Some Reaction of 2-Mercapto-1, 3-diazaazulene

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Nozoe, Mukai and Murata[1] reported that the reaction of tropolone methyl ether and thiourea in ethanol, in the presence of sodium alcoxide, resulted in the condensation to form 2-mercapto-1, 3-diazaazulene (I). Later, the same condensation reaction was carried out on tropolones with methyl[2], isopropyl[3], phenyl[4] and styryl[5], and oxidative desulfurization reaction on 2-mercapto-1,3-diazaazulene thereby formed. No studies, however, have been made on the nature of the mercapto group in 2-position of these compounds and it seemed of interest to examine reactivity of a mercapto group in this kind of new, nitrogenous heterocyclic compound. Therefore, examinations were made with I which has no carbon-containing side chain.

Oxidation of I with nitric acid or 10% hydrogen peroxide with heating affords 1,3-diazaazulene (II)[1] in over 80% yield. Application of 10% hydrogen peroxide at room temperature or of sodium nitrite in acetic acid affords only the 2-disulfide (III)[1] in almost quantitative yield. Application of hydrogen peroxide to III with heating produces II, but the possible intermediate in this reaction, the sulfonic acid or sulfinic acid[6], was not isolated. III is easily reduced to I by aqueous solution of sodium sulfide.

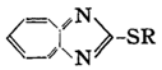
The sodium salt of I undergoes facile reaction in ethanol with various alkyl iodides, polynitrochlorobenzenes, benzyl chloride, chloroacetone, phenacyl chloride, chloroacetic acid, and 2-chloro-1,3-diazaazulene[7] to form the corresponding thioethers (Table I).

TABLE I. 2-SR-1,3-DIAZAAZULENE

Compd. No.	R	Cryst. form*	m. p., °C	Recrystn. solvent**	Analysis					
					Calcd.			Found		
					C	H	N	C	H	N
IV	CH_3	py. P.	101~102	P+B	61.36	4.58	15.90	61.01	4.82	16.67
V	C_2H_5	py. P.	95~ 96	C+B	63.15	5.30	14.73	63.32	5.01	14.38
VI	n-C_3H_7	py. N.	98~ 99	C+B	64.69	5.92	13.72	64.61	5.46	13.65
VII	n-C_4H_9	py. N.	66~ 67	C	66.03	6.47	12.84	65.95	6.11	12.18
VIII	CH_2-CH=CH_2	y. P.	72~ 74	P+B	65.33	4.98	13.86	64.84	4.94	13.82
IX	$CH_2C_6H_5$	y. N.	94~ 95	B+C	71.41	4.80	11.11	71.25	4.84	11.09
X	$C_6H_3(NO_2)_2$	y. N.	224(d.)	D+A	51.22	2.46	17.07	51.29	2.30	17.63
XI	$C_6H_2(NO_2)_3$	y. N.	194	D+A	45.05	1.89	18.77	44.86	2.07	15.35
XII	$CH_2COC_6H_5$	y. N.	164	A	68.56	4.32	10.00	68.50	4.47	9.70
XIII	CH_2COCH_3	py. S.	68~ 69	C	60.54	4.62	12.84	60.80	4.43	13.31
XIV	CH_2COOH	py.	300	—	54.55	3.66		54.62	3.63	
XV	$C_3H_5N_2$	y. P.	254(d.)	A			19.30			19.12

* y, yellow; py, pale yellow; N, needles; P, prisms; S, scales.

** A, ethanol; B, benzene; C, cyclohexane; D, dioxane; P, petroleum ether.



(IV)—(XV)

1) T. Nozoe, T. Mukai and I. Murata, *J. Am. Chem. Soc.*, **76**, 3352 (1954).
2) H. Akino, K. Sato and Y. Suzuki, *Science Repts. Tohoku Univ., I*, **40**, 92 (1956).
3) T. Nozoe and T. Sato, unpublished data.
4) K. Kikuchi and T. Muroi, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **77**, 1081 (1956).
5) H. Matsumura, ibid., **78**, 669 (1957).
6) The intermediate formed by oxidative desulfurization of 2-mercaptoimidazole is said to be a sulfinic acid. Cf. I. E. Balaban and H. King, *J. Chem. Soc.*, **1927**, 1858; I. D. Lamb and F. L. Pyman, ibid., **125**, 706 (1924).
7) T. Nozoe, T. Mukai and I. Murata, *Proc. Japan Acad.*, **30**, 482 (1954).

TABLE II. U. V. ABSORPTION MAXIMA OF 2-SR-1,3-DIAZAAZULENES

Compd. No.	λ_{max}^{MeOH}, mμ (log ε)
IV	239(4.47), 270(4.29), 362(4.26)
V	239(4.48), 270(4.30), 362(4.27)
VI	239(4.50), 271(4.32), 362(4.30)
VII	239(4.51), 271(4.32), 364(4.31)
VIII	240(4.41), 268(4.27), 362(4.17), 435(3.74)
IX	240(4.47), 270(4.29), 360(4.28)
X	242(4.59), 270(4.36), 370(4.29)
XI	238(4.58), 270(4.45), 340(4.17), 380(sh.)
XII	241(4.55), 270(4.35), 358(4.26)
XIII	238(4.45), 270(4.35), 358(4.26)
XIV	240(4.40), 270(4.19), 365(4.18)
XV	248(4.72), 275(sh.), 368(4.41)

The ultraviolet absorption maxima of these thioethers are presented in Table II.

The nucleophilic substitution reaction of I was then examined. Examples of nucleophilic substitution of a mercapto group are extremely rare and only the reaction with ammonia or amine[8] is known. Heating of I with 40% aqueous ammonia or methylamine in a sealed tube for a few hours at 170~180°C only results in quantitative recovery of I. Heating of I with concentrated hydrochloric acid in a sealed tube for 6 hr. at 160°C results in its hydrolysis and 2-hydroxy-1,3-diazaazulene (XVI)[1,7] is obtained in a good yield.

The methylthio group may be considered to undergo more facile nucleophilic substitution than the mercapto group and there is a comparatively large number of examples[9]. Actually, IV reacts with a number of nucleophilic reagents to form the corresponding 2-substituted derivatives (Table III).

Experimental[10]

2-Mercapto-1,3-diazaazulene (I). — Synthesized from tropolone methyl ether and thiourea according to the method described earlier[1]. Reddish orange microneedles, m. p. >300°C.

Oxidation of I.—a) To a suspension of 1 g. of I in 10 cc. of water, 5 cc. of 30% hydrogen peroxide was added and the mixture was warmed on a water bath, by which the reaction proceeded immediately with effervescence to form a clear, orange solution. After cooling, the mixture was rendered weakly alkaline with sodium hydrogen carbonate and extracted with chloroform. The extract was washed with water, dried, and chloroform was evaporated. The residue was dissolved in benzene and passed through a short column of alumina from which 620 mg. of yellow needles, m. p. 110~112°C, was obtained. Mixed fusion with 1,3-diazaazulene (II) showed no depression of the melting point.

b) To a suspension of 100 mg. of I in 1 cc. of water, 1.2 cc. of 10% hydrogen peroxide was added dropwise with stirring at room temperature and the mixture was stirred for further 3 hr. The precipitate formed was collected by filtration and 80 mg. of yellow microneedles (III), m. p. 203°C (decomp.), was obtained.

c) A solution of 45 mg. of sodium nitrite dissolved in 0.5 cc. of water was added dropwise to 100 mg. of I suspended in 2 cc. of glacial acetic acid, cooled in ice. The precipitate formed changed from orange to yellow. After stirring for 2 hr., the precipitate was collected by filtration to 85 mg. of III, m. p. 204°C (decomp.).

Reaction of Disulfide (III).—*a) Oxidation with hydrogen peroxide.*—A mixture of 100 mg. of III suspended in 0.5 cc. of water, with 1 cc. of 30% hydrogen peroxide added, was heated on a water bath by which effervescence occurred immediately to form an orange solution. The mixture was neutralized with sodium hydrogen carbonate, extracted with chloroform, and the extract was washed with water. After drying, chloroform was distilled off and 70 mg. of yellow needles, m. p. 110~113°C, was obtained. This showed no

TABLE III. NUCLEOPHILIC SUBSTITUTION OF 2-METHYLTHIO-1,3-DIAZAAZULENE

Compd. No.	Reagent	Yield, %	m. p., °C	Calcd.	Found	Ref.
XVI	Concd. HCl	72	245	—	—	1
XVII	40% aq. NH_3	36	295(d.)	—	—	10
XVIII	40% aq. NH_2CH_3	55	172~173	26.40	26.32	—
XIX	40% aq. $NH(CH_3)_2$	74	133~134	—	—	7
XX	80% aq. NH_2NH_2	71	189	—	—	7
XXI	$C_6H_5NH_2$	56	239	18.99	19.00	—
XXII	$C_6H_5CH_2NH_2$	74	175	17.86	17.92	—
XXIII	$NaOCH_3$	27	94	—	—	7

8) G. H. Hitchings and P. B. Russell, *J. Chem. Soc.*, **1949**, 2454; E. C. Taylor, J. A. Carbon and D. R. Hoff, *J. Am. Chem. Soc.*, **75**, 1904 (1953).

9) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 273 (1951).

10) All melting points are uncorrected. Ultraviolet absorption spectra were used for identification of high-melting substances and decomposition products. Measurement was made with a Beckman Model DU spectrophotometer. The microanalyses were carried out by Mr. S. Ohyama and Miss A. Iwanaga, to whom the author's deep gratitude is hereby expressed.

depression in the melting point on admixture with II.

b) Reduction with sodium sulfide. — Aqueous solution of 200 mg. of sodium sulfide was added to 65 mg. of III, suspended in 1 cc. of ethanol by which the precipitate disappeared to form an orange solution. The mixture was diluted with 2 cc. of water, acidified with glacial acetic acid, and the precipitate was collected by filtration to give 50 mg. of I, m. p. >300°C.

Reaction of Sodium Salt of I and Halides.—*a) General procedure for preparation of methyl- (IV), ethyl- (V), n-propyl- (VI), n-butyl- (VII), allyl- (VIII), benzyl- (IX), phenacyl- (XII) and acetonylthio-1,3-diazaazulene (XIII).* — Ethanolic solution of 1.1 molar equivalents of halide was added to the sodium salt of I dissolved in ethanol and the mixture was refluxed for 0.5~1.0 hr. Ethanol was distilled off, the residue was dissolved in benzene, and the benzene solution was passed through a short column of alumina. The crystalline residue obtained on evaporation of benzene was recrystallized 2~3 times from the solvent listed in Table I.

b) General procedure for preparation of 2,4-dinitrophenyl- (X), 2,4,6-trinitrophenyl- (XI) and 2-(1,3-diazaazulenylthio)-1,3-diazaazulene (XV).— Sodium salt of I was mixed with halide in ethanol and the precipitate formed after some time was recrystallized twice from a solvent as listed in Table I.

c) 2-Carboxymethylthio-1,3-diazaazulene (XIV). —To a solution of 500 mg. of I dissolved in 2 cc. of 2 N sodium hydroxide, 300 mg. of monochloroacetic acid neutralized with sodium hydrogen carbonate was added and the mixture was heated on a water bath at 90°C for 15 min. After cooling, the mixture was acidified with acetic acid, the yellow precipitate was collected by filtration, and washed with water and then with ethanol, affording 640 mg. of crystalline powder, m. p. >300°C.

2-Hydroxy-1,3-diazaazulene (XVI).—*a) From I.* — A mixture of 100 mg. of I and 2 cc. of concentrated hydrochloric acid was sealed in a tube and heated at 160°C for 6 hr. Evaporation of hydrochloric acid left 120 mg. of colorless crystals, m. p. >300°C, which was dissolved in a small amount of water, and the solution was neutralized with a saturated solution of sodium hydrogen carbonate. The crystalline precipitate thereby formed was collected by filtration and 95 mg. of pale yellow needles, m. p. 234°C, was obtained. Recrystallization from dilute ethanol raised the melting point to 244°C, undepressed on admixture with XVI.

b) From IV.—A mixture of 50 mg. of IV and 1 cc. of concentrated hydrochloric acid was refluxed, in an oil bath for 2 hr., hydrochloric acid was evaporated, and the residue was treated as in a) from which 30 mg. of XVI was obtained.

Nucleophilic Substitution Reaction of IV.—*a) 2-Amino-1,3-diazaazulene (XVII).*—A mixture of 50 mg. of IV and 1 cc. of ammonia water was sealed in a tube and heated at 100°C for 6 hr. The mixture was allowed to cool overnight and crystals that formed were collected by filtration to 15 mg. of crystals melting at 290°C with decomposition. Recrystallization from hot water afforded yellow needles (XVII), m. p. 294°C (decomp.). Ammonia mother liquor was diluted with 3 cc. of water and extracted with chloroform from which 20 mg. of IV was recovered.

b) 2-Methylamino- (XVIII) and 2-dimethylamino-1,3-diazaazulene (XIX).—A mixture of 50 mg. of IV and 40% aqueous solution of monomethylamine or dimethylamine was sealed in a tube and heated at 100°C for 6 hr. The reaction mixture was diluted with water, extracted with chloroform, and the chloroform residue was recrystallized from the benzene-petroleum ether mixture to XVIII, m. p. 173~174°C, or XIX, m.p. 134°C. There was no recovery of IV in this case.

c) 2-Hydrazino-1,3-diazaazulene (XX). — To a solution of 70 mg. of IV dissolved in 1 cc. of ethanol, 0.5 cc. of 80% aqueous solution of hydrazine was added and the mixture was refluxed for 2 hr. When cooled, crystals formed, they were collected by filtration and recrystallized from ethanol to 45 mg. of XX, m. p. 187°C (decomp.).

d) 2-Anilino- (XXI) and 2-benzylamino-1,3-diazaazulene (XXII).—A mixture of 70 mg. of IV dissolved in 1 cc. of ethanol and 50 mg. of aniline or benzylamine was heated in a sealed tube at 160~170°C for 8 hr. The crystals formed on cooling were recrystallized from benzene to yellow needles (XXI), m. p. 238~239°C, or yellow scales (XXII), m. p. 175°C.

e) 2-Methoxy-1,3-diazaazulene (XXIII). — To a solution of 30 mg. of sodium methoxide dissolved in 3 cc. of dehydrated methanol, 90 mg. of IV was added and the mixture was refluxed on a water bath for 25 hr. After evaporation of methanol, the benzene-soluble portion afforded 30 mg. of XXIII and the benzene-insoluble portion afforded 15 mg. of XVI.

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