CHEMISTRY LETTERS, pp. 519-522, 1976. Published by the Chemical Society of Japan

3-METHYLSULFONYL-3H-BENZ[d]AZEPINE

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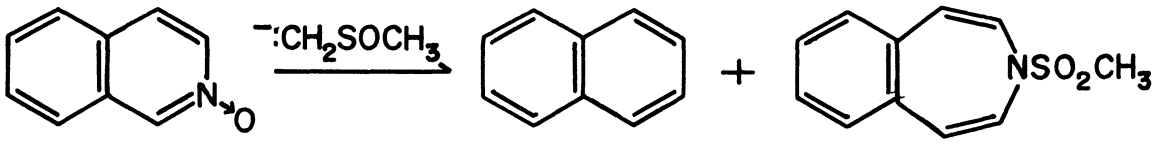
3-Methylsulfonyl-3H-benz[d]azepine was prepared by the reaction of methylsulfinylmethyl carbanion with isoquinoline N-oxide, and its structure was determined by spectroscopic measurements.

Benzazepine derivatives are of interest since they are expected to show antiaromatic character to some extent[1], and their syntheses have been reported by several authors. Dimroth and Freyschlag[2] obtained 3-phenyl-3H-benz[d]azepine-2,4-dicarboxylic acid and its esters by the condensation of phthalaldehyde with corresponding phenyliminodiacetates. Johnson and Nasutivicus[3] prepared 3-acetyl-4-bromo-2-diacetylamino-3H-benz[d]azepine from 2-amino-4-bromo-1H-benz[d]azepine. On the other hands, the dihydrobenzazepine derivatives have been prepared by the ring expansion of the corresponding isoquinoline.[4-6]

The present authors wish to report the formation of the title compound (3) in the reaction of methylsulfinylmethyl carbanion toward isoquinoline N-oxide (1) according to the following sequence.

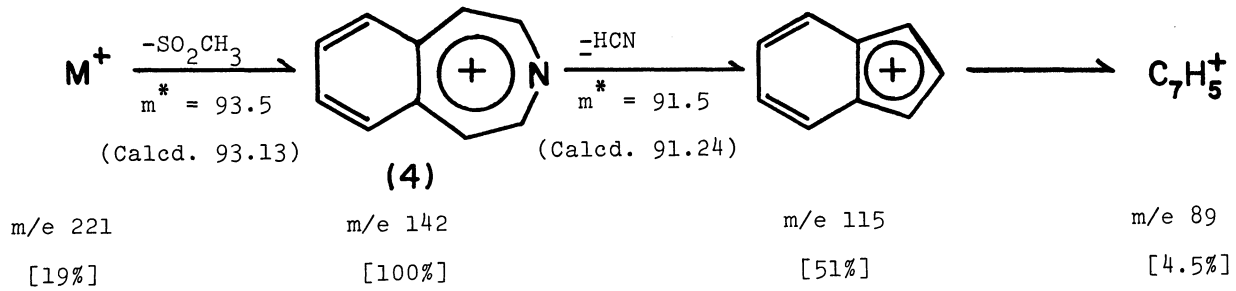


(1) (2) 0.8% (3) 8.0%

Sodium hydride (2.46g) was dissolved in 80ml of dimethyl sulfoxide under nitrogen atmosphere, and solution of isoquinoline N-oxide (2.9 g) in dimethyl sulfoxide (20ml) was poured into

the solution. The reaction mixture was kept at 70°C and stirred for 30 min. Then, the mixture was poured into a large excess of water and the brownish yellow solid separated from the solution was collected by filtration. The reaction products were separated by column chromatography (silica gel and chloroform), and 0.35g (8.0%) of 3-methylsulfonyl-3H-benz[d]azepine (3) and 0.02g (0.8%) of naphthalene (2) were obtained.[8] Recrystallization from ethyl acetate gave yellow leaflets of pure 3: mp 138-140°C; uv max 244 nm ($\log \epsilon$ 4.50); mass spectrum m/e 221(M^+); ir(solid) 1335, 1165 cm^{-1}(ν_{SO}). Found: C, 59.87; H, 4.93; N, 6.21%. Calcd for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33%.

The structure of 3 is deduced from the spectral evidences. The indication for the 3H-benz[d]azepine structure is found by observing a set of doublets, J=5.3 Hz, centered at δ 5.48 and 5.91, which is the typical of cis-disubstituted olefinic protons, and assigned to the protons on the azepine ring. Its ultraviolet spectrum resembles closely to that of methyl 3-phenyl-3H-benz[d]azepine-2,4-dicarboxylate (λ_{max} 248 nm, $\log \epsilon$ 4.65).[1] Much less intense band near 315 nm ($\log \epsilon$ 3.0) was observed. The PPP-CI MO calculation gives 269.0 and 368.9 nm, respectively, for the wavelengths of these transitions. The bathochromic shift of the allowed $\pi - \pi^*$ transition compared with that of isoquinoline system was supported by the calculation, and the presence of a weak absorption at a longer wavelength is also predicted. Rather intense absorption bands located at 1335 and 1165 cm^{-1} in the infrared spectra could be attributed to the two SO stretching modes (ν_{as} and ν_s) of the sulfonamido group. Mass spectrum of 3 shows an intense peak of benzazepinylium (4) at m/e 142, which is proved by the metastable peak at m/e 93.5 to be generated from the parent molecular ion by the elimination of CH_3SO_2 group. This may be another evidence for the presence of the benzazepine structure.



Relative intensities of the peaks are given in brackets [ ].

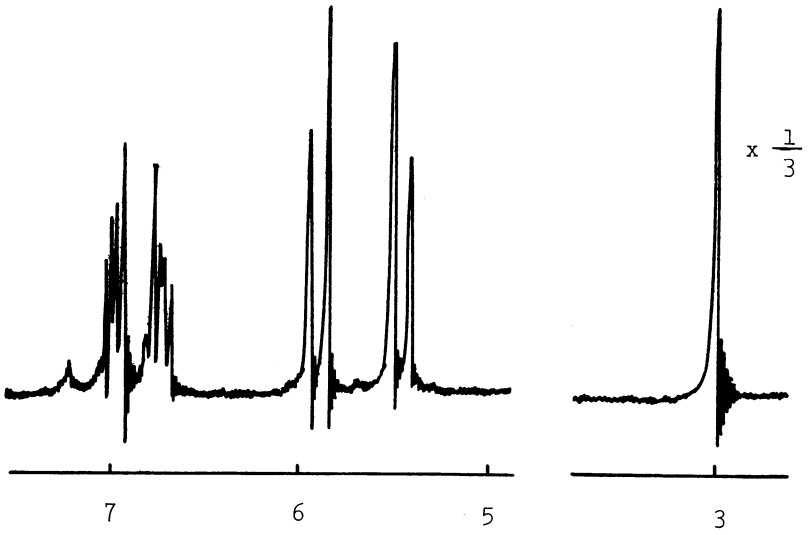


Fig. 1 Nmr spectrum of 3-methylsulfonyl-3H-benz[d]azepine (3).

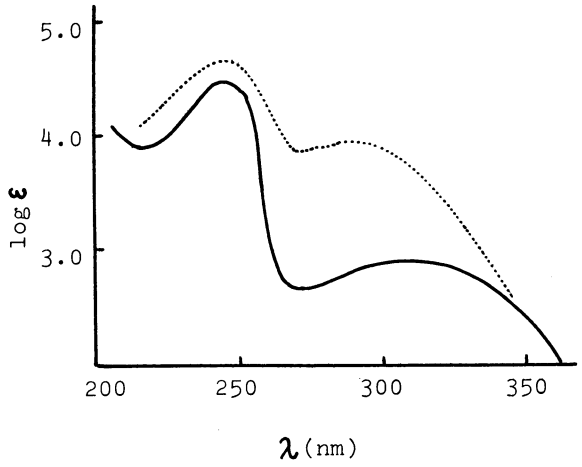
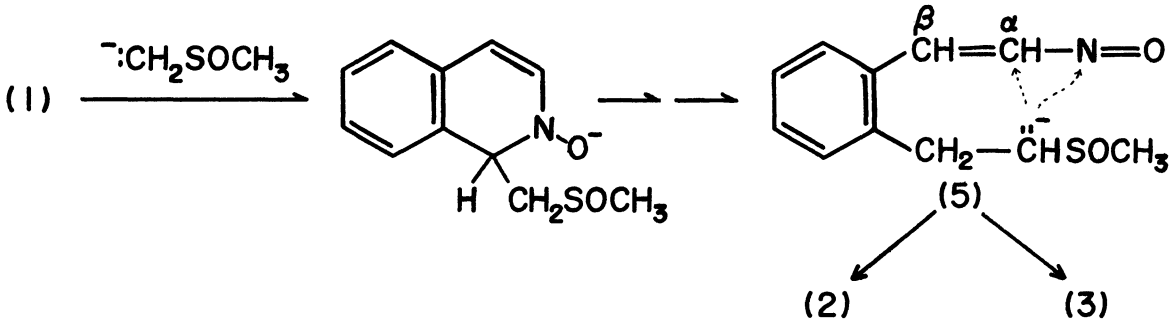


Fig. 2 Ultraviolet spectrum of 3-methylsulfonyl-3H-benz[d]azepine (3). The spectrum of 3 (————) is similar to that of dimethyl 3-phenyl-3H-benz[d]azepine-2,4-dicarboxylate (·····) reported in ref. 2.

Formation of naphthalene (2) during the reaction is supposed to be another example of the unusual formation of aromatic hydrocarbon.[7]

The reaction is supposed to proceed through the cyclization of intermediate carbanion (5), and the intramolecular nucleophilic attack both to α-carbon atom and to nitrogen atom might occur to produce finally 2 and 3, respectively. Further investigation to prove the reaction pathway is in progress by employing deuterium labelled materials.



References and Notes

1) Resonance energies for azepine and 3H-benz[d]azepine are estimated to be -1.80 and 17.53 kcal mol^{-1} by MINDO calculations. See M. J. S. Dewar and N. Trinajstic, Tetrahedron, 26, 4269 (1970).

2) K. Dimroth and H. Freyschlag, Chem. Ber., 90, 1628 (1957).

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4) H. O. Bernhard and V. Snieckus, Tetrahedron, 27, 2091 (1971).

5) T. J. Van Bergen and R. M. Kellogg, J. Org. Chem., 36, 978 (1971).

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8) A considerable amount of unidentified tarry product was obtained besides these products, and the starting isoquinoline N-oxide was not recovered.

(Received February 17, 1976)