Thermolysis of Δ^3-1,3,4-Oxadiazolin-2-ones

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Δ^3-1,3,4-Oxadiazolin-2-ones are decomposed at moderate temperatures, either neat or in solution, by two parallel, first-order processes. One of these results in the formation of the appropriate diazomethane and carbon dioxide while the other leads to ketone, nitrogen, and carbon monoxide. Rates of these competing processes are reported along with some solvent effects and substituent effects on the product ratios.

Les Δ^3 oxadiazoline-1,3,4 ones-2, soit pures soit en solution sont décomposées à des températures modérées selon deux processus parallèles du premier ordre. L'un deux a pour résultat la formation de diazométhane et du gaz carbonique alors que l'autre conduit à la cétone, l'azote et l'oxyde de carbone. Les vitesses de ces réactions compétitives sont rapportées ainsi que quelques effets de solvants et de substituants sur les rapports des produits.

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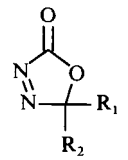
Introduction

Lactones of azocarboxylic acids (**1***a*, *b*) were isolated recently and were found to be remarkably reactive (1). For example, **1***a* was found to decompose to acetone azine with a half-life of about 3 weeks at 3° (1). Both **1***a* and *b* reacted in distilled water at room temperature to yield the appropriate ketone as well as the corresponding azine $(R_1R_2C{=}N{-})_2$. In view of the much greater thermal stability of α,β-unsaturated-γ-lactones (**2**), it was of interest to investigate the mechanism of decomposition of the former. In particular it was important to establish whether decomposition of **1** is strictly unimolecular or whether decomposition is also in some way induced by one of the products. Should dissociation turn out to be unimolecular, it would be of interest to determine the timing, stepwise or concerted, of the bond changes involved. This report is concerned with the first question, the kinetics of the reactions. Scheme 1 outlines possible decomposition pathways, including alternative routes to ketazine.



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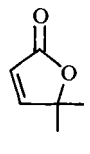

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a $R_1 = R_2 = CH_3$
b $R_1 = CH_3$; $R_2 = CH_2CH_3$
c $R_1 = CH_3$; $R_2 = C_6H_5$
d $R_1 = R_2 = C_6H_5$

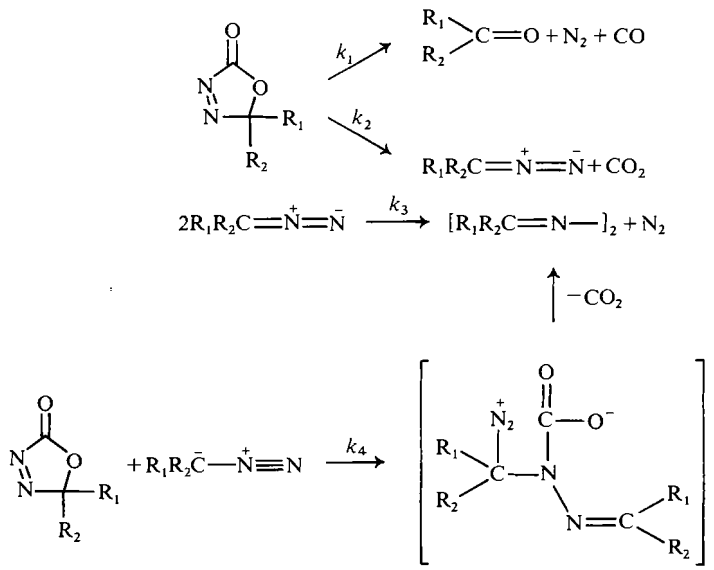
Methods and Results

The two possible mechanisms of ketazine formation should be distinguishable from the kinetics of disappearance of the oxadiazolinone. Reaction of the substrate with one of the products should be detectable in the form of either a deviation from first-order kinetics or a dependence of the apparent first-order rate constant on the substrate concentration. Furthermore the azine:ketone ratio in the product mixture should decrease with time in a given run and its final value should depend on initial oxadiazolinone concentration if induced decomposition of substrate by diazo compound were important. Accordingly, the rate of disappearance of **1***a* and

Table 1. Kinetics of thermolysis of 5,5-dimethyl-Δ^3-1,3,4-oxadiazolin-2-one at 84°*

Initial concentration of **1***a* (*M*)	$k_1 \times 10^4$ (s^{-1})	$k_2 \times 10^4$ (s^{-1})	Product ratio, ketone/azine
0.51	1.1	0.27	8.1
0.79	0.90	0.21	8.6
1.03	0.85	0.24	7.1
1.58	0.80	0.21	7.6
2.03	0.84	0.22	7.6
2.30	0.82	0.19	8.6
1.84†	0.88†‡	4.0†‡	0.52†‡

*In CCl_4, unless otherwise indicated. Rate constants are those defined in Scheme 1.
†In CH_3OH.
‡Isopropyl methyl ether, about 13% of the initial 2-propyl groups, was also present. Individual rate constants were calculated from the total first-order rate constant ($k_1 + k_2$) and the product distribution; k_1/k_2 being set equal to the ratio of integrals, ketone/(azine + ether), in which the ether integral was the doublet portion from the isopropyl signal only.



SCHEME 1

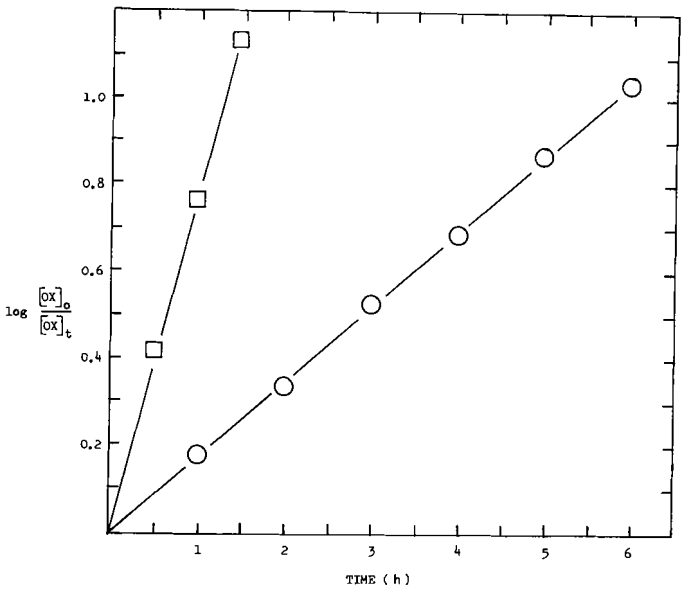


FIG. 1. Decomposition of **1***a* in CCl_4 (circles) and in CH_3OH (squares) at 84°.

the azine:ketone ratio were followed simultaneously by p.m.r. spectroscopy using benzene as internal standard for integration. Results are collected in Table 1 and Fig. 1.

Phenyl-substituted oxadiazolinones **1***c* and *d* are much less stable than **1***a* or *b* and could not be isolated in pure form. Solutions of those compounds in CCl_4 or ether turned red at room temperature and absorbed in the i.r. near 2025 cm^{-1} (2) as a result of decomposition to the appropriate diazo compounds. In CCl_4 at 84°, **1***d* decomposed with a half-life of approximately 30 s, corresponding to an overall rate constant of 2×10^{-2} s^{-1}, assuming first-order decomposition. The major products were diphenyldiazomethane and benzophenone (1653 cm^{-1})

with the former predominating. Benzophenone azine (1730 cm^{-1}) was always present in freshly prepared solutions of **1***d* but little, if any, additional azine was formed during the short time required for its decomposition at 84°.

Heating crude **1***c* (neat), at 85° for 25 min, gave acetophenone azine and acetophenone in the ratio 2:1 which corresponds to $k_1/k_2 = 0.25$ (Scheme 1). In solution (CCl_4 or ether) **1***c* also gave much more diazo compound and azine than ketone. Thus phenyl substituents at C-5, relative to methyl groups, enhance the rate of decomposition to CO_2 and diazo compound. Changing the solvent from carbon tetrachloride to methanol also favors decomposition to those products (Table 1).

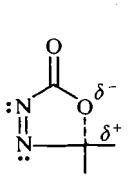
Discussion

The data of Table 1 and Fig. 1 show that **1***a* decomposed with first-order kinetics in carbon tetrachloride and in methanol. That behavior, together with a concentration–independent product ratio (Table 1), points toward unimolecular first steps. Ketazine must therefore arise by a process other than the last reaction of Scheme 1. Presumably the acetone azine is formed in a bimolecular process from two molecules of dimethyldiazomethane. The latter, which is reported to be quite unstable (3), did not accumulate to a level detectable by p.m.r. Applequist and Babad (4) studied the silver- and zinc-iodide-promoted decomposition of dimethyldiazomethane as well as diphenyldiazomethane and suggested that carbenes are not intermediates in those processes. Ketazines were the main products, with only traces of tetramethylethylene and tetraphenylethylene (4). Our results support their conclusion; propylene, from a 1,2-hydrogen shift in dimethylcarbene, was not detectable in the p.m.r. spectra of our product mixtures although formation of olefins from dialkyl carbenes is a facile process (5). Furthermore, decomposition of **1***a* in styrene gave mainly acetone and acetone azine, plus a small amount (<5%) of phenyl-2,2-dimethylcyclopropane. An upper limit is thus set on the amount of dimethylcarbene that could have been formed, for some of the cyclopropane may have come from decomposition of a pyrazoline intermediate.

During decomposition of **1***d* the concentration of diphenyldiazomethane builds up to substantial levels, for it is relatively stable at about 80°. Thus there is no reason to assign anything other than a unimolecular mechanism to the decomposition of **1***d*. The same probably applies for **1***c*. In what follows we discuss possible mechanisms of unimolecular decomposition of oxadiazolinones and suggest a reason for their instability, relative to lactones **2**.

The weakest bonds in oxadiazolinones (**1**) should be the N—CR_2 and the O—CR_2 bonds of the ring. Homolytic cleavage of the former is well known azo chemistry and stepwise decomposition is possible in view of the fact that some unsymmetric azo compounds may decompose by breaking N—C bonds one at a time (6). A diradical-like, rather than a dipolar transition state for C—N bond-breaking is in keeping with the small solvent polarity effect on k_1 (Table 1). Alternative processes leading to N_2, CO, and ketone by concerted breaking of two or three bonds could also be relatively insensitive to solvent polarity and cannot be excluded at this time.

Decomposition to carbon dioxide and diazo compound probably involves a more polar transition state as depicted by structure **3**. The increase in k_2 on changing the solvent from CCl_4 to CH_3OH (Table 1) is consistent with a polar transition state and the substituent effects (CH_3 *vs.* C_6H_5) are accommodated well in such a mechanism. Moreover, in the series of compounds **5**, which also decompose to di-



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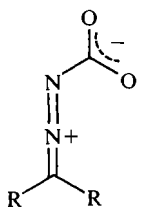

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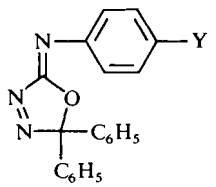


5

phenyldiazomethane, substituents Y which are electron-withdrawing enhance the rate of that decomposition (7), indicating development of negative change at benzylic nitrogen.

At first sight one might expect **2** to be equally suited to heterolytic C—O bond cleavage, as the negative end of the resulting zwitterionic species is again the carboxylate ion whereas the positive end is an allylic cation. However, the π-electrons of **1** and **2** are in an orbital normal to the C—O single bond and can therefore not provide stabilization until substantial C—O bond breaking, and N—CR_2 (or C—CR_2 in the case of **2**) bond rotation have occurred. Probably the most significant structural feature of **1**, which allows C—O bond-breaking to be relatively facile, is the lone pair of electrons at nitrogen, in an orbital coplanar with the stretching C—O bond. Overlap is thus possible and there may be an intermediate (**4**), at least in polar solvents, which rapidly decarboxylates. However, present data do not require a zwitterionic intermediate nor any other intermediate. Decomposition to diazoalkane and carbon dioxide fits the orbital symmetry requirements for fully-concerted bond changes (8). The solvent effect on k_2 (Table 1) is reasonable for either a stepwise mechanism, with formation of **4** rate-determining, or for a concerted mechanism leading to the polar diazoalkane directly. If the mechanism of the general reverse reaction, 1,3-dipolar cycloaddition of diazoalkanes to dipolarophiles, were firmly established, that knowledge could be used to infer the mechanism of decomposition of **1** to diazocompounds and CO_2, even though the reverse of that particular reaction is unknown. Arguments both for (9) and against (10, 11) concerted 1,3-dipolar cycloadditions have been presented and the matter is still not settled. In fact, it is possible that compounds like **1** will provide a solution, for the CO_2 formed from retrograde cycloaddition should be ideal for measurement of the $^{12}C/^{13}C$ kinetic isotope effect. Concerted decomposition must show an isotope effect whereas stepwise decomposition, through **4** or its diradical analog, with the second step fast, would not involve carbon isotope fractionation in the CO_2. We are currently carrying on such experiments.

Experimental

The u.v. and i.r. spectra were obtained with a Cary, Model 14 and a Perkin–Elmer, Model 521 instrument, respectively. The p.m.r. spectra were recorded with Varian A-60 and T-60 spectrometers and are referred to internal TMS as standard. Mass spectra were obtained with a Hitachi RMU-6A spectrometer. Melting points were determined with a Thomas "Unimelt" capillary melting point apparatus and are uncorrected.

2-Imino-Δ^3-1,3,4-oxadiazolines

A typical procedure is the following for preparation of 5-ethyl-5-methyl-2-methylimino-Δ^3-1,3,4-oxadiazoline by oxidative cyclization of the appropriate semicarbazone (12).

Butanone-4-methyl semicarbazone (13.0 g, 0.09 mol) in methylene chloride (100 ml) was added dropwise to a stirred, ice-cooled solution of lead tetraacetate (53.2 g, 0.12 mol) in methylene chloride (250 ml) under nitrogen. When addition was complete, the ice bath was removed and stirring was continued for 30 min. Ice-cold water (200 ml) was then added and the lead compounds were removed by filtering through a bed of Celite. The organic layer was washed with cold water, cold aqueous bicarbonate solution, and again with cold water. Evaporation of the dried ($MgSO_4$) solution at room temperature *in vacuo* gave an oil which appeared to decompose on chromatographic columns of silica gel, deactivated charcoal, or neutral alumina. Purification by g.l.p.c., on SE 30 at 70°, gave 5-ethyl-5-methyl-2-methylimino-Δ^3-1,3,4-oxadiazoline (3 parts) and 5-ethyl-5-methyl-Δ^3-1,3,4-oxadiazolin-2-one (1 part). The combined yield was 71%. Spectra and analyses of 2-imino-Δ^3-1,3,4-oxadiazolines are in Table 2.

5-Ethyl-5-methyl-Δ^3-1,3,4-oxadiazolin-2-one

The following procedure is typical for the hydrolysis of iminooxadiazolines.

To 5-ethyl-5-methyl-2-methylimino-Δ^3-1,3,4-oxadiazoline (200 mg) in methanol (15 ml) at 0° was added ice-cold, aqueous HCl (1 ml, 2.44 *M*). The mixture was stirred for 5 min before it was diluted with water and extracted with ether. Evaporation of ether from the washed (bicarbonate) and dried ($MgSO_4$) solution at room temperature gave the title compound (140 mg, 77%). Data for other oxadiazolinones are listed in Table 3.

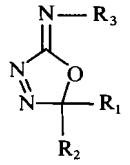
Semicarbazones

Unsubstituted semicarbazones were prepared from ketones and semicarbazide hydrochloride according to the procedure of Cheronis and Entriken (13). 4-Methyl semicarbazones were prepared from 4-methyl semicarbazide, which was made by adding hydrazine to methyl isocyanate (14). 4-(β-Phenylethyl) semicarbazones were made by transamination of the appropriate unsubstituted semicarbazones with β-phenylethyl amine, as described below for one member of the series.

Acetone semicarbazone (57.5 g, 0.5 mol) was added all at once to β-phenylethyl amine (84.7 g, 0.7 mol) at 130–140°. The well-stirred mixture was kept at that temperature until evolution of ammonia ceased. The mixture was then poured into aqueous acetic acid (10%) to precipitate the product which was crystallized from aqueous ethanol (82% yield). Data for new semicarbazones are in Table 4.

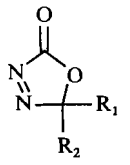
Ketazines

The azines of acetone, butanone, acetophenone, and benzophenone were prepared according to a published procedure (15).

TABLE 2. 2-Imino-Δ^3-1,3,4-oxadiazolines, 

Compound	m.p. (°C)	i.r. (cm^{-1}) (C=N, CCl_4)	p.m.r. (δ, CCl_4)*	Analysis† C	H	N
$R_1 = R_3 = CH_3$ $R_2 = C_2H_5$	oil	1713	0.77, t(7.5), 3 1.57, s, 3 2.02, q(7.5), 2 3.12, s, 3	51.05 51.31	7.85 7.97	29.76 29.53
$R_1 = R_2 = R_3 = CH_3$	oil	1712	1.65, s, 6‡ 3.12, s, 3	§	§	§
$R_1 = R_2 = CH_3$ $R_3 = CH_2CH_2C_6H_5$	oil	1715	1.37, s, 6 2.85, t(7.0), 2 3.55, t(7.0), 2	66.34 66.51	6.96 7.22	19.34 18.98
$R_1 = CH_3$ $R_2 = C_6H_5$ $R_3 = CH_2CH_2C_6H_5$	56–58	1715	1.73, s, 3 3.01, t(7.0), 2 3.81, t(7.0), 2	73.10 73.16	6.13 6.18	15.04 15.18
$R_1 = R_2 = C_6H_5$ $R_3 = CH_2CH_2C_6H_5$	65–66	1715	3.00, t(7.0), 2 3.80, t(7.0), 2	77.40 77.64	5.61 5.82	12.31 12.44

*Signals from aromatic hydrogens are not tabulated. The first entry is the chemical shift, followed by a multiplicity term (with coupling constant in brackets), followed by the relative integral.
†Calculated values in upper rows. Analytical results in lower rows.
‡In $CDCl_3$.
§This compound was not obtained in sufficiently pure form for satisfactory analyses.

TABLE 3. Δ^3-1,3,4-Oxadiazolin-2-ones, 

Compound	m.p. (°C)	i.r. (cm^{-1})*	u.v. (hexane)†	p.m.r. (δ, CCl_4)‡	Analysis§ C	H	N
$R_1 = R_2 = CH_3$	36–37	1835	216(3.54); 365(2.51) 373(2.57); 381(2.38)	1.63, s	42.11 41.97	5.30 5.35	24.55 24.81
$R_1 = CH_3$ $R_2 = C_2H_5$	oil	1835	216(3.54); 365(2.51) 373(2.57); 381(2.38)	0.82, t(7.5), 3 2.10, q(7.5), 2	46.87 47.01	6.29 5.99	21.86 21.69
$R_1 = CH_3$ $R_2 = C_6H_5$	oil	1835	‖	1.95, s, 3	‖		

*In CCl_4.
†λ_{max} (nm) followed by log ε in brackets.
‡Aromatic signals not included. The chemical shift is followed by the multiplet symbol, the coupling constant (Hz in brackets), and the relative integral.
§Calculated values in upper rows. Analyses in lower rows.
‖Purity high enough for a reliable u.v. spectrum, or for analysis, was not achieved. The corresponding diphenyl compound ($R_1 = R_2 = C_6H_5$) was obtained only as a solution in CCl_4. That solution also absorbed at 1835 cm^{-1} in the i.r. as well as at 2040 (diphenyldiazomethane), 1730 (benzophenone azine), and 1670 cm^{-1} (benzophenone).

TABLE 4. 4-Substituted semicarbazones, $R_1R_2C{=}NNHCONHR_3$

Compound	m.p. (°C)	p.m.r. (δ, CCl_4)*				Analysis† C	H	N
$R_1 = R_2 = CH_3$	87–88	1.90	1.94	2.83	3.44	65.75	7.71	19.16
$R_3 = CH_2CH_2C_6H_5$		s, 3	s, 3	t(7), 2	m, 2	65.83	7.84	19.09
$R_1 = CH_3$, $R_2 = C_6H_5$	129–130	2.33	2.87	3.58		72.57	6.81	14.93
$R_3 = CH_2CH_2C_6H_5$		s, 3	t(7), 2	m, 2		72.71	6.82	15.02
$R_1 = R_2 = C_6H_5$	87–88	2.81	3.47			76.94	6.16	12.24
$R_3 = CH_2CH_2C_6H_5$		t(7), 2	m, 2			76.93	6.20	12.34

*Aromatic and N—H signals not included. Upper rows are chemical shifts below which is the multiplicity followed where applicable by the coupling constant (Hz, in brackets) and the relative integral.
†Calculated values in upper rows. Analyses in lower rows.

Thermolysis of 5,5-Dimethyl-Δ^3-1,3,4-oxadiazolinone

Solutions of the oxadiazolinone (concentrations in Table 1) in CCl_4 containing benzene were pumped free of air with several freeze–pump–thaw cycles before they were sealed in n.m.r. tubes. The concentration of benzene was about half that of oxadiazolinone, so that integrals for that reference and the substrate were about equal at 50% reaction of the latter. The p.m.r. spectrum was recorded and integrated before tubes were placed in a bath at 84°, from which they were removed at 1 h intervals for analysis. Reaction was stopped by cooling the tubes quickly in ice water and time outside the bath was not counted. Integrals of p.m.r. signals were normalized with respect to the internal standard. The overall rate constant $(k_1 + k_2)$ for decomposition was obtained from such normalized data from a plot of log $([OX]_0/[OX]_t)$ *vs.* t where [OX] indicates oxadiazoline concentration at the time indicated by the subscript. The slope was set equal to $(k_1 + k_2)/2.303$. Individual rate constants were calculated from the total $(k_1 + k_2)$ and product data; *i.e.* the fraction of oxadiazolinone going to acetone is $k_1/(k_1 + k_2)$.

Product ratios were obtained by comparing averaged integrals, from many sweeps, of the ketazine signals with the ketone signals. In the case of 5,5-diphenyl-Δ^3-1,3,4-oxadiazolinone, where the p.m.r. spectrum is not useful, rate and product data came from measurements of the i.r. absorption bands at 1835 (oxadiazolinone), 2025 (diphenyldiazomethane), and 1730 cm^{-1} (benzophenone azine). Standard solutions of the two latter compounds were used to prepare calibration curves.

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