Cyclobutanes in organic synthesis. Part I. Fragmentation to 1,4-dicarbonyl compounds. General considerations

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Received October 15, 1969

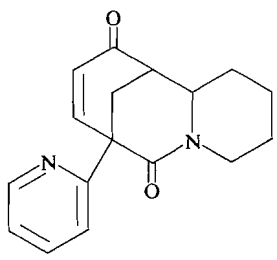
Photo-cycloaddition of vinyl acetates to 2-cyclohexenones followed by hydrolysis of the acetate group and by oxidative fragmentation leads to 2-alkyl-2-cyclohexenones in which the newly introduced alkyl group bears a 2′-carbonyl group. A similar, less generally applicable method, involving photo-cycloaddition, bromination, and heterolytic fragmentation is also described. Possible applications of this sequence in organic synthesis are discussed.

Canadian Journal of Chemistry, **48**, 1436 (1970)

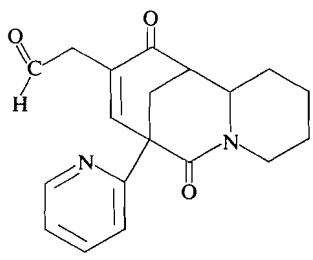
Intramolecular photo-cycloaddition of a double-bond to a cyclohexenone by Ciamician and Silber (1), Sernaggiotto (2), and Büchi and Goldman (3), followed by an extension of this cyclobutane formation to an intermolecular case by Eaton (4), introduced an important new reaction into the field of organic synthesis. In recent years, many relatively difficult syntheses of natural products and strained compounds of theoretical interest have been accomplished in a significantly simplified manner by the use of this method; some of these have been achieved with retention (5–10) and some with modification (11–15) of the cyclobutane ring. We now wish to report a fragmentation of suitably substituted cyclobutanes which promises to have wide synthetic utility.

In the course of our studies on the synthesis of *Ormosia* alkaloids (15) it became necessary to transform **1** into **2** in which the newly introduced side-chain would possess a reactive function at its terminus and in which the cyclohexenone double-bond would be retained. Clearly, a normal alkylation could not be used since the cycloalkenone function in **1** does not possess an enolizable γ-hydrogen atom. Bearing in mind the mode of photo-cycloaddition of unsymmetrical olefins to cyclohexenones (16, 17), and anticipating an easy fragmentation (18, 19) of a suitably substituted cyclobutane ring, we have been able to convert **1** into **2** in the following simple manner.

Irradiation of keto lactam (**1**) in vinyl acetate and tetrahydrofuran gave a 60% yield of crude keto acetate (**3**), which proved to be homogeneous on silica thin-layer chromatography (t.l.c.). Subsequent transformations revealed **3** to be a mixture of four stereoisomers, the major one of which could be recrystallized to a constant m.p. of 200–201 °C. Since none of the keto alcohols obtained by a basic hydrolysis of **3** underwent a reverse aldol reaction to a keto aldehyde, and since all of them gave a cyclobutanone on oxidation, it became clear that all components of the mixture possess structure **3**. Bromination of **3** with pyridinium bromide perbromide in glacial acetic acid gave a mixture of four stereoisomeric bromo ketones (**4**) in 78% yield. These could be chromatographically resolved and characterized; since all four stereoisomers could, however, potentially give the desired product, the mixture was used in the subsequent reaction.



1



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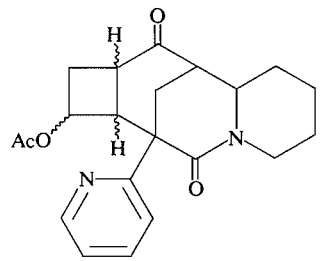

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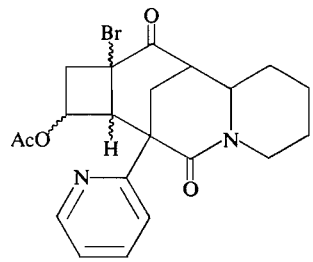

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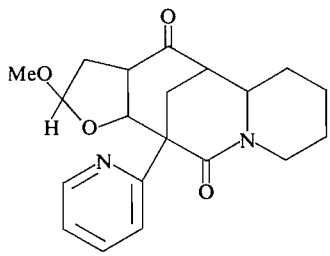

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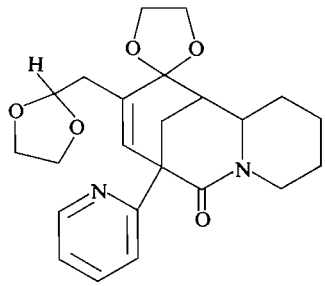
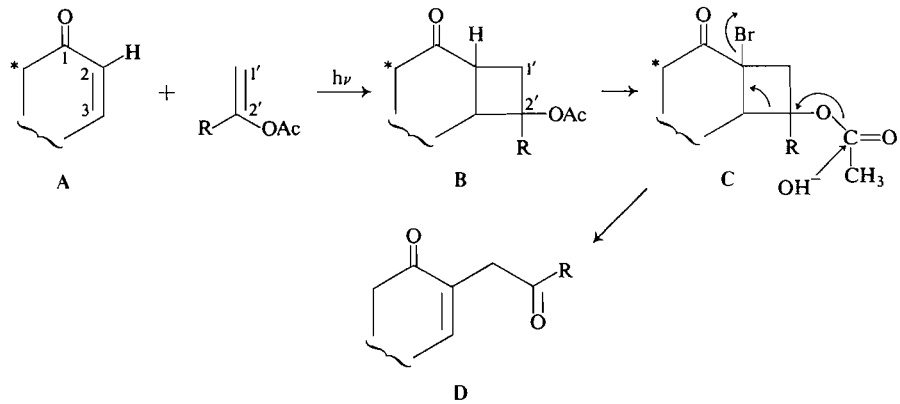


6

Treatment of **4** with aqueous sodium carbonate in methanol at room temperature, followed by chromatography on silica gel, gave the pure keto aldehyde (**2**) in 76% yield and the corresponding acetal (**5**) in 15% yield. The structures of **2** and **5** follow unambiguously from spectroscopic data (see Experimental), from the conversion of pure **2** into **5** on prolonged treatment with methanolic sodium carbonate, and from further conversions of **2** (15).[1] The fragmentation could also be achieved in acidic media. Treatment of **4** in boiling benzene with ethylene glycol and *p*-toluenesulfonic acid gave the bisdioxalane (**6**) in 70% yield.

Photoaddition

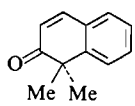
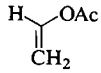
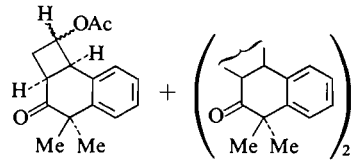
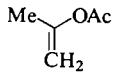
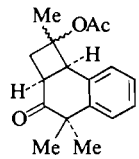
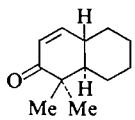
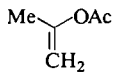
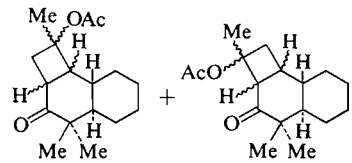
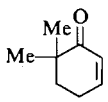
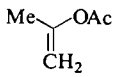
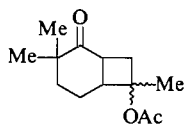
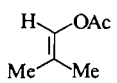
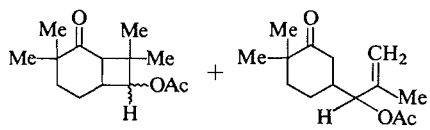
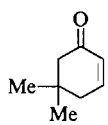
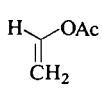
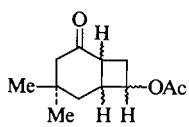
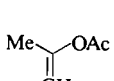
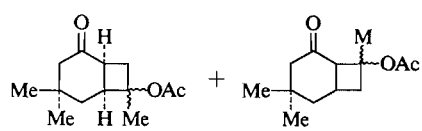
The success and ease of these initial transformations led us to consider the general applicability of the reaction sequence **A** → **B** → **C** → **D**. Concerning first the nature of **A**, it is well known that 2-cyclopentenones and 2-cyclohexenones normally undergo smooth cycloaddition and that substitution at various positions of **A**, with the exception of C-2, does not



A B C D

[1]Totally synthetic alkaloid ormosanine has now been prepared from **2** in our laboratory.

TABLE 1
Photo-cycloadditions

Cyclohexenone	Enol acetate	Photo adducts and yields (%)
		 (2 isomers 63%) (11%)
		 (2 isomers 96%)
		 (4 isomers 55%) (~10%)
		 (64%)
		 (~34%) (~31%)
		 (2 isomers after hydrolysis, 90%)
		 (2 isomers 55% after hydrolysis and extensive chromatography) (~5%)

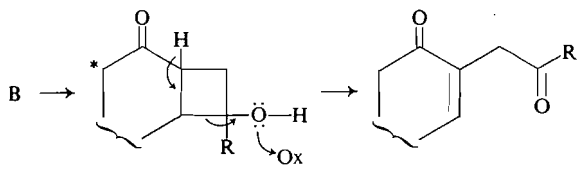
seriously affect the addition (16, 20, 21). It is also known that vinyl acetate adds preferentially in the desired sense (16, 17); as far as its substitution is concerned, our preliminary evidence listed below indicates that the cycloaddition takes place in good yields with a methyl group at C-2′ and lower yields with two methyl groups at C-1′ (see Table 1). The yields of photo adducts from the cycloaddition vary considerably and we have not made a systematic study to optimize conditions. In general, low concentrations of cycloalkenone and the use of aprotic solvents gives little or no cycloalkenone dimer and leads to cleaner photo products. Work described in this communication deals exclusively with cyclohexenones; extension to cyclopentenones will be reported later.

Activation for Fragmentation

The bromination step **B** → **C** proved to be highly efficient in all cases in which enolization of the keto group towards C* was not possible because of substitution or because of strain (cf. **3** → **4**). However, we have so far been unable to achieve a preferential introduction of a leaving group into the desired position in **B** when C* was also reactive. This is clearly a serious limitation to the generality of the above sequence since most synthetic intermediates of the type **B** will obviously have a reactive C*. This difficulty can furthermore not be circumvented by the photoaddition of vinyl acetates to α-bromocycloalkenones. Our results in this respect are completely negative, although such an addition, in an intramolecular case, has been achieved (8) and although α-acetoxycycloalkenones have been found to react (22–24).[2]

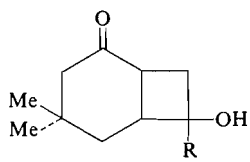
One can, however, ask the interesting question whether the presence of a leaving group is in fact essential for the desired transformation **B** → **D**. Formally, at least, one can readily visualize an oxidative fragmentation indicated in **E**, operating by an electron flow opposite to that encountered in the heterolytic fragmentation **C** → **D** and leading directly to **D** without the benefit of a conventional leaving group.

We now find that a number of methods are in fact available for this transformation and that the oxidative fragmentation of the keto alcohols (**E**) thus represents a general solution to the problem. Table 2 summarizes our findings and

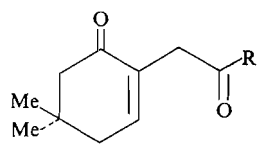


E D

gives yields of fragmentation products obtained on treatment of three keto alcohols with various oxidizing agents. Our results using Ce^{4+} are particularly encouraging. Thus, reaction of keto alcohol **7** with ceric ammonium nitrate in 75% acetic acid solution, until the characteristic reddish color due to the Ce^{4+}–alcohol complex (25) had disappeared, followed by treatment with aqueous mineral acid for several hours, gave an 86% yield of diketone **9**, while a similar oxidation of **8** furnished the desired keto aldehyde **10** in a 71% yield. Additional oxidation results make it clear that the method works equally well with unblocked substrates without oxidation of the resulting cyclohexenone to a phenol.



7 R = Me
8 R = H



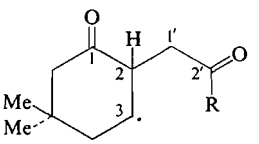
9 R = Me
10 R = H

Published work on oxidations with ceric ion (26, 27) makes it very likely that two consecutive one-electron oxidations are involved, the first leading to radical **11**, the second creating a carbonium ion at position C-3 to give **12**.[3] Experimentally, we have found varying amounts of nitrate esters (**13**) (33) in the reaction product mixture, but this mixture was cleanly converted to **9** (or **10**) by treatment with aqueous mineral acid without requiring separation.

The recent observation of Roček and Radkowsky (28) on the oxidative cleavage of cyclobutanol with Cr^{4+} offers an alternative procedure to the Ce^{4+} oxidation but suffers from

[2]We thank Professors de Mayo and Eaton for a useful exchange of correspondence on this topic.

[3]During the preparation of this manuscript, the Iowa State University group reported further results of their general study of oxidations with cerium(IV). In their interesting new report (33), the successful fragmentation of bicyclo[2.2.1]-2-heptanols and of bicyclo[2.2.2]-2-octanol, as well as the mechanism involving two one-electron processes and the formation of nitrate esters, are discussed.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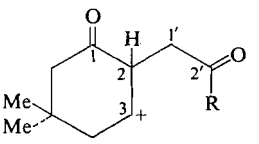
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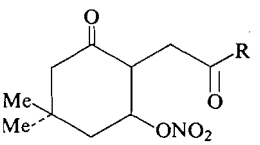
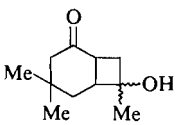
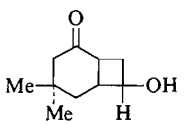
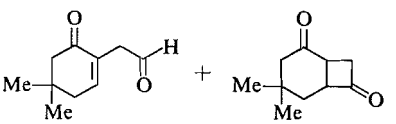
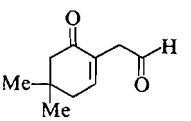
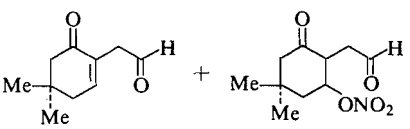
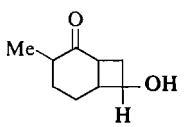
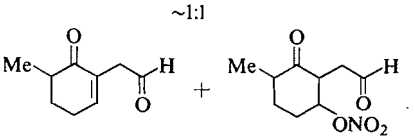
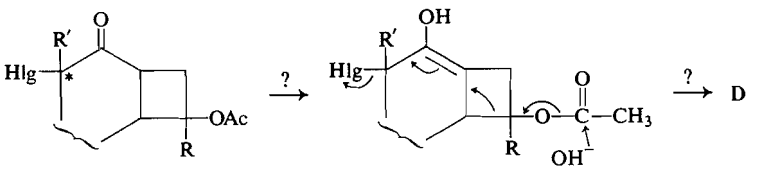

13

the requirement of *in situ* generation of Cr^{4+} and the acidic medium used.

We are presently studying the question whether the following additional methods could be applied in special circumstances for an efficient transformation **B** → **D**. In analogy to rearrangements encountered with α-substituted ketones (29, 30), a vinylogous fragmentation of ketones **F** through the corresponding enol or enolate could take place as indicated in **G**. We have so far not

TABLE 2
Homolytic fragmentations

Keto alcohol	Method	Product(s)	Yield (%)	Reference
	$Pb(OAc)_4/CaCO_3/C_6H_6$ at reflux		18	34, 35
	$HgO/I_2/h\nu/CCl_4$ at reflux	"	49	36
	$Pb(OAc)_4$/pyridine at room temperature	"	67	37
	Ceric sulfate/75% CH_3CN at reflux	"	66	38
	$Ce(NH_4)_2(NO_3)_6$/75% CH_3CN at reflux	"	65–75	26
	$Ce(NH_4)_2(NO_3)_6$/75% HOAc at room temperature	"	86	27
	$Pb(OAc)_4$/pyridine	 ~2:1	65	37
	$HgO/I_2/h\nu/CCl_4$		~45	36
	$Ce(NH_4)_2(NO_3)_6$/75% CH_3CN	"	73	26
	$Ce(NH_4)_2(NO_3)_6$/75% HOAc	 ~1:1	75	27
	$Ce(NH_4)_2(NO_3)_6$/75% HOAc	 ~1:1	70	27



F G

been able to achieve this transformation with haloketones **F** in which R′ = H. The study of systems with R′ = alkyl in which the enolization must take place in the required direction will show whether the geometry of the relevant orbitals in **G** allows the desired fragmentation.

Based on reported reactions (21, 31), **D** could furthermore possibly be prepared by the sequence **A** → **H** → **I** → **J** → **D** in which the required "leaving group" is introduced into the olefin rather than into the alkenone.

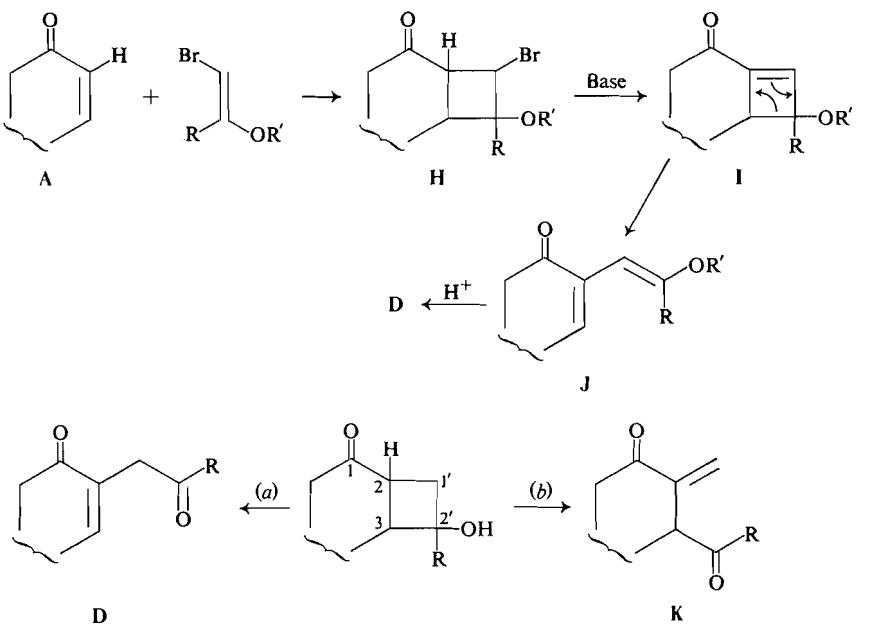
In summary, a large variety of dicarbonyl compounds of the type **D** can now be produced often in very high yields, by photo-cycloaddition followed by an oxidative fragmentation of the corresponding keto alcohols **E** with ceric ion. A second high-yield method, bromination followed by a heterolytic fragmentation, is available for photo adducts **B** which do not enolize in the direction of C*.

Direction of Fragmentation

The somewhat surprising fact that all fragmentations studied by us so far proceeded in only one sense, although two pathways, (*a*) and (*b*), are in fact available, must now be discussed.

Considering first the probable intermediate **11** of the one-electron oxidative methods, the formation of the more stable secondary radical can be used as a plausible explanation. Further study involving additional substitution at C-1′ and at C-3 should provide important information in this connection. Specifically, higher substitution at C-1′ should make pathway (*b*) more favorable if this explanation is correct.

The heterolytic fragmentation **C** → **D** was studied on a large number of *cyclohexanones* (Table 3) and was found to proceed invariably in a very high yield. No detectable trace of fragmentation product **K** was found in any of the studied cases, including one with a *gem*-dimethyl group at C-1′. Furthermore, study of pairs epimeric at C-2′ has shown that **D** is formed exclusively, regardless of the relative configuration of the bromine and the acetoxyl group in **C**. Although this specificity is of obvious preparative



A H I D J K

value, the full explanation for it has to await further study. It appears unlikely that the cyclobutane ring would in all cases possess an unsymmetrical conformation fulfilling the geometrical requirements for a concerted fragmentation reaction (18, 32) in only one direction. Rather, it can probably be assumed that both pathways are geometrically allowed and that pathway (*a*), involving the formation of an *endo* double-bond, proceeds via a transition state of lower energy. In this connection, the behavior of *cyclopentanones* and strained ring-systems will be of special interest.

Potential Applications

In most general terms, the reactions described above provide a synthetically attractive method for the addition, to the α-position of an α,β-unsaturated cyclohexanone (and presumably also cyclopentanone), of a single carbon chain possessing a carbonyl function. The position of double-bond in the cycloalkenone fully deter-

TABLE 3

Heterolytic fragmentations

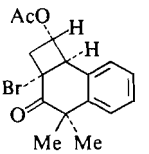
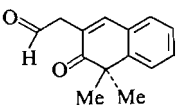
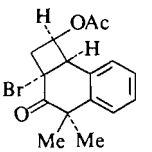
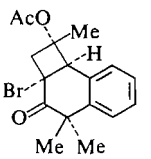
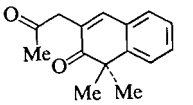
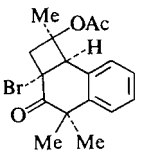
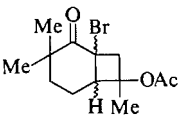
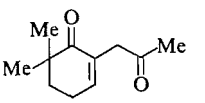
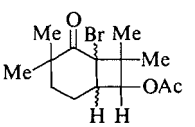
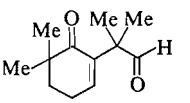
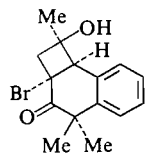
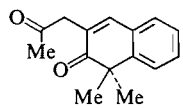
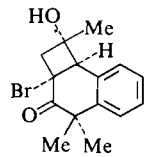
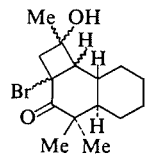
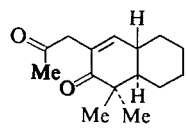
Substrate	Fragmentation media	Product	Yields (%)
	Na_2CO_3/aqueous MeOH		92 (From keto acetates)
	"		98
	NaOH/aqueous MeOH		83
	"		97
 (Mixture of isomers)	KOH/aqueous MeOH		98
 (Mixture of isomers)	KOH/aqueous MeOH		95

TABLE 3 (*Concluded*)

Substrate	Fragmentation media	Product	Yield (%)
	NaOH/aqueous MeOH		89 (From keto alcohol)
	Spontaneous loss of HBr	"	92 (From keto alcohol)
 (Mixture of isomers)	Na_2CO_3/aqueous MeOH		80 (From crude bromo keto alcohols)

mines the site of addition and, rather importantly, an enolizable hydrogen atom in the γ-position of the starting ketone is not required. Unsaturated and, after appropriate reduction, saturated 1,4-dicarbonyl compounds are thus produced.

In principle, chains of arbitrary length (longer than one-carbon) and branching can be added either directly or by subsequent reactions of the side-chain carbonyl group. The relative position of the carbonyl groups furthermore permits a wide variety of special applications.

Five-membered carbocyclic rings can, for instance, be formed by aldol condensations while the corresponding saturated 1,4-dicarbonyl compounds are immediately suited for the preparation of furanes, pyrroles, and thiophenes. We furthermore find that a conversion of the side-chain carbonyl group in **D** into a leaving group followed by an attack with a suitable nucleophile leads to a high-yield production of α-cyclopropyl ketones.

Special applications of the sequence as well as mechanistic and stereochemical details of the described reactions are under further study and will be reported later.

Experimental

General

The infrared (i.r.) spectra were recorded on Perkin–Elmer Infracord or Perkin–Elmer model 237B spectrophotometers. The mass spectra were determined on a Hitachi Perkin–Elmer model RMU-6D spectrometer. The nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian Associates 56.4 Mc.p.s. instrument using tetramethylsilane as internal standard. A Kofler hot stage apparatus was used to determine the melting points which are uncorrected. Photolysis was carried out using one of the following lamps depending on the reaction scale: Hanovia High-Pressure Quartz Mercury Vapour Lamps, 100 W, Type SOL:608A36; 200 W, Type S:654A36 or 450 W, Type L:679A36.

General Procedure for Photo-cycloadditions

The apparatus used for the photochemical reactions consisted of a cylindrical Pyrex reaction vessel with a nitrogen bubbler which served to agitate the solution, a side-arm for a condenser, and a neck to accommodate a quartz-jacketed water-cooled immersion well which could be fitted with Pyrex or Corex filters and any of the lamps used in the procedure. The cycloalkenone used for the photoaddition was dissolved in hexane (or other appropriate, aprotic solvents) such that the concentration of alkenone was less than 0.05 *M*. The enol acetate to be used for the photoaddition was usually added in a large excess (20 to 50% of the solvent used). The vessel was covered with aluminum foil and, with a good flow of water through the water-jacket, the reaction vessel was immersed in an ice-bath. The system was flushed by bubbling

nitrogen through and then irradiated under a nitrogen flow to facilitate mixing. The progress of the reaction was followed by evaporating aliquots and measuring the i.r. absorption. In some cases, t.l.c. was also used.

At the completion of photolysis, the solvent was removed by distillation under reduced pressure and the photo adducts were purified either by distillation under reduced pressure or by chromatography on silica gel. In some cases, the best purification was achieved by hydrolysis of the keto acetate photo adducts to the corresponding alcohol followed by chromatography on silica gel.

Photoaddition of Vinyl Acetate to Keto Lactam (1)

To a solution of the keto lactam (**1**) (1.37 g) in tetrahydrofuran (65 ml), was added vinyl acetate (65 ml). The solution was irradiated with a 100 W lamp, using a Pyrex filter, for 1 h at 0 °C and 2 h at 20 °C. The solution was evaporated to dryness under reduced pressure to give a viscous oil which contained polymeric compounds. The oil was chromatographed on silica gel; the polymeric compounds were eluted with benzene and the photo adduct **3** (1.073 g) was eluted with ether. The photo adduct crystallized from ether to give colorless crystals, m.p. 200–201 °C. The i.r. spectrum showed acetate absorption at 1735 and ketone stretching at 1710 cm^{-1}. The n.m.r. spectrum was completely consistent with the assigned structure.

Anal. Calcd.: C, 68.46; H, 6.56; N, 7.60. Found: C, 68.95; H, 6.60; N, 7.59.

Bromination of Photo Adduct 3

To a solution of the four-membered ring acetate (**3**) (1.66 g) in glacial acetic acid (50 ml) was added pyridinium bromide perbromide (1.71 g) and 46% aqueous hydrobromic acid (1.5 ml). The solution was stirred at room temperature for 16 h. The solution was then basified with saturated aqueous sodium bicarbonate and extracted with chloroform. After drying over magnesium sulfate, filtration, and evaporation *in vacuo* to dryness, the chloroform solution afforded an oil (1.72 g) which by t.l.c. showed mainly four compounds. Column chromatography on silica gel resulted in separation of these four compounds (total 1.58 g). They showed identical i.r. spectra and the mass spectra gave *m/e* 448 and 446. These four compounds were thus four stereoisomers of the bromo acetate (**4**). The isomeric mixture was used in the subsequent reaction.

General Procedure for Bromination of the Photo Adducts

The keto acetate photo adduct (1 mmole) was treated with bromine (1.1 mmole) in 20 ml of Reagent Grade carbon tetrachloride. The time required for bromination varied considerably (usually several hours); the progress of the reaction could be conveniently followed by t.l.c. on silica gel. The organic solution was washed with water, dried over sodium sulfate, and evaporated to dryness *in vacuo* to give the bromo keto acetate in high yield and purity. The bromo keto acetates were homogeneous on t.l.c. and gave i.r., n.m.r., and mass spectra completely consistent with the structures assigned in Table 3.

Heterolytic Fragmentation of Bromo Acetate (4)

To a solution of the isomeric mixture of bromo acetates (**4**) (4.244 g) in methanol (50 ml) was added saturated aqueous sodium carbonate (10 ml). After stirring at 0 °C for 1 h, the mixture was poured into water (500 ml) and extracted with chloroform. The chloroform solution was dried over magnesium sulfate, filtered, and evaporated *in vacuo* to dryness yielding an oil (3.31 g). Column chromatography of the crude product on silica gel gave, in addition to recovered starting material (0.825 g), two new products. The acetal (**5**) (0.408 g) was obtained on elution with ether as a foam; its i.r. spectrum showed a saturated ketone stretching absorption at 1725 cm^{-1}. Elution with methanol–ether (1:50) gave the unsaturated keto aldehyde (**2**) as a foam. Molecular weight (by mass spectrometry): 324. The i.r. spectrum indicated characteristic aldehyde absorptions at 2730 and 1730 cm^{-1} and unsaturated ketone stretching absorption at 1680 cm^{-1}. In the n.m.r. spectrum, the aldehydic proton was recorded at 0.32 τ.

In general, the heterolytic fragmentation proceeded cleanly on base treatment of the bromo keto photo adducts to give the corresponding dicarbonyl compounds (Table 3) in high yield and purity. The dicarbonyl compounds could be further purified by chromatography on silica gel when necessary. Their spectral and analytical data were completely consistent with the assigned structures.

Preparative Scale Ceric Ammonium Nitrate Oxidation of Keto Alcohol (7)

To the keto alcohol (7) (1.1199 g; 6.15 mmole) in 40 ml of 75% aqueous acetic acid at room temperature was added ceric ammonium nitrate (8.439 g; 15.4 mmole) in one portion. The initial red color of the Ce^{4+}–alcohol complex disappeared after several minutes and the reaction mixture was stirred an additional 1.5 h. To this reaction mixture was added concentrated hydrochloric acid (2 ml) and the solution was allowed to stand at room temperature for 3.5 h. Saturated salt solution (150 ml) was added to the reaction mixture and the resulting solution was extracted with methylene chloride (2 × 50 ml) and ether (2 × 50 ml). The combined organic extracts were washed with 10% sodium bicarbonate and saturated salt solution, dried ($MgSO_4$) and evaporated to dryness to yield the diketone (**9**) as a pale yellow oil (0.9584 g; 5.27 mmole; 85.7%). The i.r. spectrum indicated carbonyl absorptions at 1720 and 1677 cm^{-1}. The n.m.r. spectrum showed signals at 8.9 (6H), 7.88 (3H), 7.8 (2H), 7.75 (2H, d), 6.85 (2H), and 3.45τ (1H, t). The mass spectrum gave the molecular ion peak at *m/e* 180.

Oxidative Preparation of Diketone 9 and Nitrate 13 ($R = CH_3$)

The keto alcohol (7) (0.6793 g; 3.73 mmole) was dissolved in 75 ml of 75% aqueous acetonitrile at reflux and ceric ammonium nitrate (4.110 g; 7.50 mmole) was added in one portion. The mixture was stirred at reflux for 25 min during which time the color changed from orange to pale yellow. The solvent was partially removed under reduced pressure and water was added; the mixture was then extracted with ether and methylene chloride. The organic extract was washed with 10% sodium bicarbonate and saturated salt solution, dried ($MgSO_4$) and the solvent removed under reduced pressure. The mixture of diketone (**9**) and nitrate (**13**) (0.6484 g) was obtained as a pale yellow oil. Chromatography on silica gel (60 g) gave on

elution, with 2% ether in benzene, compound **13** (R = CH_3) (0.0651 g; ~10%). The i.r. spectrum of **13** indicated strong absorptions at 1720, 1640, 1280, and 860 cm^{-1}. The n.m.r. spectrum showed a characteristic methyl absorption at 7.80 τ. Further chromatography yielded the diketone (**9**), the spectra of which were superimposable with those of **9** obtained in the preparative scale reaction.

Oxidation of Keto Alcohol (7) in Lead Tetraacetate/ Pyridine Solution

The keto alcohol (**7**) (1.9816 g; 10.88 mmole) was dissolved in 10 ml of benzene and 40 ml of pyridine. To this solution was added lead tetraacetate (9.659 g; 21.8 mmole) and the mixture was heated under reflux for 3.5 h (the oxidation at room temperature was about five times slower), 1.5 ml of ethylene glycol was added to destroy the excess lead tetraacetate and the mixture was stirred until it had cooled to room temperature. The p*H* was adjusted to ≃2 with 10% HCl and the flocculent precipitate was filtered off and washed with water, ether, and chloroform. The acidic aqueous filtrate was extracted with ether (3 × 100 ml) and chloroform (3 × 100 ml). The ether and chloroform extracts were combined, washed with 10% sodium bicarbonate and water, dried ($MgSO_4$), and evaporated *in vacuo* to dryness to give 1.2312 g of product. The acidic solution was continuously extracted with ether for 16 h. This ether extract upon similar work-up yielded an additional 0.2906 g of product. The i.r. spectrum of the product indicated that some β-acetoxy ketone was present, probably from addition of acetate anion or radical to the carbonium ion **12** or radical **11**. When these fractions were combined and treated overnight in a 50:50 solution of 10% hydrochloric acid:tetrahydrofuran, and worked-up in the usual way, the diketone **9** (1.3136 g; 7.30 mmole; 67.1%) was obtained as a dark yellow oil. The spectra of **9** obtained from **7** by this method were identical in all respects to those of **9** obtained by ceric ion oxidation of **7**.

Support of this work by the National Research Council of Canada in the form of scholarships to N. R. H. (1967–1970), G. A. MacA. (1968–1970), and H. J. L. (1967–1968) is gratefully acknowledged.

1. G. Ciamician and P. Silber. Chem. Ber. **41**, 1928 (1908).
2. E. Sernaggiotto. Gazz. Chim. Ital. **47**, I, 153 (1917); **48**, I, 52 (1918).
3. G. Büchi and I. M. Goldman. J. Amer. Chem. Soc. **79**, 4741 (1957).
4. P. E. Eaton. J. Amer. Chem. Soc. **84**, 2454 (1962).
5. E. J. Corey, R. B. Mitra, and H. Uda. J. Amer. Chem. Soc. **86**, 485 (1964); **85**, 362 (1963).
6. J. D. White and D. N. Gupta. J. Amer. Chem. Soc. **88**, 5364 (1966); **90**, 6171 (1968).
7. M. Brown. Chem. Commun. 340 (1965); J. Org. Chem. **33**, 162 (1968).
8. P. E. Eaton and T. W. Cole. J. Amer. Chem. Soc. **86**, 3157 (1964); **86**, 962 (1964).
9. P. E. Eaton. 155th National Meeting of the American Chemical Society, San Francisco, California, April 1968. p. 1.
10. K. Wiesner, Lizzie Poon, I. Jirkovsky, and M. Fishman. Can. J. Chem. **47**, 433 (1969).
11. R. W. Guthrie, Z. Valenta, and K. Wiesner. Tetrahedron Lett. 4645 (1966).
12. E. J. Corey and S. Nozoe. J. Amer. Chem. Soc. **86**, 1652 (1964); **87**, 5733 (1965).
13. B. D. Challand, H. Hikino, G. Kornis, G. Lange, and P. de Mayo. J. Org. Chem. **34**, 794 (1969) and earlier work quoted therein.
14. Z. Valenta, B. Balenovic, P. Cavanagh, and W. L. Wilson. Synthetic work on a ryanodine reduction product completed in this Department.
15. H. J. Liu, Z. Valenta, J. S. Wilson, and T. T. J. Yu. Can. J. Chem. **47**, 509 (1969).
16. E. J. Corey, J. D. Bass, R. Lemahieu, and R. B. Mitra. J. Amer. Chem. Soc. **86**, 5570 (1964).
17. Y. Yameda, H. Uda, and K. Nakanishi. Chem. Commun. 423 (1966).
18. C. A. Grob and P. W. Schiess. Angew. Chem. Internat. Ed., **6**, 1 (1967).
19. C. F. Wilcox, Jr., and D. L. Nealy. J. Org. Chem. **28**, 3450 (1963); L. J. Dolby and C. L. Wilkins. Tetrahedron, **25**, 2381 (1969).
20. P. E. Eaton. Accounts Chem. Res. **1**, 50 (1968) and references quoted therein.
21. T. S. Cantrell, W. S. Haller, and J. C. Williams. J. Org. Chem. **34**, 509 (1959).
22. P. de Mayo. Private communication.
23. S. Kagawa, S. Matsumoto, S. Nishida, S. Yu, J. Morita, A. Ichihara, H. Shirahama, and T. Matsumoto. Tetrahedron Lett. 3913 (1969).
24. T. Matsumoto, H. Shirahama, A. Ichihara, S. Kagawa, and S. Matsumoto. Tetrahedron Lett. 4103 (1969).
25. See reference 4 in the paper by P. M. Nave and W. S. Trahanovsky. J. Amer. Chem. Soc. **90**, 4755 (1968).
26. P. M. Nave and W. S. Trahanovsky. J. Amer. Chem. Soc. **90**, 4755 (1968).
27. W. S. Trahanovsky, L. H. Young, and M. H. Bierman. J. Org. Chem. **34**, 869 (1969).
28. J. Roček and A. E. Radkowsky. J. Amer. Chem. Soc. **90**, 2986 (1968).
29. R. A. Bell and M. B. Gravestock. Can. J. Chem. **47**, 3661 (1969).
30. F. G. Bordwell and R. M. Wellman. J. Org. Chem. **28**, 2544 (1963).
31. C. H. Krauch and W. Metzner. Chem. Ber. **99**, 88 (1966).
32. C. A. Grob, H. R. Kiefer, H. J. Lutz, and H. J. Wilkens. Helv. Chim. Acta, **50**, 416 (1967).
33. W. S. Trahanovsky, P. J. Flash, and L. M. Smith. J. Amer. Chem. Soc. **91**, 5068 (1969).
34. R. E. Partch. J. Org. Chem. **28**, 276 (1963).
35. M. Amorosa, L. Cogliotti, G. Cainelli, H. Immer, J. Keller, H. Wehrli, M. LJ. Mihailovic, K. Schaffner, D. Arigoni, and O. Jeger. Helv. Chim. Acta, **45**, 2674 (1962).
36. M. Akhtar and D. H. R. Barton. J. Amer. Chem. Soc. **86**, 1528 (1964).
37. R. E. Partch and J. Monthony. Tetrahedron Lett. 4427 (1967).
38. G. Mino, S. Kaizerman, and E. Rasmussen. J. Amer. Chem. Soc. **81**, 1494 (1959).