1-azaphenalene would be ascribed to the destruction of aromatic stability of the naphthalene nucleous in 9. However, occurence of this cyclization at peri position would be assisted by effect of methoxy or methylthio group to delocalize the positive charge in 9.

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6) Spectral data of 5c. IR (nujol, cm^{-1}) 3350s, 1710vs. NMR (δ in $CDCl_3$) 1.32 (3H, t J=7 Hz), 3.74 (3H, s), 4.32 (2H, q J=7 Hz), 5.93 (1H, dd J=2 and 6 Hz), 6.37-7.54 (6H, m). UV [λ_{max}(ε) in cyclohexane] 241 (31000), 288 (9200), 351 (10300), 367 (12200), 510 (2600).

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