The Chemistry of 1,3,4-Oxadiazin-2-ones. Preparation and Thermal Stability¹

M. Rosenblum, A. Longroy,² M. Neveu,³ and C. Steel

Contribution from the Department of Chemistry, Brandeis University, Waltham, Massachusetts 02154. Received August 2, 1965

The thermal decomposition of the dihydrooxadiazinone derivative (4), which affords a mixture of cis- and transstilbene, has been shown to take place by a stepwise loss of CO_2 and N_2 . On treatment with 2 equiv. of sodium triphenylmethide, 4 is rearranged to the isomeric dihydrooxadiazinone derivative (9). Oxidation of this substance with lead tetraacetate led to the formation of tolane in low yield. Treatment of cis-stilbene oxide with carbethoxyhydrazine afforded the tetrahydrooxadiazinone derivative (6), which on oxidation with lead tetraacetate smoothly lost CO_2 and N_2 and gave trans-stilbene exclusively in high yield.

Thermally induced fragmentation and rearrangement reactions, which do not involve the intermediacy of either ionic or free-radical species, are processes of some synthetic importance and theoretical interest. The thermal decomposition of esters⁴ and amine oxides⁴ as well as the Claisen⁵ and Cope⁵ rearrangements represent some of the many reactions of this class.

In principle, the offtimes severe stereochemical constraints which characterize many of these reactions should be largely obviated when the process of concerted bond making and breaking is able to take place within a pre-existing ring. Furthermore, the formation of thermodynamically stable gaseous molecules such as CO, CO₂, and N₂ in fragmentation reactions of this class may be expected to provide considerable driving force for these processes.⁶ Both of these structural conditions are met in the oxadiazinone system (1) and two of its three isomeric dihydro derivatives (2 and 3), the syntheses of which were undertaken in these laboratories some time ago.



In our previous paper⁷ we described two general procedures, summarized in Figure 1, for the construction of derivatives of 3 from α -ketols and α -diketones. At elevated temperatures, these substances were ob-

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(2) Author to whom inquiries should be addressed at Indiana University, Fort Wayne Campus, Fort Wayne, Ind.

(3) College Teacher Summer Research Participant supported by National Science Foundation Grant 20452.

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(5) S. J. Rhoads in "Molecular Rearrangements," Vol. 1, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 11.

(6) P. D. Bartlett and R. R. Hiatt, J. Am. Chem. Soc., 80, 1398 (1958), and subsequent papers; C. Walling "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 467.

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served to decompose, with loss of CO_2 and N_2 , to give olefins. While the sequence therefore constitutes a new and potentially useful method for the conversion of α ketols and α -diketones to olefins under nonreductive conditions, our more immediate purpose lay in examining the mechanism by which these heterocycles undergo thermal decomposition.

Mechanism Studies. In the present paper, the chemistry of 1,3,4-oxadiazin-2-ones is further explored, and the mechanism of the thermal decomposition of 5,6diphenyldihydrooxadiazin-2-one (4) is elucidated. This substance, which is readily prepared from benzoin, has been shown to give a mixture of cis- and transstilbene in approximately 70% yield, on pyrolysis in benzene solution at 180°.⁸ Excluding a radical chain process (vide infra), the decomposition of 4 may be depicted as involving an initial isomerization of 4 to a 5,6-dihydrooxadiazinone followed by the simultaneous expulsion of CO_2 and N_2 (Figure 2, reaction path a). There is some evidence that the decomposition of 2pyrazolines to cyclopropanes proceeds through a closely analogous tautomerization of these heterocycles to the corresponding 1-pyrazolines.⁹ Alternatively, the loss of CO_2 and N_2 may take place stepwise as shown by mechanism b. The loss of CO_2 from 3,6-dihydro- α pyrones¹⁰ forms a close parallel with the first step of this mechanism, while the recent work of Cram and Bradshaw¹¹ on the decomposition of alkyldiimides would appear to provide sufficient precedent for the second step.12

In order to distinguish between these mechanisms, the kinetics of the decomposition of 4 and of its N-deuterio derivative were examined. Pyrolyses were carried out in both benzene and dimethylformamide solutions in sealed tubes, and the progress of reaction was followed by determining the volume of nitrogen evolved. The rate of nitrogen evolution was found to follow first-order kinetics to at least 90% of complete reaction in both solvents (Figures 3 and 4) and to be equal to the rate of CO₂ formation (Figure 4). Rate constant data derived from these plots are summarized in Table I.

The absence of free-radical intermediates in the decomposition of 4 is evidenced by the invariance of the rate constant of the reaction over a twofold change in

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(1956). (9) W. M. Jones, J. Am. Chem. Soc., 81, 5153 (1959); 82, 3136 (9) W. M. Jones, J. Am. Chem. Soc., 81, 5153 (1959); 82, 3136

(1960); C. G. Overberger and J. Anselme, *ibid.*, **86**, 658 (1964).
(10) O. Diels and K. Alder, *Ann.*, **490**, 257 (1931); H. J. Hagemeyer, *Ind. Eng. Chem.*, **41**, 765 (1949). The formulation of the dihydropy-rones in this paper is probably incorrect: *cf.* F. G. Young, *J. Am. Chem. Soc.*, **71**, 1346 (1949). (11) D. J. Cram and J. S. Bradshaw, *ibid.*, **85**, 1108 (1963).

(12) Alkenyldiimides similar to 5 have likewise been suggested as possible intermediates in the transformation of α -halo ketones and α amino ketones to olefins by hydrazine: P. S. Wharton, S. Dunny, and L. Soto Krebs, J. Org. Chem., 29, 958 (1964); N. J. Leonard and S. Gelfand, J. Am. Chem. Soc., 77, 3269, 3272 (1955).





Figure 2.

concentration of **4**, by the failure of benzoyl peroxide to initiate its decomposition, and by the observation that neither triphenylmethane nor cyclohexene had any perceptible effect upon either the rate or the products of the pyrolysis reaction.

Table I

Temp., °C.	Solvent	Concn., mole/l.ª	k, sec. ⁻¹ $ imes 10^{5}$	ΔH^* , kcal./mole	Δ S* , e.u.
152	Benzene	0.01	1.61		
180	Benzene	0.01	16.8		
180	Benzene	0.02	16.5		
180	Benzene	0.01^{b}	16.6	31.1	-7.9
134	DMF ^c	0.01	0.43		
152	DMF ^c	0.01	2.38		
180	DMF ^o	0.01	25.3	31.6	-6.0

^a Concentration of dihydrooxadiazine (4). ^b N-Deuteriodihydrooxadiazinone. ^c Dimethylformamide.

Furthermore, the rate-limiting step of the reaction does not appear to involve appreciable charge separation since the reaction rate is only slightly affected by a relatively large change in both the polarity and dielectric constant of the solvent.¹⁸

The yields of both *cis*- and *trans*-stilbene could be determined independently in each of the kinetic runs by vapor phase chromatographic analysis. However, these were found to constitute a less reliable measure of the extent of reaction, since the yield of these olefins was highly variable. In some kinetic runs, the combined yield of stilbenes accounted for 95% of the nitrogen evolved, but in others it was considerably below this value. Separate exploratory experiments suggest that traces of base in the reaction vessel may be responsible

(13) Cf. J. F. Leffler, J. Am. Chem. Soc., 72, 67 (1950), and J. F. Leffler and C. C. Petropoulos, *ibid.*, 79, 3068 (1957), in which a significant increase in the rates of thermal decomposition of unsymmetrical diaroyl peroxides in nitrobenzene compared with their rates in benzene has been ascribed to the intervention of an ionic mechanism.



Figure 3. First-order rate plots for the decomposition of diphenyldihydrooxadiazinone (4) in benzene solution: \bigcirc , 0.01 *M* solutions at 180°; \triangle , 0.02 *M* solutions at 180°; \square , 0.01 *M* solutions at 152°.



Figure 4. First-order rate plots for the decomposition of 0.01 M solutions of diphenyldihydrooxadiazinone(4) in dimethylformamide: \triangle , 180°; O, 152°; \Box , 134° (from N₂ evolution); •, 152° (from CO₂ evolution).

for the decreased yield of olefin, but a precise definition of the manner in which the reaction is diverted is, for the present, not possible.

The ratio of *cis*- to *trans*-stilbene formed in the decomposition of 4 exhibited a pronounced solvent dependence. This ratio, which did not vary appreciably over the temperature ranges studied for each solvent, and which does not appear to depend on the yield of olefin, was found to be 1.2 in benzene and 0.6 in dimeth-



Figure 5. First-order rate plot for the decomposition of 0.01 M solutions of N-deuteriodiphenyldihydrooxadiazinone (4): O, in benzene at 180°; •, in 0.1 M solutions of cyclohexane in benzene; Δ , in benzene saturated with D₂O.



Figure 6.

ylformamide. In separate experiments it was determined that *cis*-stilbene, which is the thermodynamically less stable of the two olefins,¹⁴ was not isomerized in either benzene or dimethylformamide solution at the reaction temperatures employed in the decomposition of **4**. The observed ratio of these olefins must consequently be a measure of the proportion in which they are formed in the pyrolysis reaction in each solvent, but the factors which determine this ratio remain as yet unknown.

Deuteration of 4 was carried out by acid-catalyzed exchange in benzene solution containing D_2O . After one such treatment, the product was found to have incorporated 0.8 g.-atom of D as N-D, as estimated from its n.m.r. spectrum. Measurements of the rate of decomposition of this substance at 180° were carried out both in benzene and in benzene containing 0.1 *M* solutions of cyclohexene. In addition, two runs were carried out in benzene saturated with D_2O , in order to obviate possible exchange of deuterium with fortuitous traces of water in the organic solvent. These data are plotted in Figure 5, and the calculated first-order rate constant for the decomposition of the deuterio compound is given in Table I.

The fact that the rate of decomposition of 4 at 180° is indistinguishable from that of its N-deuterio deriva-

Figure 7.

tive requires that, for reaction path a to obtain, the first step involving hydrogen transfer must be fast and the second rate limiting, while the converse must be true for mechanism b.

Elimination of one of these alternatives was accomplished as follows. Treatment of *cis*-stilbene oxide with carbethoxyhydrazine at 150° gave the tetrahydrooxadiazinone **6**, the stereochemistry of which follows from its likely mode of formation *via* the carbethoxyalkylhydrazine **7**. This substance was unaffected by mercuric oxide, but on treatment *at room temperature* with lead tetraacetate it lost CO₂ and N₂ spontaneously and gave *trans*-stilbene exclusively in 89% yield. The 5,6-dihydrooxadiazinone **8**, which should be the direct product of this oxidation, must therefore be considerably less stable thermally than its isomer (**4**), and hence mechanism a for the thermal decomposition of this latter substance may be excluded (see Figure 6).¹⁵

Base-Catalyzed Isomerization. In order to examine the possibility that 4 might undergo facile decomposition by an ionic route through the anion 4a, the substance was treated with 1 equiv. of sodium triphenylmethide in benzene. Although the dihydrooxadiazinone rapidly consumed 1 equiv. of base, the resulting anion was not decomposed after heating at reflux temperature for 1 hr., since 4 could be recovered in good yield from these solutions (see Figure 7).

In the course of these experiments we noted that 4 titrated as a dibasic acid in the presence of sodium triphenylmethide. In contrast to 4a, the dianion 4b afforded only a low yield of 4 on neutralization. The major product was a substance isomeric with 4 which is assigned the structure of a 3,4-dihydrooxadiazinone (9) on the basis of its analysis, molecular weight, infrared spectrum (NH, 3.1 μ), and n.m.r. spectrum, which exhibited absorption at τ -1.45 and 2.71 (intensity 1:11).

The thermal stability of this substance, which melts without decomposition at 217° and remains unchanged up to 300° , is quite apparently due to the fact, in contrast to 4 and 8, that no plausible path exists by which multiple bond cleavage can lead directly to stable molecular fragments.

The oxidation of this substance, like that of 6, was effected by lead tetraacetate in benzene, but instead of

⁽¹⁴⁾ G. B. Kistiakowsky and W. S. Smith, J. Am. Chem. Soc., 56, 638 (1934); T. W. J. Taylor and A. R. Murray, J. Chem. Soc., 2078 (1938).

⁽¹⁵⁾ This conclusion is predicated on the reasonable assumption that the rearrangement of 4, as depicted in mechanism a, would yield both the *cis* and *trans* forms of the isomeric 5,6-dihydrooxadiazinone. Failing this, it would be necessary to assume that the *cis* isomer alone is formed in this step, and that its thermal stability is remarkably greater than the *trans* isomer (8). Attempts to prepare the *cis* isomer from *trans*-stilbene oxide have thus far been unsuccessful.

the oxadiazinone 10, the only product, isolated in low yield, was tolane. It seems likely that the oxadiazinone is in an intermediate in this reaction and, that like 8, it readily loses CO₂ and N₂.

The investigation of the chemistry of these new heterocycles and of their use as intermediates in the transformation of α -ketols and α -diketones to olefins and acetylenes is being continued.

Experimental Section

Kinetic Runs. A 3-ml. tube with break-seal and side arm was charged with 0.5 ml. of dihydrooxadiazinone solution, and this was degassed three times on a highvacuum line and finally sealed. The tube was placed in an oil bath thermostated at 180, 152, or 134°. At the end of the reaction period, the reaction vessel was withdrawn and cooled in an ice bath to room temperature. It was then placed on the vacuum line, and the seal was broken. Nitrogen was collected by a Toeppler pump and determined in a gas buret, after removing carbon dioxide in a liquid nitrogen trap. The purity of the nitrogen was confirmed by gas chromatographic analysis using a molecular sieve column. The tube was then opened to the atmosphere and analyzed for cis- and trans-stilbene by v.p.c., employing a 3-ft. 4% RC polymeric BGA column on Chromosorb W treated with hexamethyldisilazane (column temperature 160°). Calibration curves for the stilbenes were determined and were checked prior to each sample determination.

In those runs in which the volumes of both carbon dioxide and nitrogen were determined, the above procedure for collecting nitrogen was followed, after which the liquid nitrogen trap was replaced by a Dry Iceacetone trap. The reaction solution was then allowed to warm to room temperature and distilled over into the carbon dioxide trap, while the carbon dioxide gas was pumped into the calibrated bulb and its volume measured.

The relative volumes of nitrogen and carbon dioxide were checked by injecting the collected gas directly into a 2-ft. silica gel chromatographic column maintained at 90°, and previously calibrated for these gases.

N-Deuterio-5,6-diphenyl-2,3-dihydro-6H-1,3,4-oxadiazin-2-one. The dihydrooxadiazinone 4^7 (1.70 g., 6.75 mmoles) was dissolved in 100 ml. of hot dry benzene. A few crystals of *p*-toluenesulfonic acid were added. The solution was brought to reflux and three 1-ml. portions of D₂O were added, while the solution was allowed to distill slowly. Crystallization of the product from benzene gave 1.55 g. (91%) of deuterated substance, m.p. 190–191°. The n.m.r. spectrum of this product indicated 80% N–D.

trans-5,6-Diphenyltetrahydro-1,3,4-oxadiazin-2-one(6). cis-Stilbene oxide (2.00 g., 0.010 mole), prepared from cis-stilbene and perbenzoic acid, ¹⁶ was heated in a sealed tube in the presence of 2.00 g. of carbethoxyhydrazine at 150° for 4 days. The tube was then opened and the product was taken up in ether and filtered from insoluble material. The ether solution was then washed with water, dried, and evaporated to give 1.92 g. of a gum. This was crystallized from ethanol to give 365 mg. of product, m.p. 113-114° (14%). *Anal.* Calcd. for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.85; H, 5.58; N, 11.01.

Lead Tetraacetate Oxidation of 6. Formation of trans-Stilbene. A solution of 50 mg. (0.20 mmole) of tetrahydrooxadiazinone (6) in 10 ml. of dry benzene was treated with 94 mg. (0.21 mmole) of freshly recrystallized lead tetraacetate dissolved in 10 ml. of dry benzene. Evolution of gas was immediately evident on mixing these solutions. When gas evolution had ceased, the solution was filtered and then diluted to 25 ml. The yield of trans-stilbene, determined by v.p.c. analysis, was 90%. No cis-stilbene could be detected.

Solvent was removed from the reaction solution after v.p.c. analysis and the product was recrystallized from ethanol to give 32 mg. of *trans*-stilbene (89%), m.p. 124-125°, m.m.p. 124-125°.

Isomerization of Dihydrooxadiazinone 4 to 9. The diphenyldihydrooxadiazinone 4 (1.00 g., 3.96 mmoles) was taken up in 150 ml. of dry benzene and treated, in a nitrogen atmosphere, with 54 ml. of a 0.155 M solution (8.3 mmoles) of triphenylmethide in ether. The first molar equivalent of base was consumed instantaneously, while the second reacted more slowly and required heating. The mixture was poured into water, the aqueous phase was withdrawn, and the organic solution was washed with water and 2 N sodium hydroxide solution. The combined organic washings were acidified with hydrochloric acid and extracted with ethyl acetate. The extracts were combined and washed with 2 N sodium hydroxide solution, and the aqueous solution was acidified. The product which separated was collected and washed with water to give 637 mg. of dihydrooxadiazinone 9, m.p. 213–215°. Recrystallization from ethyl acetate-benzene solution gave 547 mg., m.p. 216.5-217°. The initial benzene solution yielded 143 mg. of starting material on removal of solvent, ultraviolet $\lambda_{\max}^{\text{EtOH}}$ 297 m μ (ϵ 12,000) and 217 m μ (ϵ 13,000). Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.41; H, 4.80; N, 11.11; mol. wt., 252. Found: C, 71.14; H,

4.76; N, 11.14; mol. wt., 252. Found: C, 71.14; H, 4.76; N, 11.14; mol. wt., 248 (isothermal distillation).

Lead Tetraacetate Oxidation of 9. Formation of Tolane. Lead tetraacetate (125 mg., 0.28 mmole), dissolved in 15 ml. of dry benzene, was added dropwise to a refluxing solution of 65 mg. of dihydrooxadiazinone 9 in 15 ml. of dry benzene. The solution was allowed to reflux for an additional 45 min., then was cooled, and lead acetate was removed by filtration. The solvent was removed *in vacuo* and the residue was taken up in 1.0 ml. of benzene. The yield of tolane, determined by v.p.c. analysis on a 4-ft. column of 10% RC polymeric BGA on Chromosorb W, was 14% (column temperature 190°).

(16) D. Swern, Org. Reactions, 7, 378 (1953).