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# The Synthesis and the Thermal Decomposition of 1, 3, 4-Dioxazole Derivatives

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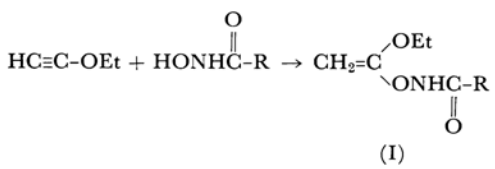
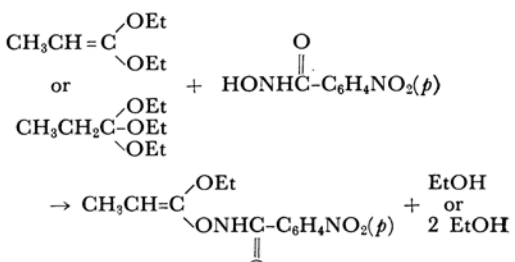
2, 2, 5-Tri-substituted-1, 3, 4-dioxazoles have been prepared by the reactions of benzhydroxamic acids with the diethylketals of such ketones as acetone, cyclohexanone, acetophenone and benzophenone. These dioxazoles decompose at elevated temperatures (above 150°C) into phenylisocyanates and ketones. A kinetic study of the decomposition reaction in nitrobenzene has been attempted, and the first-order rate constants have been obtained.

In a previous paper,[1] the dehydration reactions of hydroxamic acids by means of acetylenic ether to give isocyanates have been described. It has been there assumed that addition compounds (I) are necessary intermediates for these reactions.

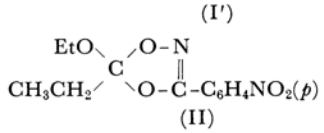


(I)

A crystalline intermediate, which has been isolated from an analogous reaction of *p*-nitrobenzhydroxamic acid with methylketene diethylacetal or ethyl orthopropionate, has also been considered to have a structure of the I type, as is shown below (I');



(I')



(II)

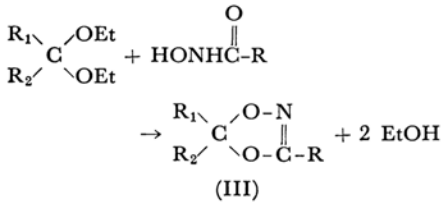
Further study of the structure of the intermediate, however, has suggested that the 1, 3, 4-dioxazole ring system (II) is a more reasonable structure for this compound, for it has been found that analogous substances are isolable from the reactions of benzhydroxamic acids with the diethylketals of such ketones as acetone, cyclohexanone, acetophenone and benzophenone.

1) T. Mukaiyama, H. Nohira and S. Asano, This Bulletin, **35**, 71 (1962).

TABLE 1. $R\text{-}\overset{\overset{O}{\|}}{C}\text{-}NHOH + \begin{matrix} R_1 \\ R_2 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} OEt \\ OEt \end{matrix} \longrightarrow \begin{matrix} R_1 \\ R_2 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} O\text{-}N \\ \| \\ O\text{-}C\text{-}R \end{matrix}$

| No. | R | $R_1$ | $R_2$ | Yield % | Mp (Bp °C/mmHg) | Formula | | Analysis, % C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $C_6H_5$- | $CH_3$- | $CH_3$- | 75 | (86—88/4) | $C_{10}H_{11}NO_2$ | Found | 67.51 | 6.47 | 7.88 |
| | | | | | | | Calcd. | 67.78 | 6.26 | 7.91 |
| 2 | $C_6H_5$- | $CH_3$- | $C_6H_5$- | 44 | 61—62 | $C_{15}H_{13}NO_2$ | Found | 75.12 | 5.42 | 5.95 |
| | | | | | | | Calcd. | 75.30 | 5.48 | 5.85 |
| 3 | $C_6H_5$- | $C_6H_5$- | $C_6H_5$- | 33 | 122—123[a] | $C_{20}H_{15}NO_2$ | Found | — | — | 4.82 |
| | | | | | | | Calcd. | — | — | 4.65 |
| 4 | $C_6H_5$- | -$(CH_2)_5$- | | 60 | 40—42 (106—108/0.04) | $C_{13}H_{15}NO_2$ | Found | 71.94 | 6.86 | 6.56 |
| | | | | | | | Calcd. | 71.86 | 6.96 | 6.46 |
| 5 | $p$-$NO_2$-$C_6H_4$- | $CH_3$- | $CH_3$- | 76 | 147—148 | $C_{10}H_{10}N_2O_4$ | Found | 54.43 | 4.77 | 12.56 |
| | | | | | | | Calcd. | 54.05 | 4.54 | 12.61 |
| 6 | $p$-$NO_2$-$C_6H_4$- | $CH_3$- | $C_6H_5$- | 36 | 92—93 | $C_{15}H_{12}N_2O_4$ | Found | 63.78 | 4.08 | 9.80 |
| | | | | | | | Calcd. | 63.38 | 4.26 | 9.86 |
| 7 | $p$-$NO_2$-$C_6H_4$- | $C_6H_5$- | $C_6H_5$- | 28 | 151—152 | $C_{20}H_{14}N_2O_4$ | Found | 69.37 | 4.24 | 8.36 |
| | | | | | | | Calcd. | 69.36 | 4.07 | 8.09 |
| 8 | $p$-$NO_2$-$C_6H_4$- | -$(CH_2)_5$- | | 53 | 102—103 | $C_{13}H_{14}N_2O_4$ | Found | 58.95 | 5.37 | 10.38 |
| | | | | | | | Calcd. | 59.53 | 5.38 | 10.68 |
| 9 | $p$-Cl-$C_6H_4$- | $CH_3$- | $CH_3$- | 60 | 60—61 | $C_{10}H_{10}ClNO_2$ | Found | 57.50 | 5.37 | 7.02 |
| | | | | | | | Calcd. | 56.74 | 4.78 | 6.62 |
| 10 | $p$-Cl-$C_6H_4$- | $CH_3$- | $C_6H_5$- | 42 | (138—140/0.05)[b] | $C_{15}H_{12}ClNO_2$ | Found | 66.25 | 4.71 | 4.70 |
| | | | | | | | Calcd. | 65.82 | 4.42 | 5.12 |
| 11 | $p$-Cl-$C_6H_4$- | $C_6H_5$- | $C_6H_5$- | 50 | 131—132 | $C_{20}H_{14}ClNO_2$ | Found | 67.84 | 4.16 | 4.20 |
| | | | | | | | Calcd. | 67.51 | 3.97 | 3.94 |
| 12 | $p$-Cl-$C_6H_4$- | -$(CH_2)_5$- | | 65 | 52—53 | $C_{20}H_{14}ClNO_2$ | Found | 61.79 | 5.82 | 5.25 |
| | | | | | | | Calcd. | 62.03 | 5.57 | 5.57 |

a) 124[2] b) Partly decomposed into $p$-chlorophenylisocyanate and acetophenone.



(III)

In this connection, Exner[2] reported the reaction of benzhydroxamic acid hydrochloride with benzophenone diethylketal to give 2, 2, 5-triphenyl-1, 3, 4-dioxazole (III; R, $R_1$ and $R_2$= $C_6H_5$-). In this case, there is no possibility of forming such a methylene-type structure as formula I. The infrared spectra of the compounds obtained here also support the 1, 3, 4-dioxazole structure. In addition, these dioxazoles decompose at elevated temperatures (above 150°C) into isocyanates and ketones. This reaction can be considered as a modified Lossen rearrangement. The present paper will also deal with a kinetic study of the thermal decomposition, as well as with the synthesis of a variety of substituted-1, 3, 4-dioxazoles.

## Procedure and Results

Various 1, 3, 4-dioxazole derivatives have been synthesized by the reaction of one-mole portions of benzhydroxamic acids with 1.2—1.5 mol portions of diethylketals of acetone, cyclohexanone, acetophenone or benzophenone in the presence of a catalytic amount of *p*-toluenesulfonic acid. The yields, melting points or boiling points, and analyses are listed in Table 1.

Similarly, bifunctional 1, 3, 4-dioxazoles have been prepared by the reaction of one-mole portions of terephthalohydroxamic acid or isophthalohydroxamic acid with 3—5 mol portions of diethylketal of acetone or cyclohexanone (Table 2).

The infrared spectra of these compounds show a characteristic absorption band in the region of 1620 $cm^{-1}$, a band which arises from the N=C

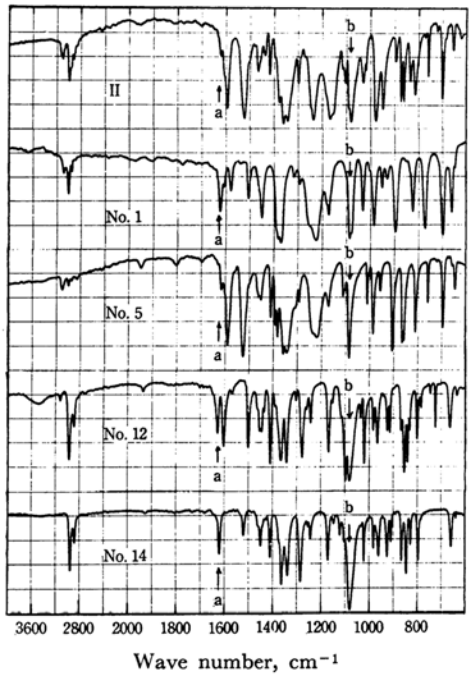
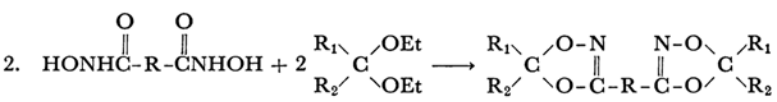
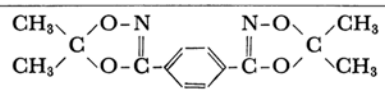
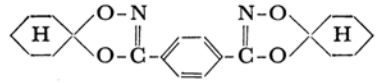
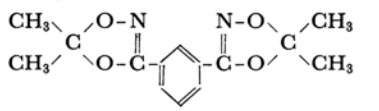
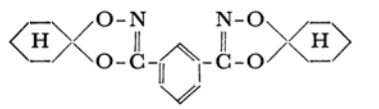



Fig. 1. Infrared spectra of 1, 3, 4-dioxazole derivatives.
II, No. 5, 12, 14 (KBr disks); No. 1 (liquid film).

TABLE 2. 

| No. | Structure | Yield % | Mp, °C | Formula | | Aanlysis, % C | H | N |
|---|---|---|---|---|---|---|---|---|
| 13 |  | 40 | 119—120 | $C_{14}H_{16}N_2O_4$ | Found<br>Calcd. | 60.95<br>60.86 | 6.43<br>5.84 | 9.68<br>10.14 |
| 14 |  | 45 | 157—158 | $C_{20}H_{24}N_2O_4$ | Found<br>Calcd. | 67.04<br>67.39 | 7.01<br>6.79 | 7.73<br>7.86 |
| 15 |  | 47 | 99—100 | $C_{14}H_{16}N_2O_4$ | Found<br>Calcd. | 60.01<br>60.86 | 5.88<br>5.84 | 10.14<br>10.14 |
| 16 |  | 55 | 109—110 | $C_{20}H_{24}N_2O_4$ | Found<br>Calcd. | 67.25<br>67.39 | 7.17<br>6.79 | 8.16<br>7.86 |

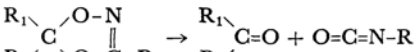
2) O. Exner, *Collection Czech. Chem. Commun.*, **21**, 1500 (1956); *Chem. Abstr.*, **50**, 15477 (1956).

TABLE 3. THE FIRST-ORDER RATE CONSTANTS FOR THE DECOMPOSITION OF 1,3,4-DIOXAZOLES IN THE PRESENCE OF DI-*n*-BUTYLAMINE IN NITROBENZENE

| R | $R_1$ | $R_2$ | $k$, $10^{-4}$ sec$^{-1}$ 158° | 150° | 140° | $E$ kcal/mol |
|---|---|---|---|---|---|---|
| $C_6H_5$- | $C_6H_5$- | $C_6H_5$- | 15 | 8.0 | 3.3 | 30 |
| *p*-$NO_2$-$C_6H_4$- | $C_6H_5$- | $C_6H_5$- | 19 | — | — | — |
| $C_6H_5$- | $C_6H_5$- | $CH_3$- | 14 | 7.8 | 3.3 | 29 |
| *p*-$NO_2$-$C_6H_4$- | $C_6H_5$- | $CH_3$- | 8.6 | 5.4 (148°) | 4.2 (145°) | — |
| $C_6H_5$- | $CH_3$- | $CH_3$- | 2.3 | — | — | — |
| *p*-$NO_2$-$C_6H_4$- | $CH_3$- | $CH_3$- | 2.7 | — | — | — |
| *p*-$NO_2$-$C_6H_4$- | -$(CH_2)_5$- | | 1.2 (160°) | — | — | — |

stretching modes of the ring system (Arrow a in Fig. 1), and strong absorption bands in the 1400—1000 $cm^{-1}$ region, bands which seem to correlate with O-C-O-C skeletal vibrations of the ring system. Above all, the band in the 1090—1080 $cm^{-1}$ region is another absorption characteristic of these compounds (Arrow b).

The kinetic study of the decomposition reaction of these dioxazoles was carried out in the presence of an excess amount of di-*n*-butylamine in a nitrobenzene solution. Di-*n*-butylamine has been known to react quantitatively with organic isocyanates to produce trisubstituted ureas; therfore, the rate of the decomposition became measurable by titrating the remaining amine.



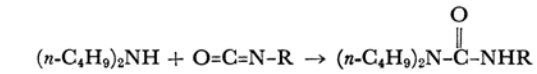


Figure 2 shows plots of $\log(c/c_0)$ against the time for the decomposition of 2, 2, 5-triphenyl-1, 3, 4-dioxazole at the temperatures of 140, 150 and 158°C; $c_0$ and $c$ represent the initial and the remaining concentrations of the dioxazole respectively.

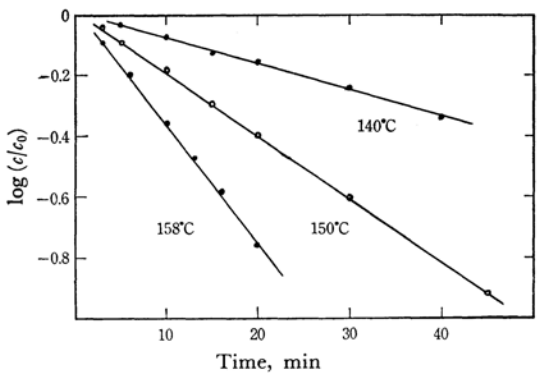
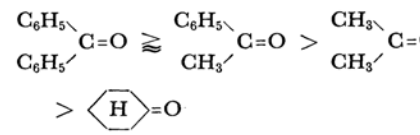



Fig. 2. The decomposition of 2, 2, 5-triphenyl-1, 3, 4-dioxazole (No. 3) in the presence of di-*n*-butylamine in nitrobenzene.

The linear relationship in this plots shows that the decomposition is first-order with respect to the dioxazole. The rate constants for this reaction were calculated according to the first-order kinetic equation; $2.303\log(c/c_0) = -kt$. The results are shown in Table 3, together with those of six other dioxazoles measured analogously. The average activation energies for these reactions are estimated to be about 30 kcal/mol from Arrhenius plots of these rate constants.

Table 3 shows, further, that 1, 3, 4-dioxazoles with any phenyl substituents on the 2-position decompose more easily than 2, 2-dialkyl-1, 3, 4-dioxazoles. In other words, the ease of the decomposition depends on the nature of the generating ketones, and can be described as follows:



On the other hand, no notable differences in reactivities between 5-phenyl-1, 3, 4-dioxazoles and 5-*p*-nitrophenyl-1, 3, 4-dioxazoles could be found.

## Experimental

**Preparation of 2, 2-Dimethyl-5-phenyl-1, 3, 4-dioxazole (No. 1).** A mixture of 13.7 g (0.1 mol) of benzhydroxamic acid, 17.2 g (0.13 mol) of acetone diethylketal, and 0.2 g of *p*-toluenesulfonic acid in 50 m*l* of pure ethyl acetate was refluxed for two and a half hours. It was then cooled, and, after the addition of 100 m*l* of ethyl ether, the solution was washed with 40 m*l* of 5% aqueous solution of sodium carbonate and then with water. The solution was dried with potassium carbonate. After the solvent had been removed, the dioxazole was distilled under reduced pressure. It weighed 15 g (75%), bp 86—88°C/4 mmHg.

Similarly, the other monofunctional dioxazoles (No. 2—12 in Table 1) were prepared from the corresponding hydroxamic acids and diethylketals. Crystalline products were recrystallized from ethyl acetate, ether, pertroleum ether, or 75—95% aqueous ethanol.

**Preparation of 1, 4-Bis(2, 2-dimethyl-1, 3, 4-dioxazol-5-yl)benzene (No. 13).** A mixture of 2.0 g

(0.01 mol) of finely-powdered terephthalohydroxamic acid, 6.5 g (0.05 mol) of acetone diethylketal, and 0.1 g of *p*-toluenesulfonic acid in 10 m*l* of a mixed solvent of ethyl acetate and dioxane (1 : 1) was refluxed for about ten hours, until the hydroxamic acid was thoroughly dissolved. It was then cooled, and after 30 m*l* of ethyl ether had been added, the solution was treated much as has been dsecribed above. The dioxazole was then recrystallized from petroleum benzine. Yield, 1,1 g (40%), mp 119—120°C.

Similarly, the other bifunctional dioxazoles (No. 14—16 in Table 2) were prepared by the reaction of terephthalohydroxamic acid or isophthalohydroxamic acid with the corresponding diethylketals.

**A General Kinetic Method for the Thermal Decomposition of 1, 3, 4-Dioxazoles.** Ten milliliters of a 0.2 N di-*n*-butylamine solution in nitrobenzene was placed in a 30 m*l* reaction tube equipped with a ground stopper, the tube was then immersed in a silicone oil thermostat controlled by a tetralin-mercury regulator for 10 min in order to obtain a constant temperature. To start the reaction, 0.001 mol of dioxazole, which had been weighed in a small paraffin tube, was put into the solution. After an appropriate interval of time, the tube was removed from the thermostat, and the reaction was stopped by rapid cooling with ice water. The amount of di-*n*-butylamine remaining was determined by titrating the mixture with 0.1 N hydrochloric acid in the presence of bromcresol green as an indicator.