Decomposition of a β,γ-Unsaturated Diazo Ketone. Evidence for the Intermediacy of a Bicyclopentanone[1]

Jerrold P. Lokensgard,* John O'Dea, and E. Alexander Hill[1b]

Department of Chemistry, Lawrence University, Appleton, Wisconsin 54911

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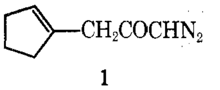
Decomposition of the β,γ-unsaturated diazo ketone **1** was carried out by photolysis, silver oxide catalysis, and thermal reaction at 150–180° in benzyl alcohol and *N,N*-diethylaniline. Thermal reactions yielded both the normal Wolff rearrangement product **5** and abnormal product **9** in which there has been an apparent allylic shift of an acetic acid residue. This compound could be made the exclusive product in the presence of small amounts of a copper salt. Its formation is rationalized in terms of an intramolecular addition to form tricyclo[3.3.0.0^{1,4}]octan-3-one, which opens to a ketene from which **9** is derived. A deuterium labeling experiment is in accord with this pathway.

The copper-catalyzed decomposition of unsaturated diazo ketones is a well-known and useful reaction leading to an intramolecular carbenoid addition to the double bond to form cyclopropyl ketones.[2] Such reactions are not common, however, for α,β- or β,γ-unsaturated diazo ketones.

The investigation of β,γ-unsaturated diazo ketones should be of interest, since an intramolecular addition here would lead to a highly strained bicyclopentanone. Of the diazo ketones of this type that have been prepared, **1**, for example, is reported to undergo normal Wolff rearrangement.[3] There are other examples, however, run under a variety of conditions, in which the double bond does participate.[4-6] In one of these cases,[5] an addition product actually survives the reaction conditions. In the other two cases,[4,6] abnormal products were isolated from attempted Wolff rearrangements. These are attributed by Wilds[4] to steric crowding in the reactive portion of the molecules.

We have had occasion to investigate the decomposition of **1** under a variety of conditions, and present here evidence that, in some cases, carbenoid interaction with the double bond does occur, with the possible intermediacy of the tricyclic ketone **2**. The diazo ketone **1** is a pale yellow liquid, which can be crystallized from hexane at low temperatures or distilled (usually with some decomposition). Because the few impurities in the crude material were shown not to affect the later reactions, the compound was used in most of our experiments in crude form. The Wolff rearrangement of this compound either using silver oxide as catalyst or by photolysis (253.7 nm) in a dioxane–water solution led to **3** as the only acidic product in 20 and 70% yield, respectively, while nearly quantitative yields of the ester **4** could be achieved by photolysis in methanol.



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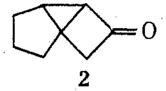

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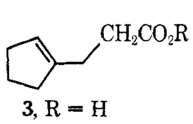
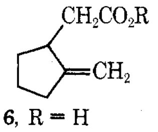
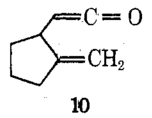


3, R = H
4, R = CH_3
5, R = $CH_2C_6H_5$



6, R = H
7, R = CH_3
8, R = C_2H_5
9, R = $CH_2C_6H_5$



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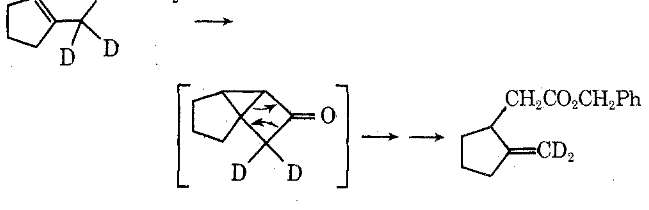
An attempt, however, to rearrange **1** using Wilds' conditions[4] (heating in a mixture of benzyl alcohol and diethylaniline[7]) yielded a mixture, nearly 1:1, of two benzyl esters, identified as **5** and **9**. The identity of **5** was established by saponification to the known acid **3**, that of **9** by direct comparison of the corresponding methyl ester **7** with material prepared by an independent route as described in the Experimental Section. The product ratio observed in the thermal reaction proved to be somewhat unreproducible, and the fraction of **5** in the ester product on later attempts varied from 5 to 95%. The total ester yield (gas chromatographic analysis), however, was always nearly quantitative, based on diazo ketone.

The variability in product ratio was traced to minute traces of copper ions, whose source was a copper steam heating coil in a large container used to soak glassware in a detergent solution. Inadequate rinsing of glassware in which the diazo ketone was handled was at fault, and increased quantities of **9** could be achieved either by deliberately using poorly rinsed flasks to handle the diazo ketone or, better, by adding traces of copper(II) acetylacetonate (**11**) to the reaction mixtures. The quantity of copper necessary to make a substantial difference in the product ratio was extremely small. A mixture of 20 mg of **1** in 300 ml of solvent, to which a few milligrams of **11** were added before heating, produced only **9** with no **5** detectable. In the absence of any copper, the ratio was reproducibly 5% **9** and 95% **5**. It was determined that other potential contaminants, including water, acid, and certain impurities separated from the diazo ketone, had no consistent effect when deliberately added to reaction mixtures.

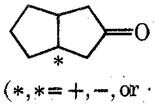
In order to clarify the structural change in the formation of **9**, a deuterium labeling experiment was performed. A sample of cyclopent-1-enylacetic acid was treated with sodium deuterioxide in D_2O, and after equilibration contained 1.5 atoms of D per molecule (nmr analysis), all in the α position. Conversion of this to the diazo ketone **1**-d_2 was accomplished without loss of label. Thermal reaction of this under conditions conducive to formation of **9** led to material still containing the same amount of deuterium, all of it in the vinyl positions. This is consistent with a process going through an intermediate such as **2**.



Several attempts were made to generate and isolate the intermediates involved in the pathway by which **9** was formed, without success. These involved reactions of **1** with suspensions of copper sulfate or solutions of **11** in dry cyclohexane, but neither **2** nor **10** was observed, nor was there evidence for volatile monomeric products of any kind. It is suspected that **2**, if formed, goes rapidly, even at room temperature, to **10** and that **10** reacts with unreacted diazo ketone[8] to form more complex products.

While the major route to **6** or its derivatives is the copper-catalyzed reaction, there appears to be another pathway, as well. In the thermal reactions run after the clarification of the role of adventitious copper, there was always at least 5–15% of **9** formed along with the major product **5**. This suggests that some intermediate in the uncatalyzed reaction, perhaps a ketocarbene, can add to the double bond to form **2** at least transiently.

In addition to the pathway we are suggesting for the formation of **9** (**1** $\rightarrow$ **2** $\rightarrow$ **10** $\rightarrow$ **9**) one can write at least two others. One of these involves an intermediate, **12** (either biradical or dipolar), in which only one new bond is yet formed (**1** $\rightarrow$ **12** $\rightarrow$ **10** $\rightarrow$ **9**). The other[9] would invoke a direct electrocyclic pathway from a carbenoid to **10** with simultaneous bond breakage and formation. In the absence of firm evidence for **2**, we prefer to consider it an intermediate for two reasons. The first is analogy to the products in larger unsaturated systems;[2] the second is the known chemistry of bicyclopentanones.



12 ($*,* = +,-$, or $\cdot,\cdot$)

There have been several photochemical studies on cyclopentenones, in which bicyclopentanones are products or presumed intermediates.[10] In two of these cases, bicyclopentanones which are sterically protected by bulky *tert*-butyl groups have been isolated at room temperature, but in the two unprotected cases, examined by Zimmerman and Agosta, only ring-opened products have been isolated from room temperature irradiations. In Zimmerman's case, the bicyclopentanone could be observed in a low-temperature irradiation, and on further irradiation it opened to a ketene in a manner analogous to the transformation of **2** to **10** in the present case. In the case of **2**, indeed, the added strain from the additional fused five-membered ring should increase the facility of ring opening and might account for our failure to isolate the compound.[17]

In summary, rearrangement of this β,γ-unsaturated diazo ketone proceeds normally under most conditions. It is possible, though, for participation of the double bond to occur, particularly in the presence of a copper catalyst. In such cases, the strained tricyclic ketone **2** is a likely intermediate, and the final product is related to the normal Wolff rearrangement product by an apparent allylic shift of an acetic acid residue. This reaction, which proceeds in high yield, may be of synthetic use.

Experimental Section

All melting points were determined on a Thomas Hoover apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer Model 337 grating spectrometer, nmr spectra on Varian A-60A or Perkin-Elmer R12-B instruments at 60 MHz, using deuteriochloroform as solvent and tetramethylsilane as internal reference, and uv spectra on a Cary 14 uv–visible recording spectrophotometer. Gas chromatographic analyses were performed on an F & M Model 609 instrument with flame ionization detector, and small-scale preparative gc was done on a Varian Aerograph 90-P3 instrument with a thermal conductivity detector. Columns used were ¼ in. × 10 ft copper columns packed with 10% SE-30 silicone oil on 60/80 Chromosorb W. Relative amounts of esters in the rearrangement reactions were determined by area measurements on the chromatograms and corrected for results on mixtures of known composition. Microanalysis was done by the Galbraith Laboratories, Inc., Knoxville, Tenn. The mass spectra were run on a Hewlett-Packard 5930A quadrupole spectrometer operating at 70 V.[11]

Preparation of (Cyclopenten-1-ylacetyl)diazomethane (1). Ethyl cyclopentylidineacetate was prepared in 81% yield according to the procedure[12] reported for the analogous six-membered case. The product was distilled at 96–104° (17–19 mm): nmr δ 5.84 (m, 1 H), 4.18 (q, 2 H), 1.45 (t, 3 H), 1.5–3.0 (4 H); ir (neat) 1705, 1650 cm^{-1}. A small amount of the unconjugated isomer was also present (ir 1730 cm^{-1}).

This ester was, without further purification, refluxed for 15 hr with 200 ml of 20% KOH. From the cooled, acidified solution was isolated cyclopent-1-enylacetic acid (**13**) which was recrystallized from petroleum ether (36–50°). The yield of solid (mp 51–52°, lit.[13] 52°) was 21.2 g (63%): nmr δ 11.4 (s, 1 H), 5.61 (s br, 1 H), 3.18 (s br, 2 H), 1.6–2.6 (6 H); ir ($CHCl_3$) 1710 cm^{-1}.

A solution of **13** (16.55 g, 0.131 mol) in 50 ml of CH_2Cl_2 was cooled to 0°. Oxalyl chloride (20 ml, 29.7 g, 0.23 mol) was slowly added to this stirred solution. The mixture was allowed to warm to room temperature over a 3-hr period, and the solvent was removed at reduced pressure. The product cyclopent-1-enylacetyl chloride (**14**) was distilled at 76–77° (25 mm) to yield 17.84 g (94%) of colorless liquid: nmr δ 5.73 (m, 1 H), 3.68 (s br, 2 H), 1.7–2.6 (6 H); ir (neat) 1795 cm^{-1}.

A solution of **14** (5.13 g, 0.036 mol) in 55 ml of anhydrous ether was added dropwise to an ice-cold, dry solution of approximately 6 g of CH_2N_2 in 500 ml of ether. The resulting solution was allowed to come to room temperature overnight and then was filtered and evaporated. The residual yellow oil was taken up in petroleum ether, dried over $MgSO_4$, and evaporated to yield 5.11 g (95%) of **1** as a light yellow oil: nmr δ 5.61 (m, 1 H), 5.37 (s, 1 H, CHN_2), 3.15 (s br, 2 H), 1.6–2.6 (6 H); ir (neat) 2100, 1630, 1360 cm^{-1}.

Decomposition of 1. A. Photolysis. A solution of crude **1** (19.2 g, 0.13 mol) in 300 ml of purified dioxane and 250 ml of H_2O was irradiated in a quartz vessel with low-pressure Hg lamps (253.7-nm maximum output) at room temperature in a Rayonet[14] photochemical reactor for 20.5 hr. The reaction was followed by observing the disappearance of diazo ketone absorbance at 250 nm in aliquots. The solution was made basic with 7.2 g of KOH (0.13 mol) and concentrated to 200 ml on a rotary evaporator. It was washed with ether, acidified, and extracted with ether. The ether layer was separated, dried ($MgSO_4$), and evaporated to provide 12.19 g (68%) of 3-(cyclopenten-1-yl)propanoic acid (**3**), mp 63.5–64.5° from petroleum ether (36–50°) (lit.[3] 64°).

B. Thermal Reactions. In general, especially for reactions in which only the product ratio of normal to abnormal products was being investigated, the procedure involved dissolving 20 μl of **1** in a mixture of 150 μl of purified[15] benzyl alcohol (BA) and 150 μl of *N,N*-diethylaniline (DEA) in a 10 × 75 mm test tube. This was immersed in a pre-heated oil bath (150–180°) for 2 min and the product ratio determined by gas chromatography of the reaction mixture.

A larger scale reaction leading to **3** was run under similar conditions. A solution of 1.56 g (10.4 mmol) of **1** in 10 ml each of BA and DEA was prepared in a 50-ml round-bottom flask fitted with a reflux condenser. This was immersed for 8 min in an oil bath heated to 180°. The cooled mixture was diluted with ether, washed with 10% HCl to remove DEA, and then dried and evaporated. The residue was stirred at reflux in 10 ml of CH_3OH, 4.5 g of KOH, and 6.5 ml of H_2O for 3 hr. The methanol was removed by evaporation. The aqueous residue was diluted with water, washed with ether, and then cooled and acidified with 10% HCl. The dark solid that separated was taken up in ether, washed with 10% HCl and then saturated NaCl, dried, and evaporated to yield 0.837 g (57%) of crude **3**.

A separate reaction in which both **3** and **6** were formed was worked up as above, and then the mixture of acids, in ether, was treated at room temperature with an excess of CH_2N_2 in ether. After reaction was complete, the solution of methyl esters was dried and evaporated to yield 46% (based on crude **1**) of a mixture of methyl (2-methylenecyclopent-1-yl)acetate (**7**) and methyl 3-(cyclopenten-1-yl)propanoate (**4**). The esters were separated and isolated by gc at 150°. The shorter retention time isomer was **7**: nmr δ 4.85 (m, 2 H), 3.70 (s, 3 H), 1.1–3.1 (9 H); ir (neat) 1745, 1655, and 883 cm^{-1}; mass spectrum molecular ion at m/e = 154, base peak 94. The longer retention time product was **4**: nmr δ 5.40 (m, 1 H), 3.70 (s, 3 H), 1.7–2.5 (10 H); ir (neat) 1740 cm^{-1}; mass spectrum molecular ion 154, base peak 79.

Synthesis of 7. In a 500-ml round-bottom flask equipped with N_2 inlet, reflux condenser, addition funnel, and stirrer was placed a solution of 33.95 g (0.25 mol) of the pyrrolidine enamine of cyclopentanone[16] [bp 103° (25 mm)] in 200 ml of acetonitrile. Ethyl bromoacetate (24 ml, 36.4 g, 0.218 mol) was added dropwise to this stirred solution. The mixture was then heated at reflux for 17 hr. When the deep red solution cooled, most of the solvent was removed at reduced pressure and replaced with 130 ml of H_2O, and the mixture was refluxed again for 45 min. The ethyl (2-oxocyclopentyl)acetate (**15**) was extracted from the cooled mixture with ether and isolated by fractional distillation: 13.3 g (36%); bp 133–135° (23 mm); ir (neat) 1730 cm^{-1}.

A 250-ml three-neck flask equipped with N_2 inlet and reflux condenser and containing 0.72 g (0.03 mol) of NaH and 25 ml of dimethyl sulfoxide (DMSO) was heated at 70–75° under N_2 for 45 min. To the cooled solution was added a solution of 10.7 g (0.03 mol) of $CH_3P(C_6H_5)_3Br$ in 33 ml of DMSO. After an additional 10-min stirring, 5.0 g (0.03 mol) of **15** in 3 ml of DMSO was added, and stirring continued at room temperature for 1.5 hr. After 40 ml of H_2O was added, the mixture was extracted with 350 ml of petroleum ether in three portions and with 50 ml of ether. The combined extracts were dried and evaporated carefully to 25 ml. Distillation in a short-path apparatus yielded approximately 1 ml of a fraction boiling 110–140° (22 mm). This was dissolved in petroleum ether and rapidly chromatographed on a silica gel column. A total of 250 mg (5%) of ethyl (2-methylenecyclopent-1-yl)acetate (**8**) was recovered. No further attempts to optimize the yield were made. Purification for analysis was accomplished by preparative gc at 230°. *Anal.* Calcd for $C_{10}H_{16}O_2$: C, 71.39; H 9.59. Found: C, 71.18; H, 9.37. Spectral data: nmr δ 4.85 (m, 2 H), 4.15 (q, 2 H), 1.27 (t, 3 H), 1.1–3.1 (9 H); ir ($CHCl_3$) 1730, 1655, 887 cm^{-1}. This was converted into **7**, identical with that derived from **1**, by treatment with $NaOCH_3$ in CH_3OH and isolation by gc.

Deuteration of 13. A sample of 2.50 g of **13** was refluxed for 2 hr in 10 ml of 8% NaOD in D_2O. The solution was cooled and acidified with 2.5 ml of concentrated H_3PO_4. The deuterated acid was isolated by filtration and dried, recovery 1.70 g. This was converted into the acid chloride as above, and nmr analysis indicated that 74% of the α-hydrogens were replaced by D. Conversion into **1** and then **9** was accomplished, and that benzyl ester isolated by gc. The vinyl protons (δ 4.85) exhibited 28% of the intensity expected by comparison with the intensity of the methylene protons of the benzyl group (δ 5.17). The nmr spectrum was otherwise identical with that of undeuterated material.

Registry No.—**1**, 5261-30-3; **3**, 2910-67-0; **4**, 52358-08-4; **7**, 52358-09-5; **8**, 52358-10-8; **13**, 21622-08-2; **14**, 2910-65-8; **15**, 20826-94-2; cyclopentanone pyrrolidine enamine, 52358-11-9; ethyl bromoacetate, 105-36-2; ethyl cyclopentylidineacetate, 1903-22-6.

References and Notes

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(13) G. A. R. Kon and R. P. Linstead, *J. Chem. Soc.*, **127**, 620 (1925).

(14) New England Ultraviolet Co., Middletown, Conn.

(15) Benzyl alcohol was washed successively with saturated $NaHSO_3$, 45% KOH, and saturated NaCl, dried, and distilled at reduced pressure.

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(17) Since the initial submission of this paper, a report has appeared presenting evidence for the detection of an intermediate analogous to **2** arising in a copper-catalyzed decomposition of another β,γ-unsaturated diazo ketone; H. E. Zimmerman and R. D. Little, *J. Amer. Chem. Soc.*, **96**, 4623 (1974).

Chlorocyclophosphazene–Epoxide Reactions. Catalysis by Lithium Halides

David F. Lawson

Central Research Laboratories, The Firestone Tire and Rubber Company, Akron, Ohio 44317

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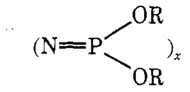
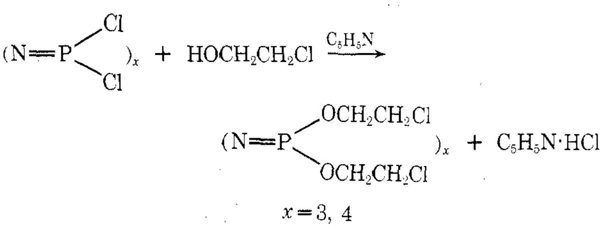
The reactions of chlorocyclophosphazenes with epoxides catalyzed by soluble salts were investigated. Lithium halide catalysts were found to be most effective for the preparation of fully substituted β-chloroethyl phosphazene esters from $(NPCl_2)_4$ and ethylene oxide. Tetraalkylammonium halides, lithium perchlorate, or cesium fluoride–hexamethylphosphoramide gave significantly lower oxirane incorporations. All reactions were extremely slow. The relative effectiveness of lithium halide catalysts is believed to be due to their ability to cleave an oxirane ring; promotion of reaction through a salt effect is also possible. Rearrangement of β-chloroethoxyphosphazene to *N*-(β-chloroethyl)oxophosphazanes appears to be a facile process.

Although the alkoxyphosphazene esters **1** are fairly well known as a general class of compounds,[1] studies of phosphazene esters which contain haloalkyl substituents other than fluoroalkyl have been limited in number and scope. The first reported haloalkyl ester was prepared by the bromination of an allyloxycyclotriphosphazene ester.[2] More recently, β-chloroethoxy- and 2,3-dichloropropoxy esters were prepared by reactions of the chlorophosphazene oligomers with the corresponding alcohols in pyridine,[3] *e.g.*, reaction 1.



$$\left(N{=}P\begin{smallmatrix}OR\\ OR\end{smallmatrix}\right)_x$$

1, R = alkyl, aryl; $x = 3, 4, \ldots n$



$$\left(N{=}P\begin{smallmatrix}Cl\\ Cl\end{smallmatrix}\right)_x + HOCH_2CH_2Cl \xrightarrow{C_5H_5N} \left(N{=}P\begin{smallmatrix}OCH_2CH_2Cl\\ OCH_2CH_2Cl\end{smallmatrix}\right)_x + C_5H_5N\cdot HCl \quad (1)$$

$x = 3, 4$

An appealingly direct route to chloroalkoxy phosphazene esters, *e.g.*, **3**, is through the reaction of chlorophosphazenes with epoxides, (reaction 2). The analogous prep-