SYNTHESES OF 1-METHYL-2-AZATHIABENZENE 1-OXIDE AND 1-METHYL-4-AZATHIABENZENE 1-OXIDE DERIVATIVES

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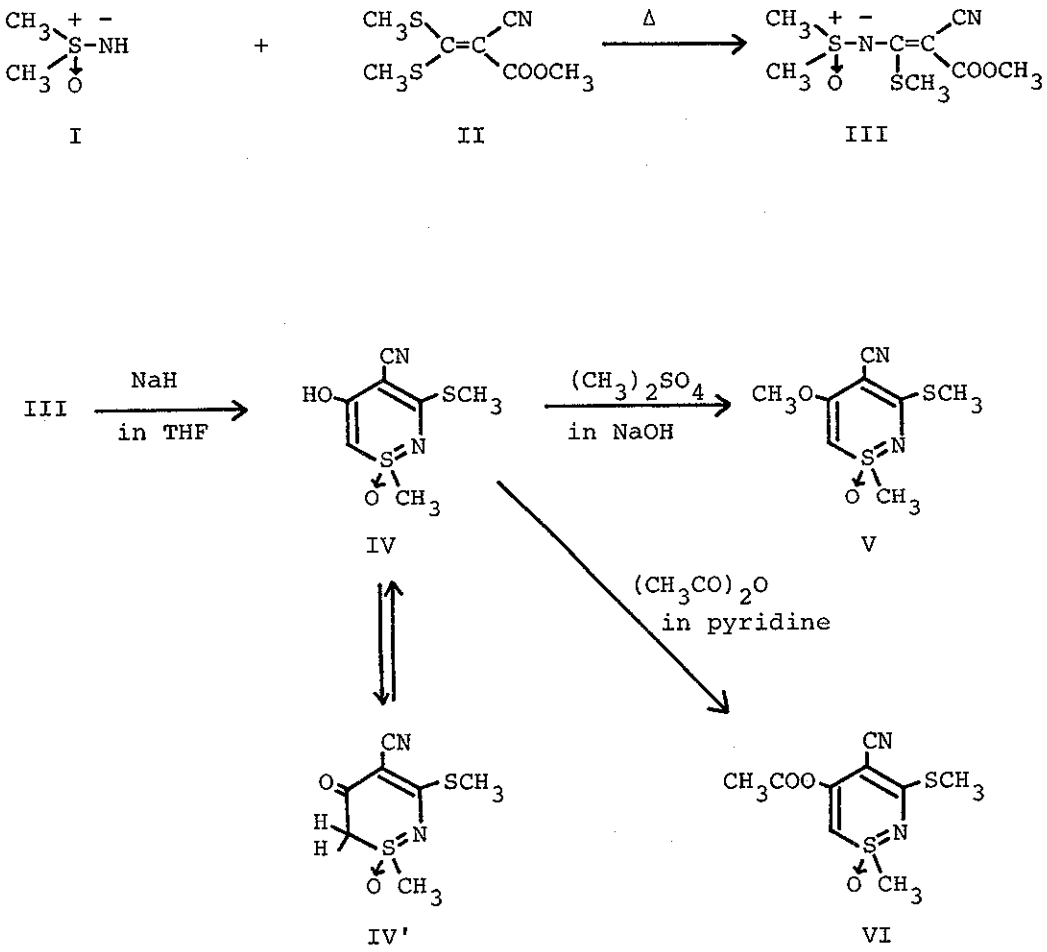
1-Methyl-2-azathiabenzene 1-oxide derivatives are synthesized by the reaction of dimethylsulfoximine and ketenethioacetal derivatives. Reaction of dimethyloxosulfonium methylide with cyanamide derivatives affords 1-methyl-4-azathiabenzene 1-oxide derivatives.

Previously, we reported[1] the synthesis of 1-methyl-2-acylthiabenzene 1-oxide derivatives in good yields.

There are much interests in the aromaticity and chemical behavior of azathiabenzene 1-oxides, new heterocyclic systems. Recently, several groups have been reported on the synthetic methods and characteristic properties for 2-azathiabenzene 1-oxides, which were prepared by the reaction of dimethylsulfoximine and ethoxyethylene[2] or acylacetylene derivatives[3]. In this paper, we wish to report a new synthetic route to 1-methyl-2-azathiabenzene 1-oxides by use of ketenethioacetal


I
II
III
NaH
in THF
IV
$(CH_3)_2SO_4$
in NaOH
V
$(CH_3CO)_2O$
in pyridine
IV'
VI

Scheme 1

derivatives as electrophiles (Scheme 1).

A mixture of dimethylsulfoximine (I) and methyl 3,3-bis(methylthio)-2-cyanoacrylate[4] (II) was heated in an oil bath at 100° in the absence of solvent for 0.5 hr. After cooling, ether was added to the resultant oil and the precipitate was collected by filtration and recrystallized from ethyl acetate to give N-(1'-methylthio-2'-cyano-2'-methoxycarbonylvinyl)dimethylsulfoximine (III) as yellow needles, mp 124°, in 90% yield. On the other hand, the chloroform solution of I and II was refluxed on a water bath in the presence of triethylamine to give no product, and the starting materials were recovered quantitatively.

The structure assignment of III was based on elemental analysis, infrared (IR) absorption (KBr) at 2200 cm^{-1} (CN) and 1680 cm^{-1} (CO), ultraviolet (UV) spectrum [λ_{max}^{EtOH} nm (log ε)] revealing maxima at 246 (3.78) and 318 (4.27), and the nuclear magnetic resonance (NMR) spectrum (δ in $CDCl_3$) showing three sharp singlets due to methyl protons at 2.90 (3H, s, SCH_3), 3.36 (6H, s, $(CH_3)_2\overset{+}{S}O$), and 3.80 (3H, s, OCH_3). It was observed that the azaylide (III) was stable at room temperature during about three months.

Treatment of III with sodium hydride in THF at room temperature for 48 hr afforded IV as pale yellow fine prisms, mp 196°, in 48% yield. Elemental analysis of IV corresponded to $C_7H_8O_2N_2S_2$ (Calcd.: C, 38.89; H, 3.73; N, 12.96; S, 29.60. Found: C, 38.77; H, 3.77; N, 12.67; S, 29.25). The NMR spectrum (δ in DMSO-d_6) showed the signals at 2.46 (3H, s, SCH_3), 3.56 (3H, s, $SOCH_3$), and 5.68 (1H, broad, C_6-H). The UV spectrum [λ_{max}^{EtOH} nm (log ε)]

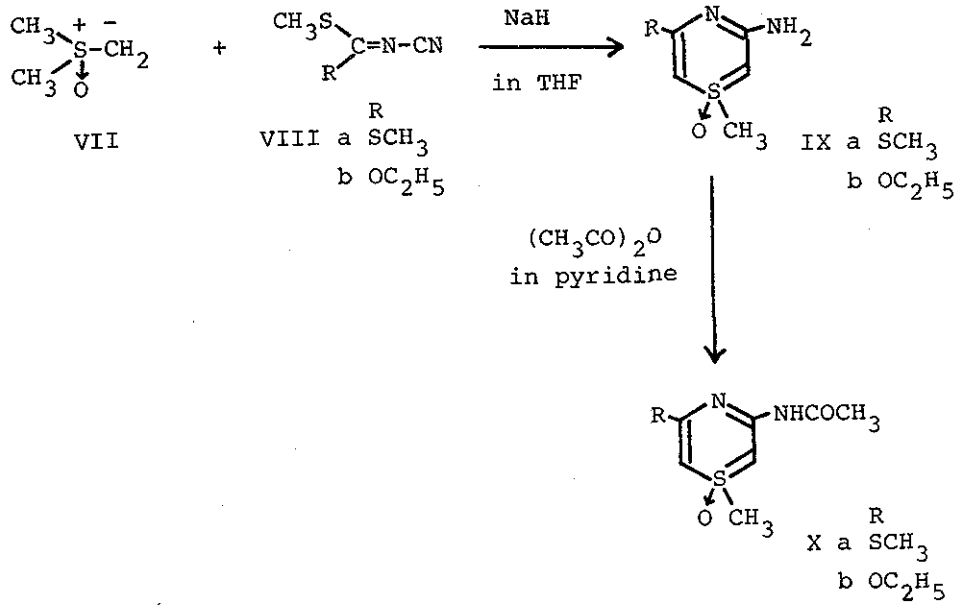
revealed maxima at 230 (4.48), 256 (3.75), and 317 (3.97). The IR spectrum (KBr) showed the cyano band at 2195 cm^{-1}, the carbonyl band at 1624 cm^{-1}, and hydroxy band at 3400 cm^{-1}. From the IR spectrum of IV, the structure may be deduced to exist two forms (enol form IV and keto form IV'). On the basis of these spectral data and elemental analysis, IV was confirmed to be 1-methyl-3-methylthio-4-cyano-5-hydroxy-2-azathiabenzene 1-oxide.

The reaction of IV with dimethyl sulfate give 1-methyl-3-methylthio-4-cyano-5-methoxy-2-azathiabenzene 1-oxide (V) as colorless fine needles, mp 226° [mass spectrum m/e 230 (M^+), IR (KBr) 2180 cm^{-1} (CN), NMR (δ in $CDCl_3$) 2.50 (3H, s, SCH_3), 3.36 (3H, s, $SOCH_3$), 3.82 (3H, s, OCH_3) and 5.20 (1H, s, C_6-H), UV λ_{max}^{EtOH} nm (log ε) 231 (4.32), 254 (3.67), and 315 (3.91)]. The UV spectrum exhibited an absorption pattern quite similar to that of IV.

The reaction of IV with acetic anhydride afforded 1-methyl-3-methylthio-4-cyano-5-acetoxy-2-azathiabenzene 1-oxide (VI) as colorless needles, mp 150°, which was confirmed by the elemental analysis and IR, UV, mass, and NMR spectra.

König and coworkers[5] reported that the reaction of trimethyloxosulfonium chloride with benzonitrile in the presence of sodium hydride afforded 1-methyl-3,5-diphenyl-4-azathiabenzene 1-oxide in low yield. We carried out the reaction of dimethyloxosulfonium methylide (VII) with cyanamide derivatives and synthesized 1-methyl-4-azathiabenzene 1-oxide derivatives as outlined in Scheme 2.

A THF solution of VII (prepared from trimethyloxosulfonium



Scheme 2

chloride and sodium hydride in THF) and dimethyl cyanamidedithiocarboxylate[6] (VIIIa) was refluxed for 2 hr and the resulting mixture was chromatographed on silica gel, eluting with chloroform followed by recrystallization from ethyl acetate to afford 1-methyl-3-amino-5-methylthio-4-azathiabenzene 1-oxide (IXa) as colorless prisms, mp 189°, in 30% yield.

The structure assignment of IXa was based on elemental analysis, mass (M^+: 190), IR (KBr) [3400 cm^{-1} (NH_2)] and NMR spectra (δ in DMSO-d_6) which showed the signals at 2.30 (3H, s, SCH_3), 3.37 (3H, s, $SOCH_3$), 4.68 (1H, d, J=4 Hz, C_2-H), 5.42 (1H, d, J=4 Hz, C_6-H), and 5.84 (2H, broad, NH_2, disappeared by addition of D_2O).

Similarly, the reaction of VII to O-ethyl-S-methylcyanamide-

thiocarboxylate[6] (VIIIb) gave 1-methyl-3-amino-5-ethoxy-4-aza-thiabenzene 1-oxide (IXb), mp 135-136°, in 20% yield, whose structure was also assigned on the basis of the elemental analysis and IR, UV, and NMR spectra. Acetylation of IXa and IXb with acetic anhydride in pyridine gave the corresponding N-acetyl compounds, Xa (mp 180°) and Xb (mp 169°).

Further work is in progress on the chemical properties and reactivities of 1-methyl-2-aza(4-aza)thiabenzene 1-oxide derivatives.

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