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STUDIES OF PYRAZINES. V. PREPARATION OF 2-ALKYLPYRAZINES FROM ALKYL 2-PYRAZINYL SULFONES[1]

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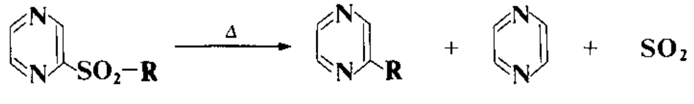
Abstract — The pyrolysis of 10 alkyl 2-pyrazinyl sulfones was performed to give 2-alkylpyrazines, pyrazine, and sulfur dioxyde with some tarry products. The *primary* alkyl 2-pyrazinyl sulfones (R = *n*-C_nH_{2n+1}; $n = 1 \sim 5$ and *i*-C_4H_9) gave the corresponding 2-alkylpyrazines as the major product (25 ∿ 53% yield). Contrary to the above, pyrazine was the major product (22 ∿ 49%) in the pyrolysis of the *secondary* and *tertiary* alkyl sulfones (R = *i*-C_3H_7, *t*-C_4H_9 and 1,2-dimethylpropyl) except for *s*-butyl one. An isomerization of the alkyl group in the 2-alkylpyrazine and the formation of alkene, alkane and 2-pyrazinesulfinic acid could not be found. The formation of 2-pyrazinol *via* successive intermediates of sulfinate and 2-alkoxypyrazine was not also observed.

Although various kinds of synthetic methods of alkylpyrazines have been reviewed by Cheeseman and Werstiuk,[2] the principal difficulties encountered in these methods are either the preparation of the precurser compounds or the unsuitability for a laboratorial preparation. Alkylation of 2-sodiomethylpyrazine with alkyl halide is an excellent method to prepare an 2-alkylpyrazine, but it is difficult to separate the unreacted 2-methylpyrazine from the reaction mixture including the lower alkyl substituted pyrazine and the polysubstitution of the methyl group is unavoidable. In this paper, we wish to report the preparation of 2-alkylpyrazines (2), especially the lower alkyl derivatives, by the pyrolysis of alkyl 2-pyrazinyl sulfones (1), which are easily prepared from 2-chloropyrazine and sodium alkanethiolates followed by oxidation with hydrogen peroxide.

Both a pyrolytic and a photolytic extrusion of sulfur dioxide from 1,3-dihydro-2-benzothiophene 2,2-dioxide have been reported.[3∿5] Although there have been many reports on the analogous reactions,[6,7] it is difficult to find the formation of 2 from 1 by the analogous method. On heating 1 at the boiling point for about 30 min under the atmospheric pressure, the sulfone 1 decomposed to 2, pyrazine (3), and sulfur dioxide[8] with some tarry products (Eq. 1). Table shows the results on the pyrolysis of the 10 sulfones 1. The primary sulfones (1a ∿ 1f) yielded 2a ∿ 2f as the major products in the yields of 25 ∿ 53%. Contrary to the above, 3 was the major product (22 ∿ 49% yield) in the pyrolysis of the secondary and tertiary alkyl sulfones (1h ∿ 1j) except for s-butyl one (1g), which yielded 25 ∿ 34% of 2 and 14 ∿ 15% of 3. In the pyrolysis of 1a, only 2a was obtained, and only 3 was done in the pyrolysis of 1j. No isomerization of alkyl group attached to the pyrazine ring was observed in the reaction of all compounds investigated. The results in Table show that the lower alkyl 2-pyrazinyl sulfones 1 except for 1a are effectively converted into the corresponding 2-alkylpyrazines 2 in the satisfactory yields. This serves our initial purpose.



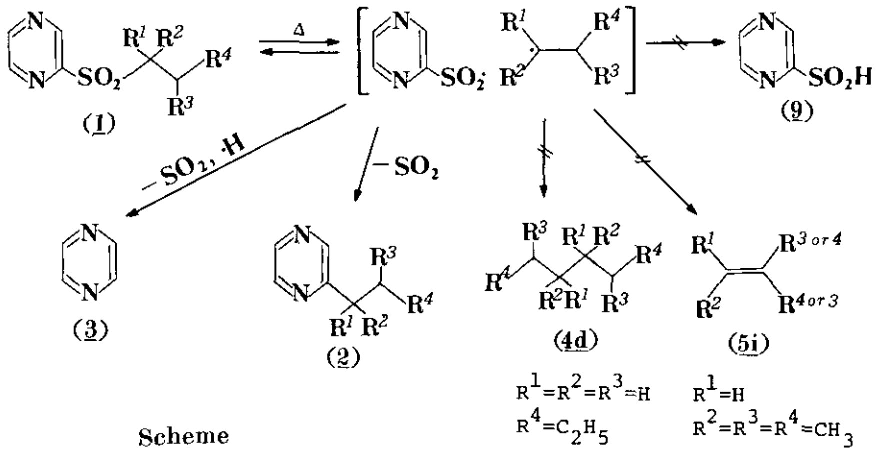
(1) (2) (3) ....(1)

a) R = CH_3
b) R = C_2H_5
c) R = n-C_3H_7
d) R = n-C_4H_9
e) R = n-C_5H_{11}
f) R = i-C_4H_9
g) R = s-C_4H_9
h) R = i-C_3H_7
i) R = 1,2-dimethylpropyl
j) R = t-C_4H_9

In Scheme was shown the reaction mechanism, which is estimated on the following facts. (a) The order of r values calculated by Eq. 2 is the same one that is found in the stability of alkyl radicals (Table). (b) No isomerization of alkyl

$$r = \frac{[3]}{[2]} \qquad \cdots\cdots\cdots\cdots (2)$$

group was observed as mentioned above. (c) Octane (4d) was not detected in the gas chromatogram for the reaction mixture of 1d, and 2-methylbutane (5i) were not also detected in the pyrolysis of 1i. (d) 2-Pyrazinesulfinates (6), 2-alkoxypyrazine (7), or 2-pyrazinol (8) could not be found in each of the reaction mixture of 1a ∿ 1j. The former two compounds, 6 and 7, have been observed in the thermal rearrangement of dibenzothiophene 5,5-dioxide,[9] and the last one 8 in the pyrolysis



Scheme

TABLE PHYSICAL PROPERTY AND PYROLYSIS OF ALKYL 2-PYRAZINYL SULFONES (1)

	Bp (°C/mmHg) of 1	Reaction Temp. t/°C	Yield (%)[a] of 2	3	r [3]/[2]
a	(45 ∿ 46)[b,c]	265 ∿ 280	25	trace	∿0
b	125/0.435[d]	290 ∿ 292	53	5.2	0.1
		—	43[e]	1.5[e]	0.03[e]
c	123 ∿ 124/0.44[f]	324 ∿ 332	43	9.3	0.2
		328 ∿ 336	41	6.2	0.1
d	139 ∿ 140/0.61[f]	298 ∿ 301	42	6.6	0.2
e	139 ∿ 140/0.45[f]	302 ∿ 305	31	6.6	0.2
		302 ∿ 312	34	3.7	0.1
f	123 ∿ 124.5/0.49[f]	297 ∿ 303	27	8.0	0.3
		285 ∿ 297	25	7.7	0.3
g	127 ∿ 130/0.58[f]	200 ∿ 280	25	14	0.6
		195 ∿ 260	34	15	0.5
h	118.5 ∿ 121/0.35[d]	206 ∿ 273	15	22	1.5
i	130 ∿ 132/0.40[f]	256 ∿ 270	6	48	8.3
		298 ∿ 304	4	46	11
j	(72.5 ∿ 73)[b,f,g]	148 ∿ 240	trace	37	large
		140 ∿ 208	trace	49	large

[a] Calculated on the basis of the reacted 1. [b] Mp (°C) in parenthesis. [c] From hexane, lit. 47 ∿ 48 °C (ref. 11). [d] Physical property for this compound has been reported previously (ref. 10). [e] Direct distillation method. [f] This compound gave a satisfactory result for C, H, N analysis and exhibited spectral properties in accordance with assigned structure. [g] From hexane-benzene.

of 7.[10]

From these facts, it is concluded that the reaction proceeds through a radical-paired intermediate. The radical pair seems to remain long enough to produce 2 before it separates from each other to give other products (for example, 4). This is also supported by the fact that the pyrolysis of 1j in the presence of 1-octene in a sealed tube (230 °C, 90 min), gave no adducts produced by an addition of *t*-butyl (or 2-pyrazinyl) radical to 1-octene.

In addition, 2-pyrazinesulfinic acid (9) was not extracted with an aq sodium carbonate solution from the reaction mixture.

Alkyl 2-pyrazinyl sulfones 1a ∿ 1j were prepared by the oxidation of the corresponding 2-alkylthiopyrazines with hydrogen peroxide, and bp (or mp) are shown in Table. The pyrolysis of 1 was performed by the following general procedure. A sulfone 1 (2 ∿ 3 mmol) was placed in a glas tube (ϕ = 10 mm) with a tapered joint, and heated cautiously for about 30 min with a small flame at the temperature shown in Table. After cooling, acetone (0.4 ml) was added to dissolve the reaction mixture. To an aliquot of the solution, appropriate internal standards were added and the sample was analyzed by means of GLC (conditions: column, Silicon GE SE-30 on Shimalite W; temp., 40 ∿ 140 °C (or 210 °C), 4 or 8 °C/min; carrier gas, N_2, 50 ml/min).

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