

1967

# Photochemical rearrangements of unsaturated acids, amides, anilides, and nitrocompounds

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PHOTOCHEMICAL REARRANGEMENTS OF UNSATUR-  
ATED ACIDS, AMIDES, ANILIDES, AND  
NITROCOMPOUNDS.

Iowa State University, Ph.D., 1967  
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PHOTOCHEMICAL REARRANGEMENTS OF UNSATURATED  
ACIDS, AMIDES, ANILIDES, AND  
NITROCOMPOUNDS

by

Peter Grant Cleveland

A Dissertation Submitted to the  
Graduate Faculty in Partial Fulfillment of  
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DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

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Head of Major Department

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Dean of Graduate College

Iowa State University  
Of Science and Technology  
Ames, Iowa

1967

## TABLE OF CONTENTS

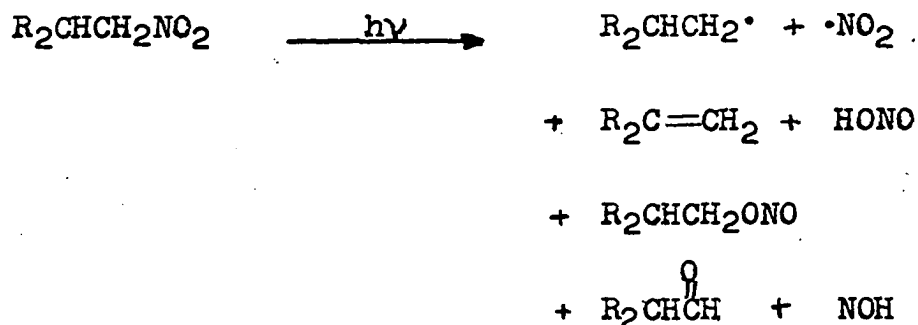
	Page
HISTORICAL	1
Photochemical Reactions of Nitro Compounds	1
Photochemical Reactions of Unsaturated Acids, Amides, and Anilides	3
RESULTS AND DISCUSSION	7
The Photochemistry of 6-Nitrocholesteryl Acetate	7
The Pyrolysis of $\beta$ -Lactones	22
The Photochemistry of Unsaturated Acids, Amides, and Anilides	25
EXPERIMENTAL	45
Instruments and Methods	45
Experimental for the Irradiation of 6-Nitrocholest-5-ene-3 $\beta$ -ol Acetate	46
Experimental for the Pyrolysis of $\beta$ -Lactones	56
Experimental for the Photochemistry of Unsaturated acids, amides, and anilides	62
LITERATURE CITED	83

## HISTORICAL

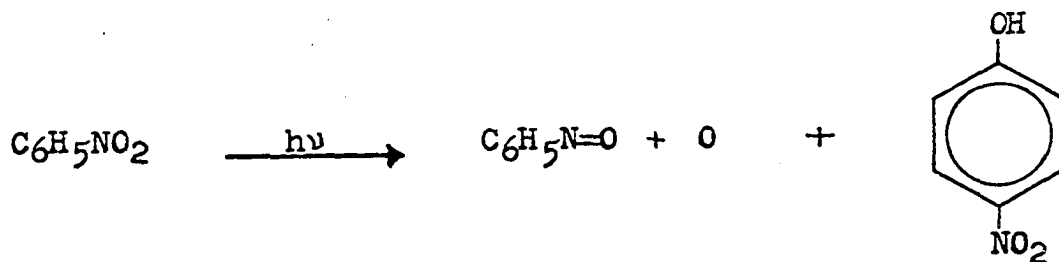
The historical section contains a brief review of the basic photochemical reactions of saturated and unsaturated nitro compounds followed by a review of the light induced reactions of unsaturated acids, amides, and anilides.

## Photochemical Reactions of Nitro Compounds

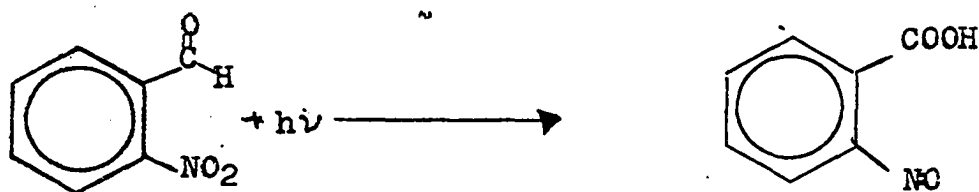
The photochemical reactions of nitro compounds has been extensively investigated in recent years. Nitro alkanes in general undergo a radical forming process on irradiation (1). In addition the nitro alkanes may fragment to form an alkene and nitrous acid when a hydrogen atom is available on the  $\beta$ -carbon (2). The rearrangement of a nitro alkane to form an alkyl nitrite is sometimes important as is the formation of an aldehyde with expulsion of hyponitrous acid (1).



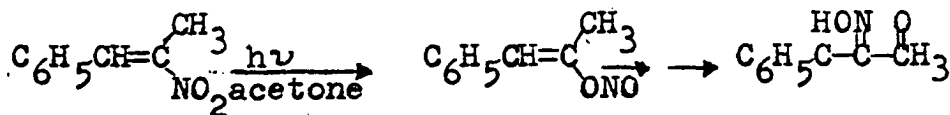
The irradiation of nitrobenzene leads to the formation of nitrosobenzene, *p*-nitrophenol and oxygen (3).



In the irradiation of *o*-nitrobenzaldehyde, an efficient transfer of an oxygen atom from the nitro group to the carbonyl C-H bond occurs (4).

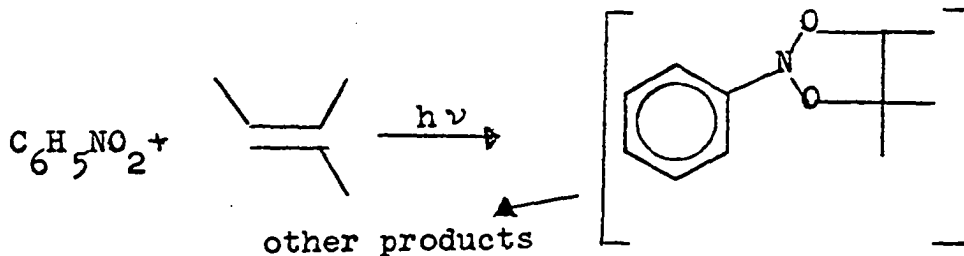


The irradiation of  $\beta$ -nitrostyrene in solution leads only to cis, trans isomerization (5), whereas the irradiation of  $\beta$ -methyl- $\beta$ -nitrostyrene is typical of a growing number of reactions where a sterically crowded nitro group is initially converted to a nitrite ester which then decomposes (6).

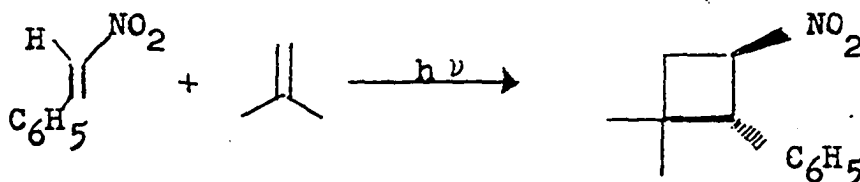


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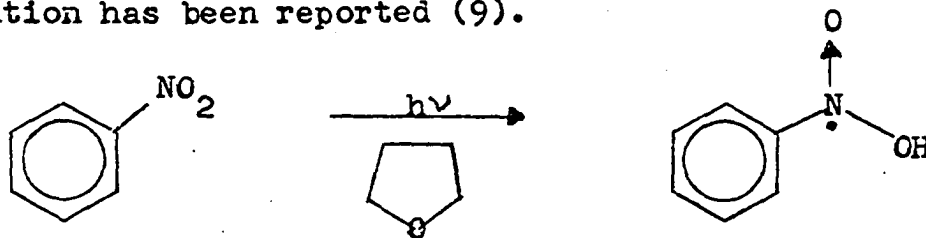
Additional reactions of nitro compounds are the intermolecular addition of a nitro group to a double bond (7),



and cycloaddition reaction of the ethylenic bond (8).



The photoreduction of aromatic nitro compounds in solution has been reported (9).



#### Photochemical Reactions of Unsaturated Acids, Amides, and Anilides

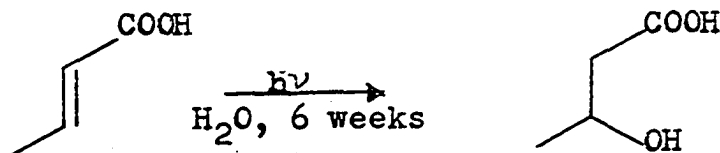
The photochemical reactions of unsaturated acids and amides have been elucidated to some extent from research over many decades. Photochemical reactions of unsaturated aliphatic acid anilides have not yet been reported.

The cis, trans isomerization of unsaturated acids has received the bulk of all attention (10), especially

the isomerization of cinnamic acids (11).

Stoermer and Robert reported that after irradiation for 11 days, trans-crotonic acid, in toluene solvent, was converted to cis-crotonic acid to the extent of 3.5% (12). The isomerization of tiglic acid to angelic acid has been investigated (see discussion section).

Photochemically induced solvent addition to unsaturated acids have been reported. Crotonic acid, if irradiated in water, for 6 weeks, forms  $\beta$ -hydroxybutanoic acid in about 10% yield. The addition of methanol and ethanol reportedly



occurs to the extent of 11.5% and 6.8% respectively (13)\*. The irradiation of the sodium salt of crotonic acid in water gives the  $\beta$ -hydroxyacid in 24% yield.

Stoermer and Robert have reported that the irradiation of trans-crotonic acid in the presence of excess aniline leads to the formation of  $\beta$ -anilinobutyric acid in about 40% yield (12).

In addition, the dimerization of cinnamic acid has

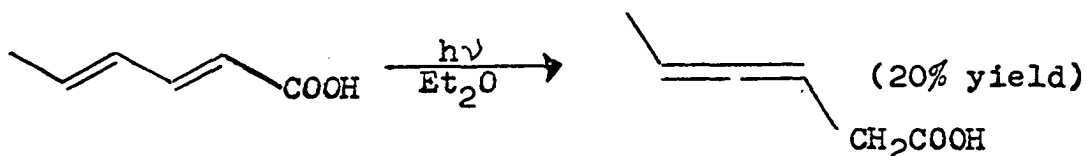
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\*This work has recently been repeated and it was found that crotonic acid did not add methanol on irradiation in the presence or absence of xylene sensitizer. Private communication. Paul Kropp, Procter and Gamble Co., Cincinnati, Ohio. 1967.

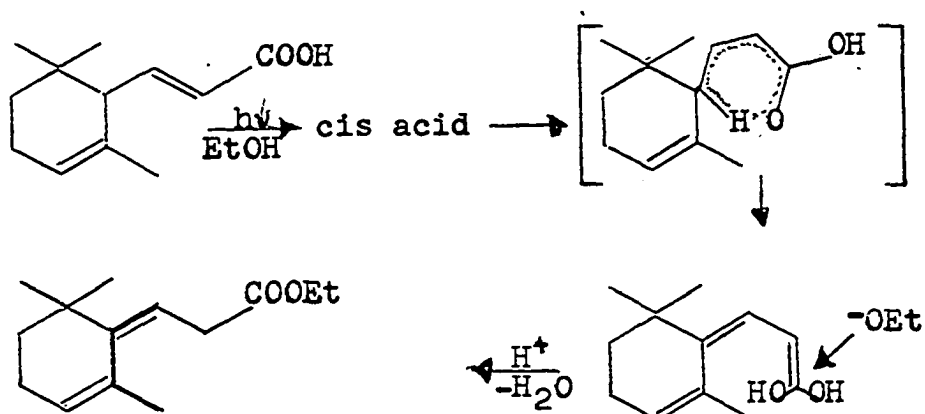


been extensively studied (11). The photocycloaddition reaction of cinnamic acid has also received attention (14).

Crowley has reported the photochemical isomerization of sorbic acid to an allenic acid (15). The methyl ester in ether containing formic acid formed the allenic acid but the irradiation of the sodium salt in water did not.

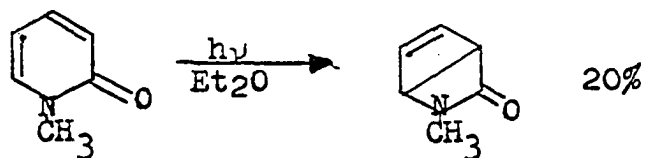


A similar isomerization occurs in the light catalyzed reaction of  $\alpha$ -ionone in ethanol (16).

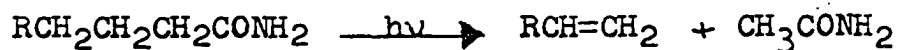


The cis, trans isomerization of cinnamic acid amides has been reported (17). The isomerization of crotonic acid amide is more extensive than the acid as 40% of the cis amide can be isolated (12).

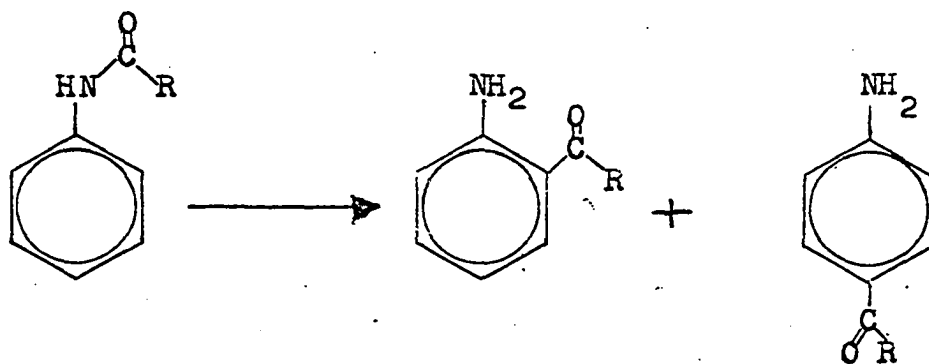
A novel reaction of an unsaturated lactam is the intramolecular cyclization of N-methyl-2-pyridone (18).



Saturated acid amides with  $\gamma$ -hydrogen atoms undergo a "Norrish Type II" cleavage analogous to other carbonyl containing compounds (19), although the parent saturated acids do not cleave in this manner.



Acid anilides, on the other hand, undergo a photo-anilide rearrangement analogous to the rearrangement of aliphatic and aromatic acid phenyl esters (20).



## RESULTS AND DISCUSSION

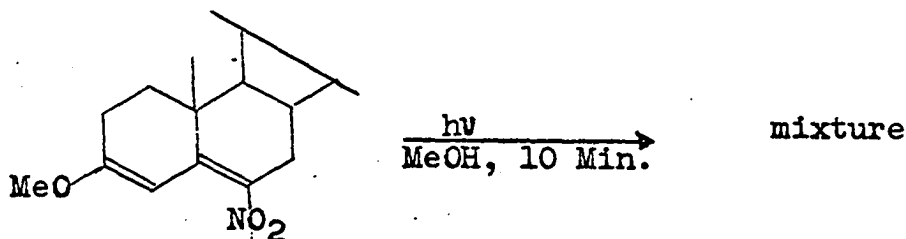
This section is divided into three parts. The first deals with the results and discussion of the photochemistry of 6-nitrocholesteryl acetate. The second section deals with the pyrolysis of  $\beta$ -lactones. The third section deals with the photochemistry of unsaturated acids, amides, and anilides.

## The Photochemistry of 6-Nitrocholesteryl Acetate

The photolysis of 6-nitrocholesteryl acetate was undertaken with the possibility of extending the known reactions of unsaturated nitro compounds. At the very least, the irradiation of the above compound would be the first definitive investigation of an alicyclic unsaturated nitro compound\*. The results expected by analogy to other work would be the formation of cycloaddition compounds and intramolecular rearrangement to 5-nitrosocholestane-6-one-

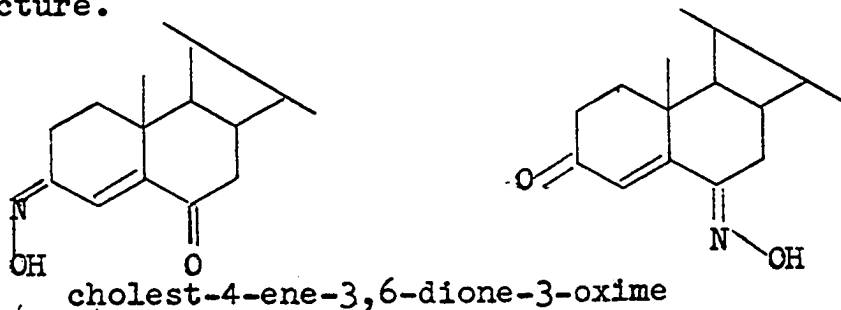
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\*The irradiation of 3-methoxy-6-nitrocholesta-3,5-diene had been reported to give a mixture of products, but the mixture was not characterized (21).



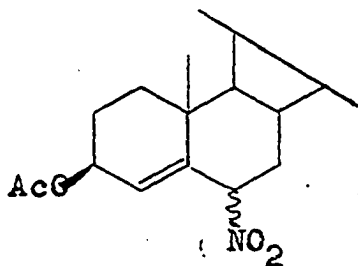
3 $\beta$ -ol acetate (6). The actual results proved to be more complex.

The photolysis of 6-nitrocholesteryl acetate in acetone solvent (purged with nitrogen) in a Pyrex immersion well vessel gave three compounds. The first was collected by filtration from the reaction solvent in 22% yield. Recrystallization from ethyl acetate gave white crystals mp. 222.5-225° d. It was obvious from the infrared spectra that the acetate group had been eliminated. Instead, there was an unsaturated ketone (5.96, and 6.27 $\mu$ ), a hydroxyl group (2.79 $\mu$ ), and one olefinic hydrogen ( $\delta$ 6.76, s) very similar to that of a 4-ene-3-keto steroid. It was apparent that the hydroxyl group was part of an oxime ( $\delta$ 8.1). In addition, the system was entirely conjugated with  $\lambda_{\max}$  (95% EtOH), 285 m $\mu$  ( $\epsilon$ 5,120). Only two structures can be derived from our starting material with the first possibility the more probable. The combustion analysis agreed with either structure.



The second compound was obtained by chromatography of the remaining reaction mixture on silica gel. The non-

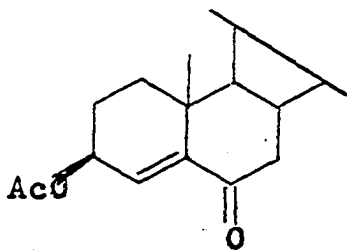
crystalline fractions eluted with Skelly-B-benzene 1:1 were homogeneous on thin layer chromatography (52% yield). A secondary acetate group was still present (5.77 $\mu$ ,  $\delta$ 2.09, and 5.16 m, 1H). A nitro group was probably present ( $\delta$ 4.97 m, 1H). The presence of a C-4 double bond was indicated by a multiplet at  $\delta$ 5.72 (1H). The structure for this compound is probably 6-nitrocholest-4-ene-3 $\beta$ -ol acetate. A mixture of epimers at the 6 position was expected since the compound did not readily crystallize. Eventually the 6 $\beta$ -epimer was



6-nitrocholest-4-ene-3 $\beta$ -ol acetate  
6 $\alpha$  and 6 $\beta$ -NO<sub>2</sub> in 1:1 ratio

obtained crystalline with mp 97-99° and the correct analysis.

A third compound was obtained by further elution with benzene-ether 95:5 in 3.4% yield, mp 106-110°. This material likewise had a secondary acetate group (5.75 $\mu$ ,  $\delta$ 5.27) and an unsaturated ketone (5.91, 6.10 $\mu$ ). A C-4 double bond was also suspected ( $\delta$ 5.99, 1H). The structure consonant with this data is cholest-4-ene-6-one-3 $\beta$ -ol acetate. The  $\lambda_{\max}$



cholest-4-ene-6-one-3 $\beta$ -ol acetate

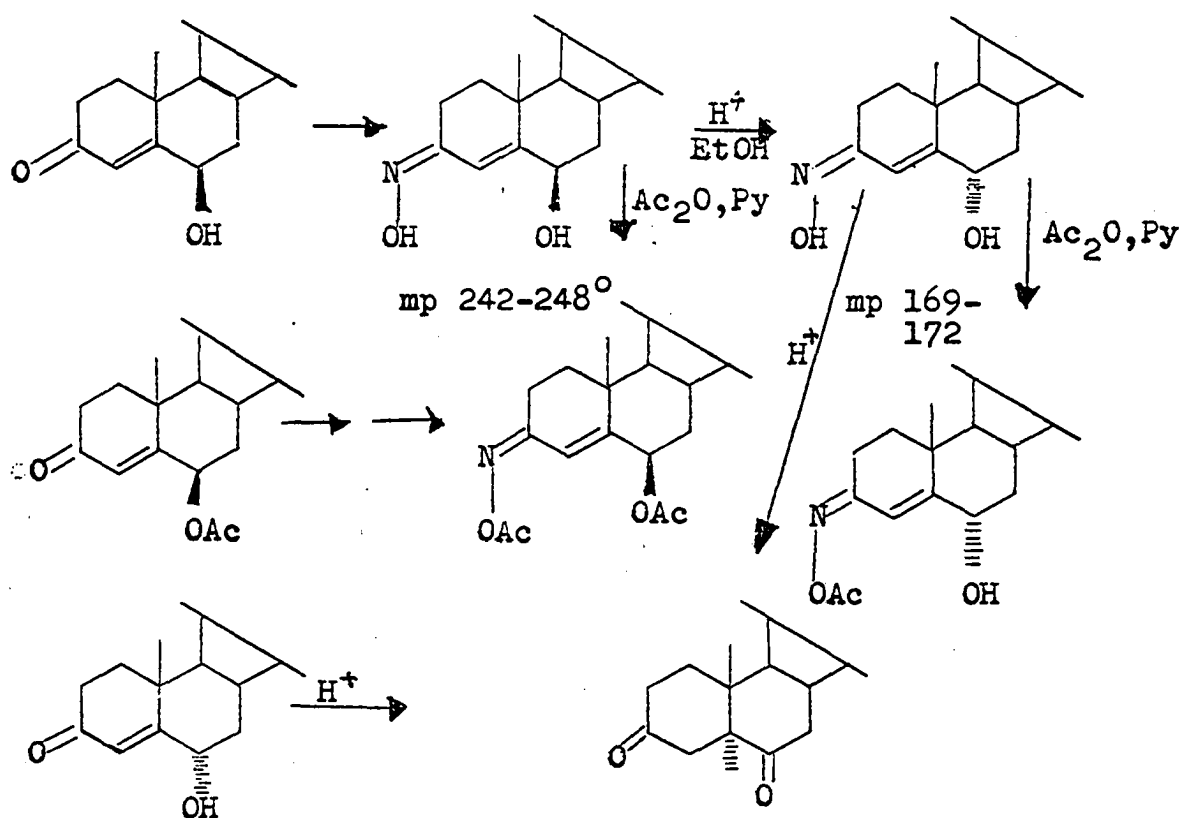
(95% EtOH), was 236  $m\mu$  ( $\epsilon$ 6,450) as expected.

The proof of structure of the above compounds was undertaken in the following manner.

That the structure of the first compound was one of the two possibilities above was demonstrated by exchange of the ketone oxime with formaldehyde catalyzed by hydrogen ion to cholest-4-ene-3,6-dione. This material was identical in every respect with a synthetic sample (22).

The synthesis of this photoproduct was then undertaken. Cholest-4-ene-3-one-6 $\beta$ -ol, synthesized directly from cholest-erol (22), was converted to its oxime in the usual manner. This oxime mp 242-248 $^{\circ}$ d was found by accident to be very labile in the presence of acid and was easily converted to cholest-4-ene-3-one-6 $\alpha$ -ol oxime mp 169-172 $^{\circ}$ . Although the infrared, UV and nmr spectra of the two oximes were quite similar, a more sophisticated rearrangement was expected since the solubility of the new compound was much greater and the melting point was significantly lower. In addition the new oxime formed only a monoacetate in good yield on acetylation in acetic anhydride-pyridine, whereas the higher melting oxime formed the expected diacetate. This diacetate was identical with that prepared from cholest-4-ene-3-one-6 $\beta$ -ol acetate oxime by acetylation. It was possible to observe the oxime acetate at about 5.64 $\mu$  and the secondary acetate at 5.76 $\mu$ . The combustion analysis

of all compounds agreed with the assigned structures. Final proof for the epimerization of the  $6\beta$ -alcohol was obtained by the acid hydrolysis of the new oxime to give  $5\alpha$ -cholestane-3,6-dione, identical with a sample obtained by catalytic reduction of cholest-4-ene-3,6-dione. Presumably then, cholest-4-ene-3-one- $6\alpha$ -ol was first formed and this rearranged to the diketone by the known route (22).

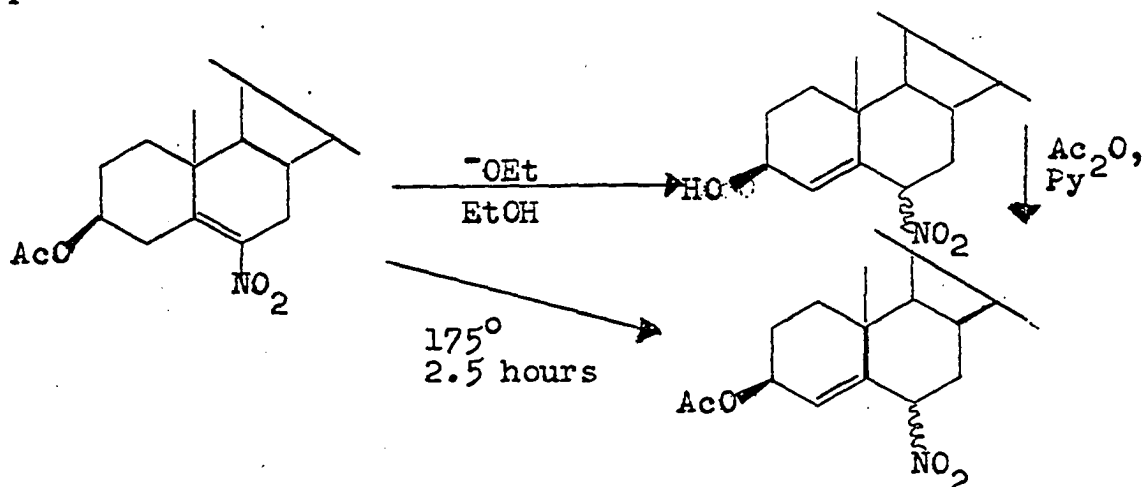


The cholest-4-ene-3-one- $6\beta$ -ol oxime  $\text{mp } 242-248^\circ$  was then oxidized with chromium trioxide in pyridine to yield cholest-4-ene-3,6-dione-3-oxime which was identical in every respect with the photoproduct.

The structure of the second photoproduct was confirmed

as follows. 6-Nitrocholesteryl acetate was hydrolyzed and isomerized by modification of a reported procedure (23,24) to yield a mixture of  $6\alpha$  and  $6\beta$ -nitrocholest-4-ene- $3\beta$ -ol. This mixture was acetylated to give a noncrystalline mixture of the two acetates. The infrared and nmr spectra were superimposable with those of the photoproduct. The epimers are also in a 1:1 ratio.

It was furthermore found that a mixture identical to the second photoproduct could be obtained simply by heating 6-nitrocholesteryl acetate for 2.5 hours at  $175^\circ$ . A pure product was obtained.



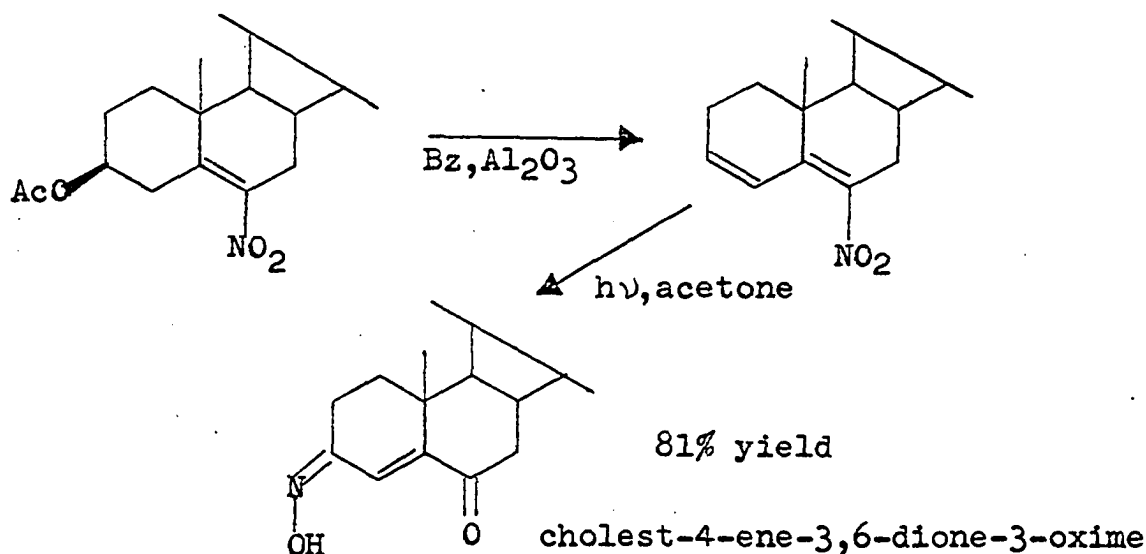
The identity of the third photoproduct was confirmed as cholest-4-ene-6-one- $3\beta$ -ol acetate by direct comparison with an authentic sample available in this laboratory.

The solvent effect on the photochemical rearrangements was partially investigated. It was found that the irradiation of 6-nitrocholest-5-ene- $3\beta$ -ol acetate in pentane solution gave a 27% yield of a mixture of  $6\alpha$  and  $6\beta$ -nitrocholest-

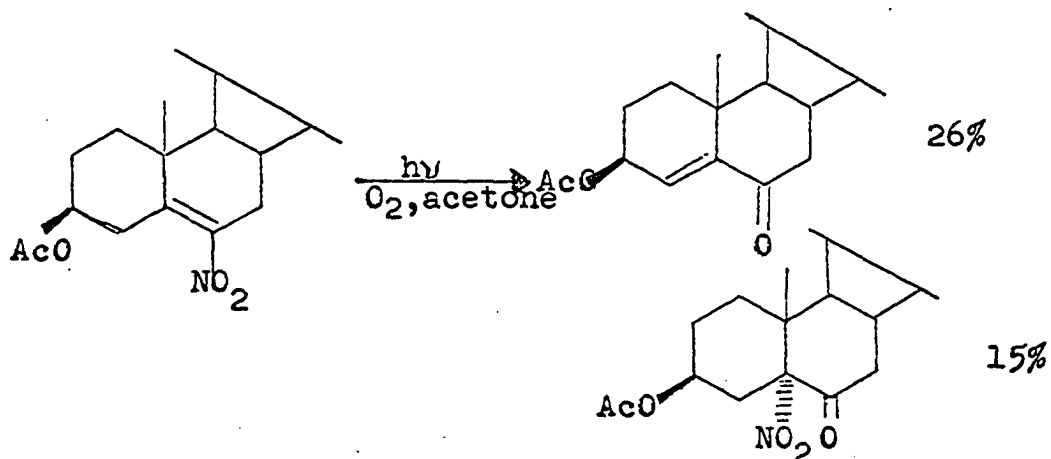


4-ene-3 $\beta$ -ol acetate and a 40% yield of the cholest-4-ene-6-one-3 $\beta$ -ol acetate. Significantly, no keto-oxime was detected or isolated. The irradiation in cyclohexene gave respectively a 56% and a 12% yield of the above photoproducts but no keto-oxime or cycloadducts. The lack of formation of cycloaddition products is analogous to the results obtained by Hoganson (8). When the unsaturated nitro group is forced by its environment to adopt a configuration that limits direct conjugation, cycloaddition does not occur.

The mechanism for the formation of the keto-oxime photoproduct was partially elucidated by the irradiation of 6-nitrocholesta-3,5-diene. This material was prepared in high yield by chromatography of 6-nitrocholesteryl acetate on alumina. Irradiation of the diene nitro compound in acetone solvent gave an 81% isolated yield of the cholest-4-ene-3,6-dione-3-oxime.



Further mechanistic evidence was uncovered by the irradiation of 6-nitrocholesteryl acetate in acetone under a stream of oxygen. The results are dramatically different than in the absence of oxygen. The crude reaction mixture was chromatographed on silica gel. The first compound eluted was cholest-4-ene-6-one-3 $\beta$ -ol acetate (26%) as shown by comparison with an authentic sample. The second compound eluted (15%) was unlike the previous photoproducts. Although it was homogeneous on thin layer plates, it had a wide melting range characteristic of a mixture of epimers. An infrared band at 5.74 and 8.15 $\mu$  is assigned to a 3 $\beta$ -acetate. Bands at 6.55 and 7.29 $\mu$  can be assigned to a nitro group. A band at 5.69 $\mu$  can be assigned to a ketone with an adjacent electronegative group. The UV absorption indicates the presence of a nitro group with a shoulder at 244 m $\mu$  ( $\epsilon$ 8,300) and  $\epsilon$ 370 at 360 m $\mu$  since an unsaturated ketone is absent. The analysis indicates a formula C<sub>29</sub>H<sub>47</sub>NO<sub>5</sub>. The probable structure, then, is 5-nitrocholestane-6-one-3 $\beta$ -ol acetate,

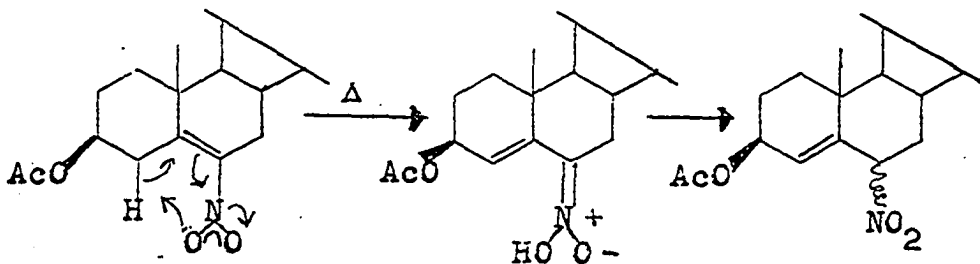


but this assignment is by no means certain. Quite significantly, however, no cholest-4-ene-3,6-dione-3-oxime, 6-nitrocholesta-3,5-diene, or 6-nitrocholest-4-ene-3 $\beta$ -ol acetate could be detected or isolated.

The irradiation of 6 $\beta$ -nitrocholest-4-ene-3 $\beta$ -ol acetate in acetone in the presence of oxygen gave only recovered starting material. It is not known if the 6 $\alpha$ -epimer behaves similarly but it would be expected to.

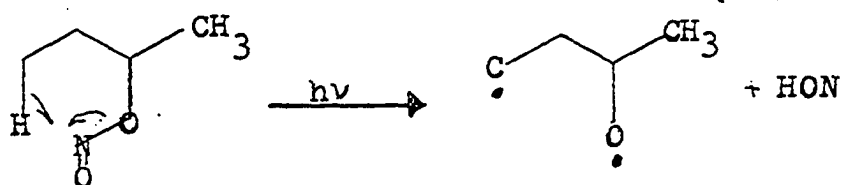
The irradiation of 6-nitrocholesta-3,5-diene in acetone and oxygen yielded several compounds but significantly no cholest-4-ene-3,6-dione-3-oxime could be detected by infrared or TLC analysis. This compound, however, does not react with oxygen in the dark in hexane solution. 6-Nitrocholesteryl acetate likewise is not affected in acetone in the presence or absence of oxygen in the dark.

The explanation for the formation of 6 $\alpha$  and 6 $\beta$ -nitrocholest-4-ene-3 $\beta$ -ol acetate is most probably that a photoexcited state of 6-nitrocholesteryl acetate is internally converted to a vibrationally excited ground state which rearranges by the thermal route. The relative yields of

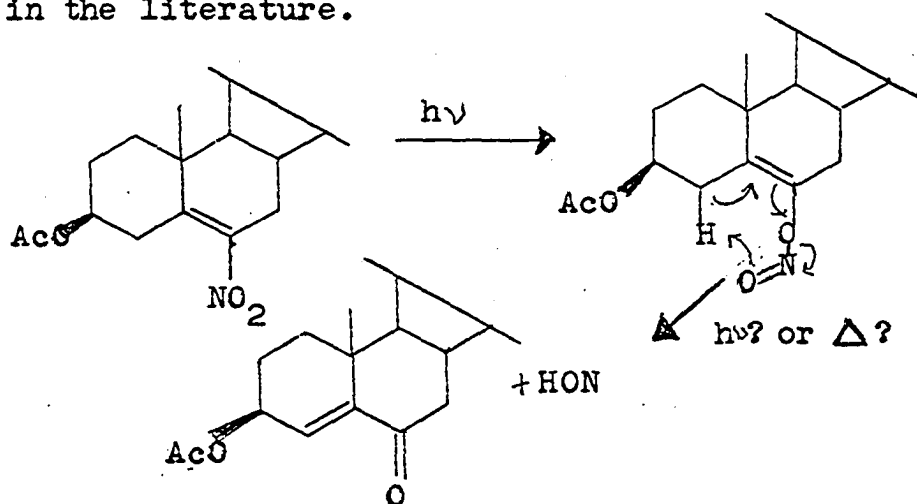


$6\alpha$  and  $6\beta$ -epimers is determined solely by the kinetically controlled tautomerization of the aci-nitro intermediate.

The formation of cholest-4-ene-6-one- $3\beta$ -ol acetate can most conveniently be explained as involving the photochemically induced nitro to nitrite rearrangement originally anticipated by analogy to  $\beta$ -methyl- $\beta$ -nitrostyrene. However, in this instance the unsaturated nitrite photochemically or thermally cleaves with the loss of hyponitrous acid and formation of the unsaturated ketone in a manner analogous to the decomposition of sec-butylnitrite (25). A thermal



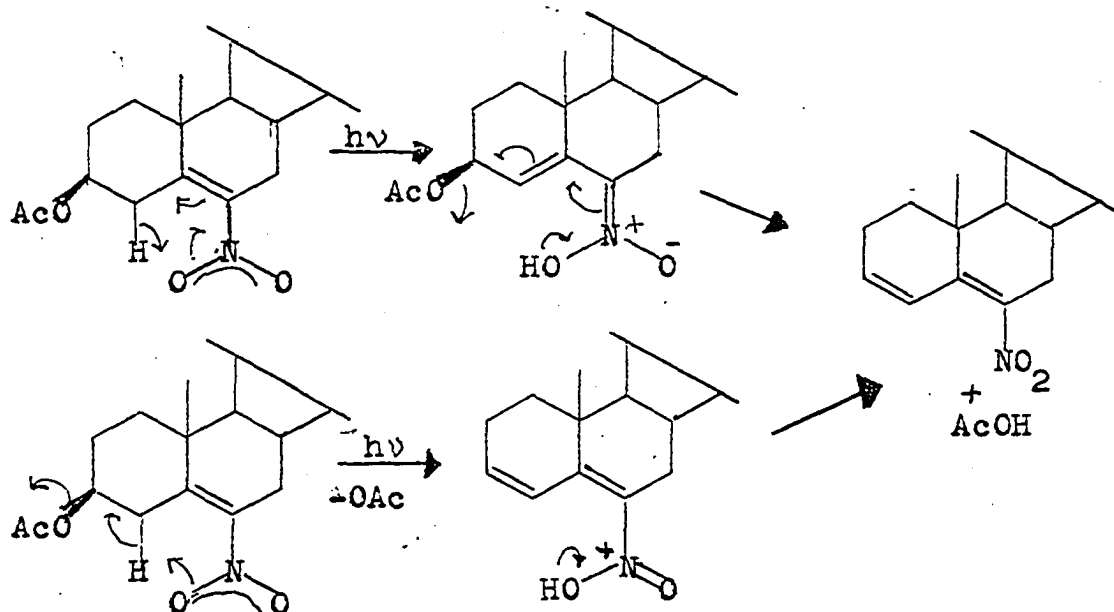
decomposition can not be excluded since an unsaturated nitrite has not been observed as a bona fide intermediate in the above reaction. Indeed, no unsaturated nitrite has been reported in the literature.



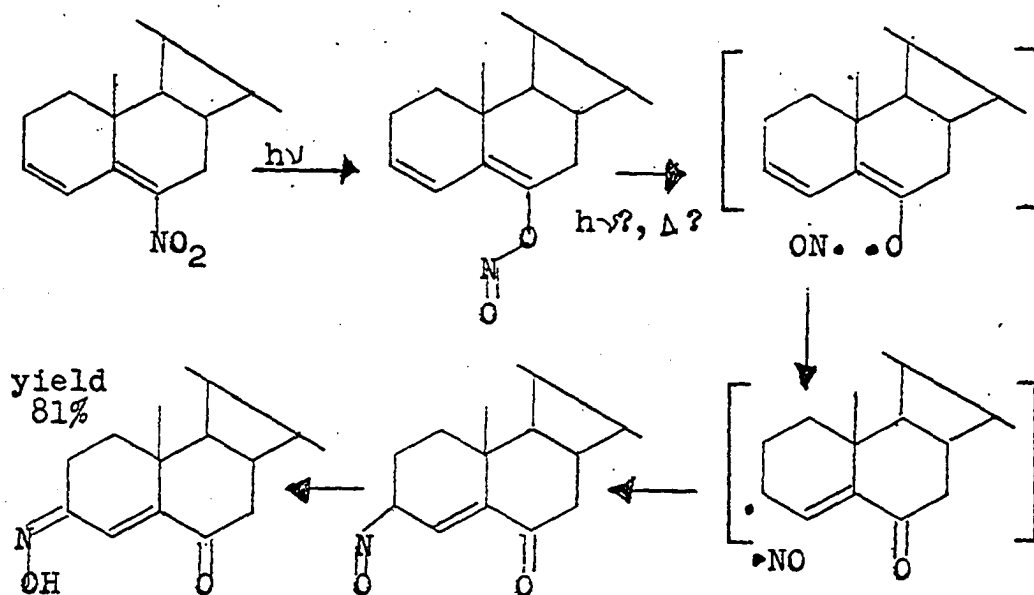
Doubtless other mechanisms could be drawn but none involving  $6\beta$ -nitrocholest-4-ene- $3\beta$ -ol acetate can be considered since this compound is not converted to the above product upon irradiation in acetone in the presence of oxygen.

The mechanism of formation of cholest-4-ene-3,6-dione-3-oxime is obviously more complex but the presence of 6-nitrocholesta-3,5-diene as an intermediate is extremely likely due to its conversion in high yield to the keto-oxime.

Several transition states for the elimination of acetic acid can be proposed under the assumption that 6-nitrocholesta-3,5-diene must be formed. The first has the same aci-nitro intermediate as involved in the formation of 6-nitrocholest-4-ene- $3\beta$ -ol acetate. The second mechanism may not be concerted as shown.

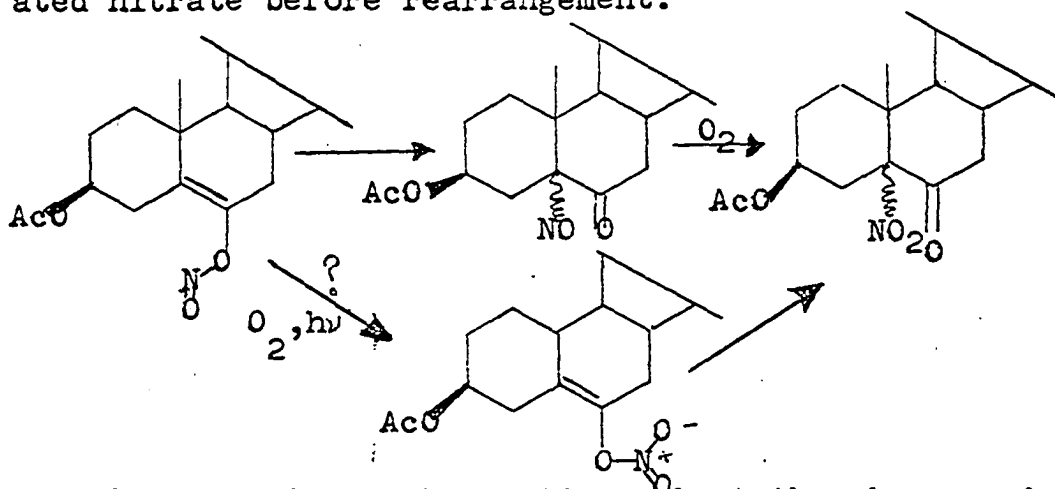


The formation of the keto-oxime proceeds via a photochemical nitro-nitrite rearrangement of 6-nitrocholesta-3,5-diene. The nitrite then thermally or photochemically cleaves to an alkoxy radical and nitric oxide. Due to the high conversion to product, it is highly probable that a radical cage intermediate is formed. The odd electron on nitric oxide then combines with the isomeric alkoxy radical. The secondary nitroso compound then tautomerizes to the stable oxime.

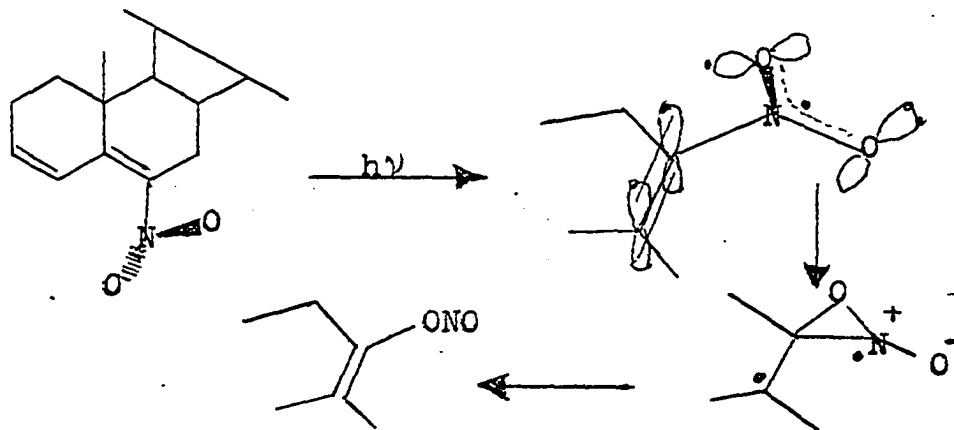


The formation of 5-nitrocholest-6-one-3 $\beta$ -ol acetate during the irradiation of 6-nitrocholesteryl acetate in acetone in the presence of oxygen is viewed as an analogy to the formation of 1-phenyl-1-oximinopropane-2-one from  $\beta$ -methyl- $\beta$ -nitrostyrene (6). The intermediate C-5 nitroso compound is believed to be oxidized to a nitro compound.

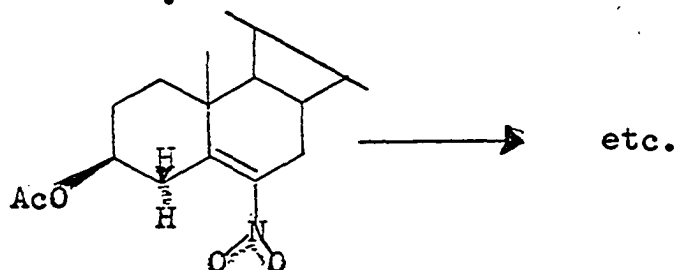
Possibly the unsaturated nitrite is oxidized to an unsaturated nitrate before rearrangement.



Some pertinent observations about the above mechanisms should be stated. It is believed that the nitro-nitrite rearrangement occurs through a non-planar non-conjugated excited state facilitated by steric interactions with hydrogens at C-4. An electron deficient non-bonding oxygen orbital may interact with the ethylenic bond to form a transient oxiziridine intermediate which rearranges rapidly to the nitrite (26). The formation of oxiziridines from the irradiation of nitrones is well known (27).



On the other hand, it is most probable that the formation of 6-nitrocholest-4-ene-3 $\beta$ -ol acetate and 6-nitrocholesta-3,5-diene are related processes partly because a planar conjugated nitro group is involved. A common transition state may be involved but the irradiations in the



presence of oxygen cast doubt on this proposal. It is not possible to predict what electronic states are involved in the above transformations. The results are not clear cut and more definitive experiments must be attempted. Still, however, it is expected that a  $n\text{-}\pi^*$  transition is quite important in one or more rearrangements\*. The multiplicity of the reactive excited state is not known.

There are many unanswered questions. Why does 6-nitrocholesteryl acetate undergo a nitro-nitrite rearrangement in the presence of oxygen, but 6-nitrocholesta-3,5-diene does not? What is the role of acetone in the above reactions?

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\*For a discussion of the excited states of the nitro group see H. H. Jaffé, and M. Orchin, Theory and Application of Ultraviolet Spectroscopy, John Wiley and Sons, Inc., New York, N. Y., 1962, p. 182 ff.



If a planar conjugated nitro group is involved in at least one transformation, why is cycloaddition not also observed even though cyclohexene is not the best choice of olefin? What is the exact structure of the new photoproduct in the irradiation of 6-nitrocholesteryl acetate in the presence of oxygen and how is it formed? What in general is the effect of oxygen on this system? Which reactions are thermal and which are photochemical?

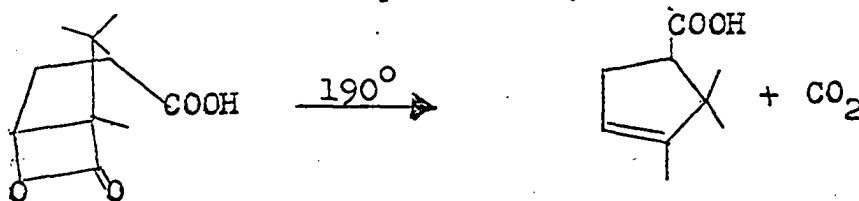
After the completion of this work, two publications appeared (28,29). The first reported some results quite different from those above. Few details were given and the results are questionable. The second reported the irradiation of 6-nitrocholesteryl acetate in ethyl alcohol and the isolation of 6-nitrocholesta-3,5-diene (2.3%) as a definite intermediate in the formation of cholest-4-ene-3,6-dione-3-oxime. The irradiation in cyclohexane yielded the mixture of epimers of 6-nitrocholest-4-ene-3 $\beta$ -ol acetate (19.6%) and cholest-4-ene-6-one-3 $\beta$ -ol acetate (40%) in good agreement with our yields of 27% and 40% respectively from an irradiation carried out in pentane solution.

A publication which originated in part from the work in this thesis is:

Chapman, O. L., P. G. Cleveland, E. D. Hoganson. Chem. Comm. 101 (1966).

The Pyrolysis of  $\beta$ -Lactones

The thermal decomposition of  $\beta$ -lactones to form carbon dioxide and an olefin has been well documented in the literature (30). In all instances the stereochemistry of the reaction is unknown except in those few cases where the decomposition is necessarily cis. For example the  $\beta$ -lactone derived from 5-hydroxycamphoric acid decomposes at  $190^\circ$  to  $\alpha$ -camphononic acid. It is not known if the thermal decomposition is cis and concerted for systems that lack gross stereochemical restraints or proceeds by a two step mechanism.

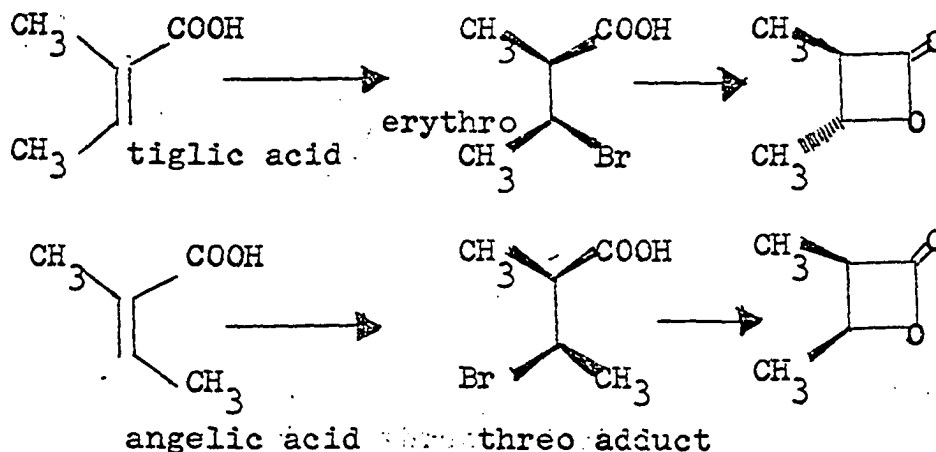


The decomposition of  $\beta$ -lactones in aqueous solution, on the other hand, has been shown by Noyce and Banitt to be a stereospecific cis elimination (31).

An experiment that would differentiate between the two thermal decomposition mechanisms is the decomposition of a set of cis and trans substituted  $\beta$ -lactones. If the reaction were a concerted elimination, a cis substituted lactone would yield a cis substituted olefin. The trans lactone would then give the trans olefin. If, however, the reaction were not concerted, the initially formed radical would rapidly invert to its most stable conformation. The breaking of the second bond would then yield carbon dioxide

and the thermodynamically stable olefin.

The cis and trans-3-hydroxy-2-methylbutanoic acid lactones were chosen since they represented the simplest isomeric set of lactones reported in the literature (32). The stereochemistry was not reported but follows from the mode of synthesis. The trans addition of hydrogen bromide to tiglic acid in 47% hydrobromic acid gives an adduct (erythro) mp 65° which is stereospecifically converted to trans-3-hydroxy-2-methylbutanoic acid lactone by solvolysis of the sodium salt. The displacement of the  $\beta$ -bromo atom must proceed with inversion of configuration. Analogously, the addition of hydrogen bromide to angelic acid should yield the threo adduct which subsequently should yield cis lactone on solvolysis of the sodium salt. The configuration of tiglic and angelic acid have been unambiguously determined by X-ray analysis (33).



A paper published in 1879, however, reported that the

addition of hydrogen bromide to angelic acid gives 60-70% of the tiglic acid adduct and possibly some angelic acid adduct which was not isolable (34).

We have found that addition of hydrogen bromide to tiglic and angelic acid occurs exactly as described in the earlier reference. Addition of hydrogen bromide to angelic acid under anhydrous conditions at room temperature or at  $-20^{\circ}$ , always produced isomerization of angelic acid to tiglic acid at a rate faster than addition of hydrogen bromide to either acid. Only a small amount of threo adduct could be formed in the presence of large amounts of erythro adduct. In spite of this result, the bulk of the erythro adduct was removed by crystallization and the solvolysis of the sodium salt of the adduct mixture yielded a mixture of the cis and trans lactones. The preparation of the trans lactone easily afforded a pure product which gave a fine second order nmr spectrum.

The pure cis lactone could not be synthesized by the reaction of erythro-3-bromo-2-methylbutanoic acid with silver oxide in anhydrous ether (31). This reaction proceeds with retention of configuration of the  $\beta$ -carbon in a few instances where the  $\beta$ -atom is stabilized by electron donating groups. In this instance a methyl group does not stabilize the developing carbonium ion as well and the reaction instead gave a 51% isolated yield of tiglic acid by trans elimination of hydrogen bromide without a trace of  $\beta$ -lactone.

The pure trans lactone in a sealed tube was pyrolyzed at 210° for 2 hours. The contents were analyzed by infrared and nmr spectroscopy. The spectra were identical with those of pure trans-2-butene. The carbon dioxide yield from another pyrolysis was 91.0%.

A sample of the cis and trans lactone mixture was pyrolyzed in the same manner. The infrared spectrum of the reaction mixture showed only cis and trans-2-butene. The relative amounts of hydrocarbons were determined by gas chromatography to be 46±5% cis-2-butene and 54±5% trans-2-butene. The yield of carbon dioxide was 87.1%. The lactone mixture was 43±6% cis lactone by nmr. Cis-2-butene is known to be stable at 450° (35). The conclusion then is that pyrolysis of  $\beta$ -lactones involves cis and concerted loss of carbon dioxide. (36).

#### The Photochemistry of Unsaturated Acids, Amides, and Anilides

The photochemical solvent additions and cis-trans isomerization of simple alicyclic  $\alpha, \beta$ -unsaturated acids are the only reported reactions of these compounds (12,13). The photochemistry of several of these acids was reinvestigated in a non-protic, non-hydroxylic solvent with the view in mind of extending the known reactions of these compounds. In particular it was of interest to determine if simple unsaturated acids could be photochemically converted

to  $\beta$ -lactones in a manner analogous to the recent lactonization of  $\alpha$ -phenylcinnamic acids (37).

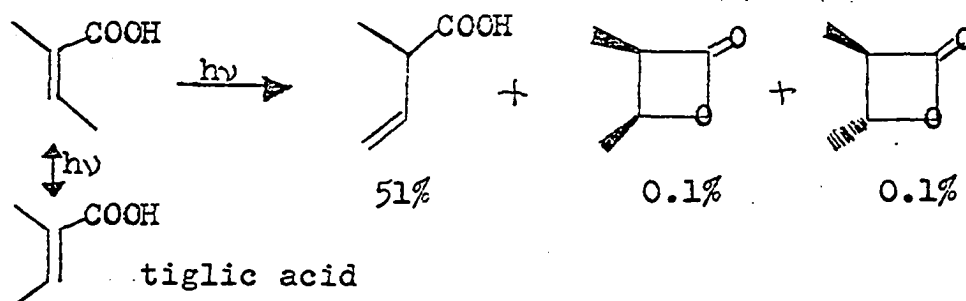
Methacrylic acid was irradiated in ether solution with a 550 watt mercury arc lamp in a quartz vessel under nitrogen. The reaction was followed by infrared analysis. After 15 hours, no starting material remained and no  $\beta$ -lactone could be observed at about  $5.50\mu$ . A white polymer mp greater than  $200^{\circ}$  was collected by filtration (18%) and an ether soluble polymer (85%) was collected on evaporation of the solvent. The infrared spectra of each fraction revealed only broad absorption bands characteristic of polymers.

On the other hand, irradiation of trans-crotonic acid in ether afforded on distillation a 60% yield of the  $\beta,\gamma$ -unsaturated 3-butenic acid. This material was identified by its infrared and spectra and by the reported properties of its amide derivative. The irradiation of 3-methyl-2-butenic acid in an analogous manner afforded a 50% yield of 3-methyl-3-butenic acid identified by its amide and spectra. In neither case could any  $\beta$ -lactone be detected.

It was first reported that the irradiation of tiglic acid in aqueous solution failed to yield any angelic acid (38). Subsequently it was shown that the irradiation of 13 g of tiglic acid powder in a quartz tube for 13 days with a 500 watt Hanovia ultraviolet lamp leads to the formation of 0.36 g of angelic acid and 1.5 g of a mixture of the

two acids (39). We have looked more closely at the irradiation of tiglic acid and its derivatives under a variety of conditions.

The irradiation of tiglic acid in a dilute ether solution with a 550 watt Hanovia lamp afforded a reaction mixture with a weak band at  $5.45\mu$  characteristic of a  $\beta$ -lactone. The mixture was distilled under reduced pressure and the first fractions which contained the  $\beta$ -lactone were combined and washed with dilute sodium bicarbonate solution. The solvent was dried and evaporated and the residue redistilled to yield an enriched lactone fraction which was again extracted with dilute aqueous sodium bicarbonate solution. Evaporation of the solvent yielded a colorless oil containing two lactones in nearly equal amounts in 0.2% overall yield. The oil had strong infrared absorption at  $5.46\mu$ . The nmr peaks ( $\text{CCl}_4$ ), for cis-3-hydroxy-2-methylbutanoic acid lactone were  $\delta$ 1.20 (d), 1.34 (d), 3.71 (m), 4.60 (m), and for the trans lactone;  $\delta$ 1.28 (d), 1.44 (d), 3.07 (m), and 4.17 (m). The spectra were nearly identical



with those of a synthetic sample of lactones.

The higher boiling fraction in the first distillation was 2-methyl-3-butenic acid (51%) characterized by its amide derivative and spectra.

The irradiation of angelic acid under the above conditions lead to the isolation of 44% of the 2-methyl-3-butenic acid and 0.2% of a nearly equal mixture of two  $\beta$ -lactones contaminated with a small amount of 2-methyl-3-butenic acid. The infrared spectrum of the lactone mixture had strong absorption at  $5.46\mu$  and a weak band at  $5.85\mu$ . The nmr peaks ( $\text{CCl}_4$ ), for cis-3-hydroxy-2-methylbutanoic acid lactone was  $\delta$ 1.22 (d), 1.41 (d), 3.66 (m), 4.66 (m), and  $\delta$ 1.36 (d), 1.53 (d), 3.15 (m), 4.24 (m) for the trans lactone.

The isolation of  $\beta$ -lactones from the irradiation of tiglic and angelic acid is the only example with non-phenyl substituted acids.

The irradiation of a more concentrated tiglic acid solution in ether with  $2537 \text{ \AA}$  light leads to a rapid formation of angelic acid then to a greater than 95% yield of the  $\beta,\gamma$ -unsaturated 2-methyl-3-butenic acid. Significantly, no  $\beta$ -lactone can be detected. This reaction is perhaps the simplest method of preparation of  $\beta,\gamma$ -unsaturated acids.

The irradiation of tiglic acid, on the other hand, in acetone solution leads to the formation of a photostationary



state after 4 days containing 51.5% tiglic and 48.5% angelic acid (by nmr). The isolated yield of pure angelic acid was however low (16%) only due to an experimental difficulty. Sensitization by acetone probably facilitates formation of the photostationary state and absorption of light by acetone prevents the isomerization to the  $\beta,\gamma$ -unsaturated isomer.

Irradiation of tiglic acid in cyclohexane solution with added benzophenone yielded only benzopinacol (68%) and cyclohexane adducts which were not fully characterized. Benzophenone prefers to abstract hydrogen atoms than to transfer energy to the unsaturated acid.

The irradiation of the sodium salt of tiglic acid in sodium hydroxide solution produced only an 18.7% yield of the rearranged acid.

The irradiation of l-cyclopentenecarboxylic acid in ether solution was undertaken with the possibility of obtaining a higher yield of  $\beta$ -lactone since the intramolecular rearrangement to the unconjugated isomer would be expected to be an unfavorable process. Several products were formed but none are  $\beta$ -lactones. The only product characterized was a dimer of starting material isolated in 4.9% yield. The irradiation in tert-butyl alcohol gave up to 40.7% of this dimer. The exact structure and stereochemistry is not known.

It was determined that tiglic and angelic acid were

not affected in the absence of light in ether solution.

The irradiation of two representative unsaturated acid amides was undertaken. Methacrylic acid amide, when irradiated in ether solution with 2537 Å light, produced 62% of a solid white polymer and a 30% recovery of starting material. In methanol solvent, the yield was 23% and 48% respectively for the same irradiation time, probably reflecting the poor hydrogen atom donating ability of the methanol solvent as compared with diethyl ether.

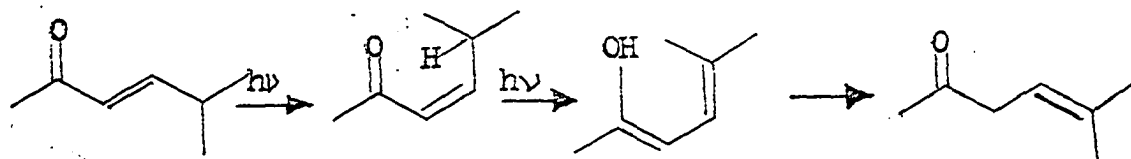
The irradiation of tiglic acid amide, on the other hand, in ether solvent gave a 52% isolated yield of 2-methyl-3-butenic acid amide in analogy with tiglic acid. Several minor compounds were not characterized. In neither case were any  $\beta$ -lactams detected.

The intervention of 2-methyl-3-butenic acid as an intermediate in the formation of the cis and trans lactones was eliminated when it was found that this acid was only degraded by light from the 550 watt lamp in ether solvent or completely unaffected by 2537 Å light in toluene solvent. The last experiment employed the conditions observed by Marshall and Kropp in the sensitized photochemical addition of alcohols to certain olefins (40,41).

There is only a single observable absorption maxima in the ultraviolet spectra of tiglic and angelic acid at 215 m $\mu$  ( $\epsilon$ 14,400) and 217 m $\mu$  ( $\epsilon$ 11,800) respectively) and

is undoubtedly a  $\pi$ - $\pi^*$  transition (42). A  $n$ - $\pi^*$  transition of low extinction is probably present under the much more intense  $\pi$ - $\pi^*$  transition. This band should be shifted from 204  $m\mu$  observed for acetic acid ( $\epsilon$ 60) to longer wavelength analogously to the bathochromic shift of simple ketone  $n$ - $\pi^*$  transitions on conjugation with an ethylenic bond (42).

It appears that with 2537 Å light in the absence of sensitizers, only cis, trans isomerization of tiglic and angelic acid followed by a slow conversion of angelic acid to the unconjugated acid occurs. A possible mechanism for this conversion is a six-membered transition state analogous to that reported by Yang and Jorgenson in the isomerization of 5-methylhex-3-ene-2-one to 5-methylhex-4-ene-2-one (43).



By analogy, a  $n$ - $\pi^*$  triplet or a low  $\pi$ - $\pi^*$  triplet would be the likely intermediate in the hydrogen abstraction and isomerization of angelic acid. This may not be the case though.

The irradiation of tiglic acid in acetone solvent and the formation of a photostationary equilibrium between tiglic and angelic acid indicates that acetone ( $E_T$  74 Kcal)

is acting here as a triplet sensitizer only for the cis, trans isomerization. The fact that the rearrangement of angelic acid to 2-methyl-3-butenoic acid fails to occur indicates that acetone does not sensitize this rearrangement. A possible explanation is that the rearrangement occurs via a singlet state which is not excited when acetone is absorbing all the light as in this experiment. Hydrogen abstraction via a singlet pi-pi\* state is not as generally observed as abstraction via other excited states (44). It is also possible the triplet state which is responsible for hydrogen abstraction ( if it is a triplet state) lies higher than the triplet of acetone and can therefore not be sensitized.

The failure of benzophenone to simply isomerize tiglic and angelic acids via energy transfer indicates that the triplet state energies for these acids are higher than 69 Kcal (45).

On the other hand, the transition state for the rearrangement process may be derived from an electronic state that has been internally converted to a thermally excited species which is the intermediate proposed in the thermal isomerization of  $\alpha,\beta$  to  $\beta,\gamma$ -unsaturated acids prior to decarboxylation (46).

It may be concluded from our experiments that light of wavelength shorter than 2537 Å from the full mercury arc

is necessary for the formation of  $\beta$ -lactones from tiglic and angelic acid since the lactones are not formed during irradiation with 2537 Å light. The low yield and the wavelength dependence of formation of the  $\beta$ -lactones agrees with the belief that a weakly absorbing n- $\pi^*$  transition is initially responsible. Furthermore, a n- $\pi^*$  singlet state is believed involved since it is the only one of the four simple electronic states that would not be available by excitation of the  $\pi$ - $\pi^*$  band with 2537 Å light. Qualitatively, the presence of oxygen does not affect the rate of formation of any product in this system. There is a slight possibility that the  $\beta$ -lactones are unstable under the reaction conditions when the 2537 Å light source is used.

If the first explanation is correct, then the predicted maximum yield of  $\beta$ -lactones from the irradiation of a simple acyclic unsaturated acid would not be greater than the ratio of the n- $\pi^*$  extinction coefficient over the  $\pi$ - $\pi^*$  extinction coefficient when both transitions are in the same spectral region. Our observed lactone yield agrees with this prediction.

It is indeed unfortunate but the interconversion of tiglic and angelic acids and the formation of a  $\beta$ -lactone mixture preclude any knowledge of steric factors important in  $\beta$ -lactone formation.

It is not known why crotonic acid, 3-methyl-2-butenic

acid and 1-cyclopentenecarboxylic acid fail to yield an observable  $\beta$ -lactone.

Since the completion of our work, it has been shown independently that trans-crotonic acid is converted to cis-crotonic acid which is then converted to 3-butenic acid in agreement with our results\*.

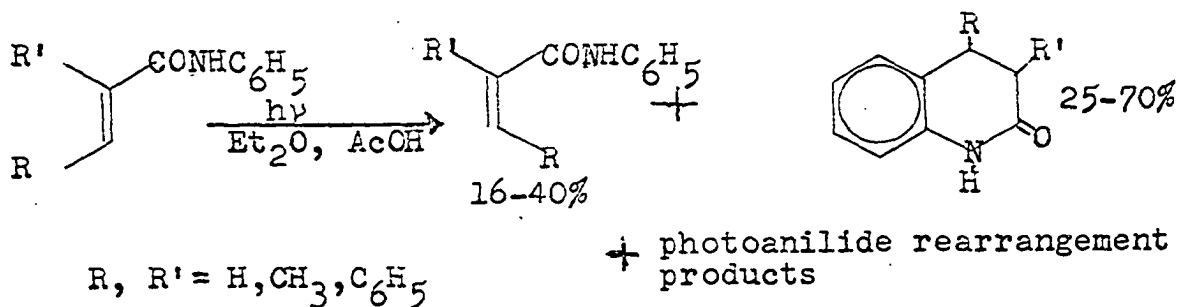
An extensive investigation of the formation of  $\beta$ -lactones from  $\alpha$ -phenylcinnamic acids has been completed (37).

The last topic for this result and discussion section is the photochemistry of unsaturated acid anilides. In general the anilides were irradiated in ether solvent in a Pyrex immersion well vessel with a 550 watt Hanovia ultra-violet lamp. The reaction progress was followed by infrared or thin layer chromatographic analysis. The reaction mixtures always contained a small amount of photoanilide rearrangement products which were removed by acid extraction during the workup. In several instances, the nmr spectra of this material indicated that the ortho and para substituted products were formed with their cis, trans isomers. The general reaction scheme is shown on the next page.

A dilute solution of tiglic acid anilide in ether was irradiated for 9 hours. The reaction mixture was separated into a basic fraction of the photoanilide rearrangement

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\*Private communication. Paul Kropp, Procter and Gamble Company, Cincinnati, Ohio. 1967.



products (1.9%) and a neutral fraction. Elution of the neutral fraction on a silica gel column with benzene yielded white crystals of angelic acid anilide (19%) identified by melting point and spectra comparison with an authentic sample. Fractions eluted with benzene-chloroform 75:25 contained a new compound (54%) whose structure was indicated by the lack of olefinic protons to be a dihydrocarbostyryl derivative (see experimental section). This compound appeared to be a mixture of diastereomers. A single diastereomer was obtained when a sample of the photoproduct was sublimed at  $115^\circ/0.03$  mm Hg with mp  $116.5-117.5^\circ$ . An authentic sample of 3,4-dimethyldihydrocarbostyryl had mp  $116.5-117.5^\circ$  and an identical infrared spectrum as the photoproduct (47).

The generality of this new cyclization reaction was investigated by irradiation of several homologues of tiglic acid anilide. The irradiation of trans-crotonic acid anilide in ether gave 2.4% of the photoanilide rearrangement products after 21 hours. The neutral fraction was chromatographed on silica gel yielding two compounds in 32% and 45% Yield. The first had mp  $100-102^\circ$  and nmr peaks as follow: A methyl

doublet at  $\delta$ 2.11, an olefinic doublet at 5.84, an olefinic quartet at 6.15, aromatic peaks from 6.9-7.7 (5H), and an N-H broad singlet at  $\delta$ 8.0. This material was therefore cis-crotonic acid anilide. The reported mp is 102<sup>o</sup> (48). The second compound was starting material by comparison of melting points and spectra. No dihydrocarbostyryl was detected in this reaction.

It seemed possible that the photoanilide rearrangement products were absorbing all the light and the formation of the dihydrocarbostyryl was prevented. The only reaction then observed was the facile cis, trans isomerization of the unsaturated acid anilide. The irradiation of trans-crotonic acid was repeated in the presence of a small amount of acetic acid which effectively moves the absorption maxima of the aniline derivatives out of the Pyrex region. This time a 25% yield of 4-methyldihydrocarbostyryl was obtained along with a small amount of the cis and trans anilides. The photochemical cyclization is slow, requiring 5 days irradiation, and much polymer is produced. The 4-methyldihydrocarbostyryl was identified by its spectra and mp 100-102<sup>o</sup>; lit. mp 98<sup>o</sup> (49).

The irradiation of methacrylic acid anilide in ether in the absence of acetic acid resulted in the recovery of 97% of the starting material and a 3% yield of the photoanilide rearrangement products. The irradiation in the



presence of acetic acid, on the other hand, gave only 39% recovered starting material but a 50% yield of 3-methyl-dihydrocarbostyryl which was identified by its spectra and reported melting point (50).

The irradiation of cis-crotonic acid anilide in ether containing acetic acid with 2537 Å light yielded only 15% recovered starting material and polymers. No 4-methyl-dihydrocarbostyryl could be detected though a very small amount of trans-crotonic acid anilide could be observed. It is indeed surprising that the cis anilide does not isomerize to the trans anilide to any significant extent but prefers to polymerize.

It was found that irradiation of trans-cinnamic acid anilide in the presence of acetic acid for 8 days yielded only cis-cinnamic acid anilide and polymer according to nmr and TLC. Trans-cinnamic acid anilide irradiated for 7 hours in the absence of acetic acid yielded only the cis anilide and polymer. The isolated cis-cinnamic acid anilide (41%) had the expected spectra and analysis. After a total irradiation time of 2 days in the absence of acetic acid, only a small amount of the photoanilide rearrangement products could be detected in addition to the cis anilide and polymers.

The irradiation of  $\alpha$ -phenylacrylic acid in a quartz immersion well vessel in the presence of acetic acid for

48 hours produced 2% of the photoanilide rearrangement products, 20% recovered starting material and polymer. At least three other compounds are found in low yield. One could still be the dihydrocarbostyryl derivative.

The photocyclization of the phenyl substituted unsaturated acid anilides does not occur to any significant extent quite possibly since the proper electronic transition is not excited. Also, cis-cinnamic acid anilide is sterically prevented from passing through a cyclization transition state and nearly all the anilide is in the cis form very soon after the irradiation has commenced.

The irradiation of tiglic acid anilide in the presence of acetic acid was now undertaken with the result that a slightly greater yield of 3,4-dimethyldihydrocarbostyryl (58%) was obtained at the expense of a lower yield of the angelic acid anilide (16%). The choice of tiglic acid anilide for further mechanistic work was made since it alone cyclized relatively cleanly in the absence of acetic acid.

The problem of the origin of the hydrogen atom in position 3 of the dihydrocarbostyryls was next undertaken.

N-Deuterotiglic acid anilide (95% N-D) was prepared and irradiated. The reaction mixture was worked up in the same manner as before so that all N-deuterium in the product was washed out to simplify analysis. The isolated angelic acid anilide did not contain any deuterium as expected according

to nmr and mass spectrometry. However, the carefully recrystallized 3,4-dimethyldihydrocarbostyryl fraction contained 14% deuterium in the 3 or 4 position by nmr and 15% deuterium by mass spectrometry. It is impossible to determine the relative deuterium content in each position directly by nmr or mass spec. The deuterium is, however, at the 3 position since it was washed out by sodium methoxide catalyzed exchange in methanol (nmr analysis only). It is apparent that 15% of the hydrogen at position 3 is derived by migration from the amide nitrogen.

Tiglic acid 2,4,6-trideuteroanilide was prepared with 93% deuterium in the ortho position by nmr and 92.8% by mass spectrometry. Irradiation of this anilide with a slightly modified work up procedure (see experimental) afforded 24% of angelic acid 2,4,6-trideuteroanilide. The nmr and mass spectra showed that no migration of deuterium had occurred during the cis, trans isomerization as expected. A 70% yield of the deuterated 3,4-dimethyldihydrocarbostyryl was obtained which now had 52% deuterium in the 3 position. This deuterium could also be washed out by methoxide catalyzed exchange in methanol. The mass spectrum indicated only a 45.5% deuterium content by a somewhat ambiguous calculation (see experimental).

It is apparent that at least 15% of the hydrogen at position 3 comes from the N-H and 56% from the aromatic ring. The rest may come from intermolecular or exchange

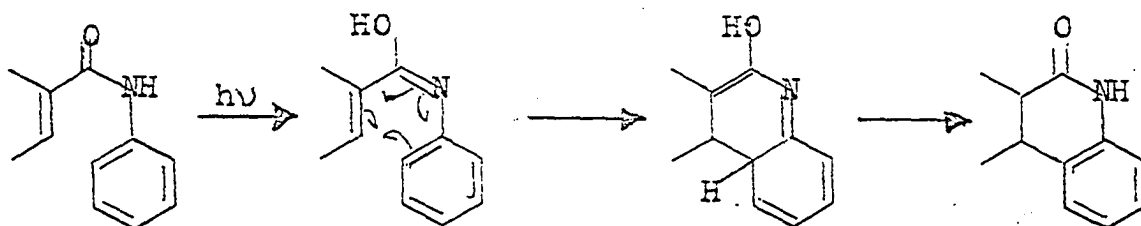
processes of an unknown nature. It was shown that deuterium is not lost from the product by continued irradiation. 3-Deutero-4-hydro-3,4-dimethyldihydrocarbostyryl was prepared with 85% deuterium in position 3 (nmr). Irradiation of this material with 2537 Å light resulted in the recovery of 99% starting material with 86% deuterium in the 3 position by nmr. Deuterium is not lost from the 3 position during the work up procedure since the synthetic 3-deutero compound was worked up exactly the same way as the photoproducts. It is quite possible that the full 44% of the hydrogen comes from the nitrogen atom and that all but 15% is lost by exchange before migration could take place.

A systematic investigation of the electronic transitions in  $\alpha,\beta$ -unsaturated acid anilides has not been reported. UV spectra of the following compounds indicates that the absorption of tiglic acid anilide is not obtained by addition of acetanilide and tiglic acid absorptions (51):

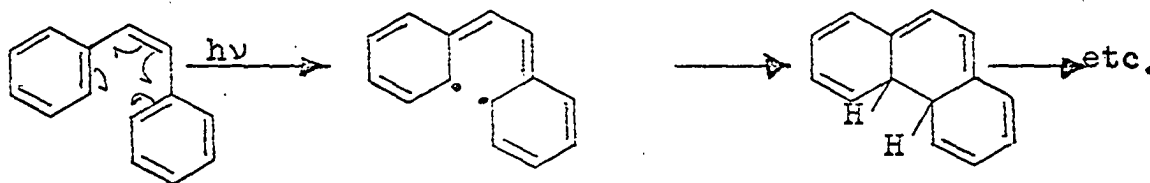
benzene	$\lambda_{\max}$ 198 m $\mu$ ( $\epsilon$ 8,000), 255 m $\mu$ ( $\epsilon$ 280)
aniline	" 230 " ( $\epsilon$ 8,600), 280 " ( $\epsilon$ 1,430)
acetanilide	" 242 " ( $\epsilon$ 14,400), 280 " ( $\epsilon$ 500)
tiglic acid	" 215 " ( $\epsilon$ 14,400)
tiglic acid anilide	" 205 " ( $\epsilon$ 22,900), 257 " ( $\epsilon$ 11,500).

Rather, it appears that extensive interaction of all pi electrons occurs and assignment of absorption bands is impossible with out further work.

Several mechanisms for the conversion of tiglic acid anilide to 3,4-dimethyldihydrocarbostryl are possible which yield an intermediate which is capable of transferring a hydrogen atom from either the aromatic ring or from the nitrogen atom.

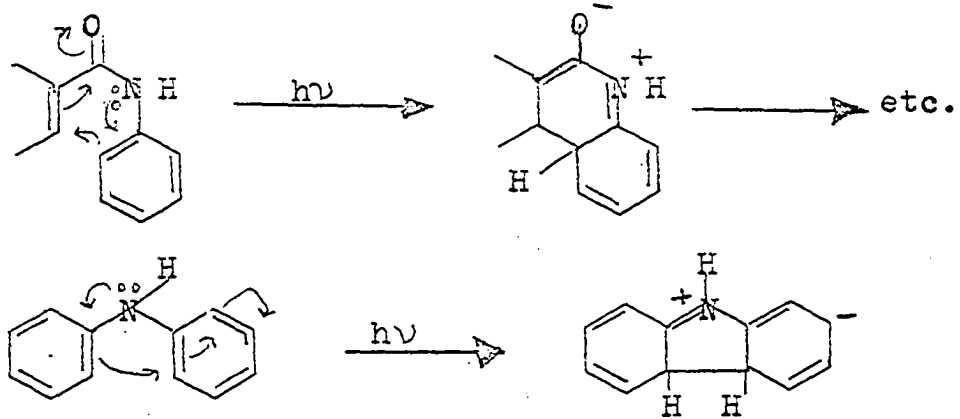


The above mechanism is somewhat analogous to the photochemical cyclization of stilbenes (52). A zwitterion intermediate is not involved. In this mechanism, one might expect a higher intramolecular hydrogen transfer from the nitrogen than was observed.

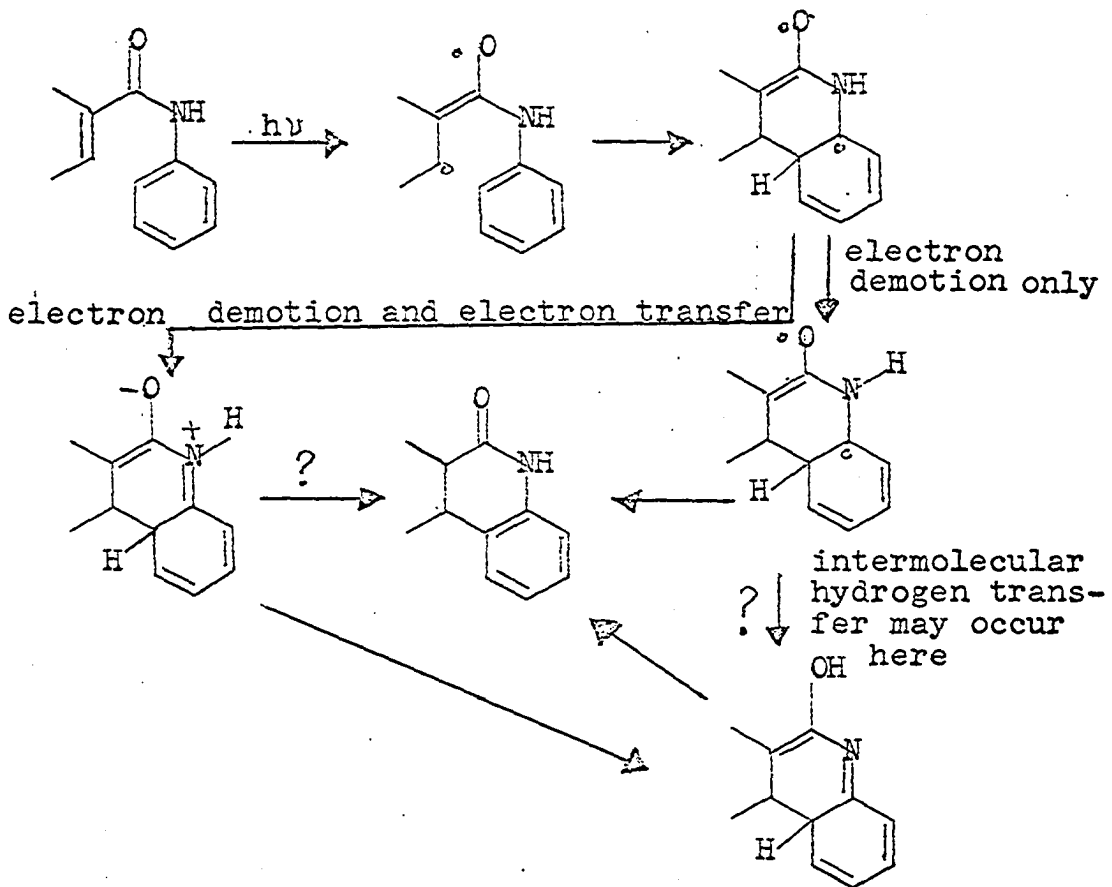


An alternate mechanism is possible which is similar to that proposed for the photocyclization of diphenylamine (53). The zwitterion intermediate has been observed with  $\lambda_{\text{max}}$  610 m $\mu$ . The protonated form of the dihydrocarbostryl precursor is exactly that predicted for the acid catalyzed

cyclization.

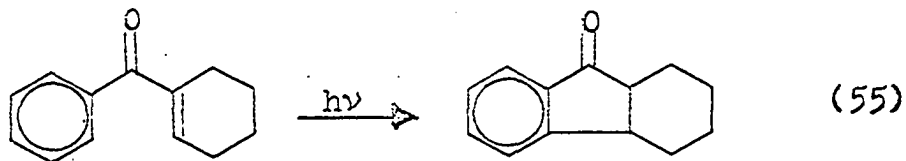


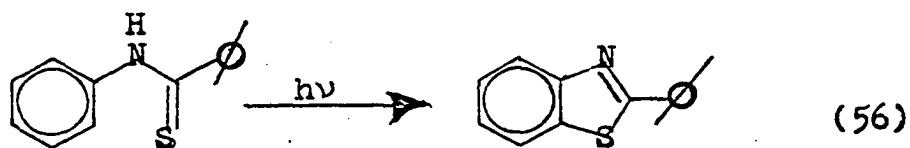
An additional mechanism which is more complex involves



bond formation in an excited state before electron demotion to a diradical intermediate or demotion with electron transfer to a zwitterion species. The intermolecular hydrogen exchange observed in the irradiation of the deuterated compounds may occur from the diradical intermediate after electron demotion. Both intermediates can undergo 1,3-hydrogen migrations from the nitrogen atom or from the potential aromatic ring. This mechanism is somewhat analogous to that proposed by Zimmermann in the rearrangement of 4,4-diphenylcyclohexadienone (54). This scheme does not imply whether a  $n\text{-}\pi^*$  or a  $\pi\text{-}\pi^*$  state is involved nor does it make any statement about the electronic state multiplicity.

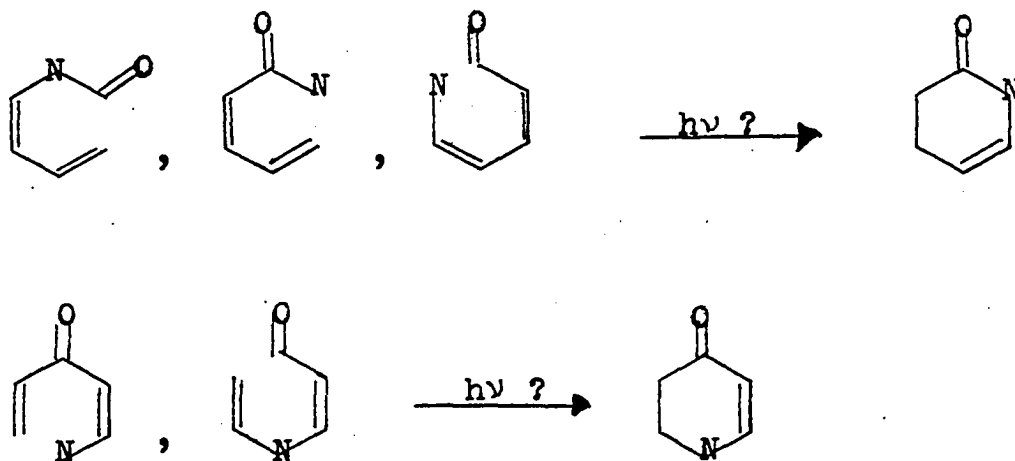
The correct mechanism for the cyclization to the dihydrocarbostyryl can not be elucidated at this time since it is not known 1) if an aromatic ring is necessary, 2) if a non-bonding pair of electrons on nitrogen or other heteroatom is required, 3) if the reaction can be sensitized or quenched (qualitatively, oxygen has no affect), or 4) what the affect of substituents on the aromatic ring might be. There are two other examples of photocyclizations that have been reported.





The first is the only cyclization which is not a formal oxidation process other than our results.

It should be noted that all the reported literature examples above are cyclizations of 6 pi electron systems. Our observed cyclization of unsaturated acid anilides is the first to occur in a formal 8 pi system. Five analogies that could extend the synthetic usefulness and theoretical understanding of our cyclization would be the following systems. Undoubtedly, many others exist.





## EXPERIMENTAL

## Instruments and Methods

All melting points are uncorrected and were measured on a Kofler microscope hot stage equipped with a polarizer.

The ultraviolet spectra were obtained in 95% ethanol or cyclohexane as noted. The spectra were recorded on a Beckman Model DK-2A spectrophotometer.

All infrared spectra were recorded on a Perkin-Elmer Model 21 spectrometer.

The nuclear magnetic resonance spectra were measured on a Varian associates Model HR-60 or A-60 spectrometer operating at 60 mc. Spectra obtained with the HR-60 spectrometer were calibrated by the side band technique using tetramethyl silane as internal standard. Chemical shifts are reported as  $\delta$ -values in parts per million.

Elemental analyses were performed by Spang Micro-analytical Laboratory, Ann Arbor, Michigan.

The source of ultraviolet light for most irradiations was the Hanovia Type-A lamp (550 watt). The spectral output of this lamp is as follows (57).

Wavelength in m $\mu$	% of Total Emission
404-578	43
366.0	15
344.0	1
313.0	7
302.5	4
296.7	2
222.4-289.4	28

Experimental for the Irradiation of  
6-Nitrocholest-5-ene-3 $\beta$ -ol Acetate

6-Nitrocholest-5-ene-3 $\beta$ -ol acetate was purchased from Aldrich Chemical Company Milwaukee, Wisconsin. Recrystallization from absolute ethanol yielded colorless crystals mp 104-105.2° (58);  $\lambda_{\max}$  (95% EtOH), 325 m $\mu$  ( $\epsilon$  53), 260 m $\mu$  ( $\epsilon$  204).

Irradiation of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate in acetone

A solution of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate (1.8 g, 3.8 m mole) in reagent grade acetone (390 ml) was purged with nitrogen then irradiated for 2 hours with a 550 watt mercury arc lamp (Hanovia Type-A) enclosed in a Pyrex immersion well vessel. The solvent was removed on a rotary evaporator. The crystalline material was filtered and washed with a small amount of ethyl acetate. Several crops of crystals were collected in addition and recrystallized from hot ethyl acetate yielding cholest-4-ene-3,6-dione-3-oxime (0.395 g, 22%) mp 220-222.5°. An additional recrystallization from ethyl acetate yielded an analytical sample, mp 222.5-225°d;  $\lambda_{\max}$  (95% EtOH), 285 m $\mu$  ( $\epsilon$  5,150); infrared (CHCl<sub>3</sub>), 2.79, 3.15, 5.96, and 6.27 $\mu$ ; nmr (CDCl<sub>3</sub>),  $\delta$  6.76 (olefinic H), and 8.1 (oxime H).

Anal. Calcd. for C<sub>27</sub>H<sub>43</sub>O<sub>2</sub>N: C, 78.41; H, 10.48; N, 2.69. Found: C, 78.32; H, 10.48; N, 2.61.

The mother liquors were combined and chromatographed on silica gel and eluted with Skelly-B-benzene 1:1. Fractions

of a mixture of epimers of 6-nitrocholest-4-ene-3 $\beta$ -ol acetate were combined (0.930 g, 52%);  $\lambda_{\max}$  (95% EtOH), 229 m $\mu$  (shoulder); nmr (CCl<sub>4</sub>),  $\delta$ 4.58 (m, 1H), 4.97 (m, 1H), 5.16 (m, 1H), and 5.72 (m, 1H). These compounds were fully characterized in a separate experiment (see below). Further elution with benzene ether 95:5 gave cholest-4-ene-6-one-3 $\beta$ -ol acetate (0.062 g, 3.4%), mp 106-110<sup>o</sup>, lit. (59) mp 110<sup>o</sup>; infrared spectra identical with an authentic sample.

Irradiation of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate in pentane

A solution of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate (0.60 g, 1.2 m mole) in pentane (1800 ml) was purged with a stream on nitrogen for 1.5 hours then irradiated as above for 2 hours. The solvent was removed on a rotary evaporator. The crude oil was combined with the product mixture from two duplicate irradiations (total 1.90 g) and chromatographed on a 1.2x 12 inch column of silica gel. The homogeneous material (0.51 g, 27%) eluted with Skelly-B-benzene crystallized after long standing. Careful recrystallization (6 times) from methanol yielded white crystals of 6 $\beta$ -nitrocholest-4-ene-3 $\beta$ -ol acetate mp 97-99<sup>o</sup>;  $\lambda_{\max}$  (95% EtOH), 229 m $\mu$  (shoulder); infrared (KBr), 5.77, 6.45, and 7.97 $\mu$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 4.66 (d, 1H), 5.28 (m, 1H), 5.80 (s, 1H).

Anal. Calcd. for C<sub>29</sub>H<sub>47</sub>NO<sub>4</sub>: C, 73.53; H, 10.01; N, 2.96. Found: C, 73.46; H, 10.06; N, 2.98.

Further elution with benzene-ether 95:5 yielded light yellow crystals (0.77 g, 40%) mp 103-111° of Cholest-4-ene-6-one-3 $\beta$ -ol acetate. Recrystallization from methanol gave crystals mp 109.2-110.7°; lit. (59) mp 110°;  $\lambda_{\text{max}}$  (95% EtOH), 236 m $\mu$  ( $\epsilon$  6,450); infrared (CCl<sub>4</sub>), 5.75, 5.91, and 6.10 $\mu$ .

Irradiation of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate in cyclohexene

A solution of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate (1.47 g, 3.1 m mole) in redistilled cyclohexene (250 ml) was irradiated under nitrogen for 6.75 hours with a 200 watt external mercury lamp in a Pyrex vessel. The solvent was removed under reduced pressure and the crude yellow oil chromatographed on a 2.4 x 26 cm column of silica gel in Skelly-B. A mixture of 6 $\alpha$  and 6 $\beta$ -nitrocholest-4-ene-3 $\beta$ -ol acetate (0.827 g, 56%) was first eluted with benzene. 6 $\beta$ -Nitrocholest-4-ene-3 $\beta$ -ol acetate was crystallized from methanol mp 97-99°. Continued elution with ether:benzene 50:50 gave cholest-4-ene-3 $\beta$ -ol acetate (0.174 g, 12%) mp 103-111°. The infrared spectrum was identical with an authentic sample.

6-Nitrocholest-4-ene-3 $\beta$ -ol acetate

A solution of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate (0.100 g, 0.21 m mole) in absolute ethanol (15 ml) containing 1.3 ml of a solution of sodium (0.8 g, 0.035 moles) in absolute ethanol (100 ml) was stirred at 38° for 6 hours. The reaction

mixture was made acid with 2 drops of acetic acid and the solvent removed under reduced pressure. The oily crystalline mixture with infrared ( $\text{CCl}_4$ ), 2.77, 2.95, 5.90 ( $\mu$ ), of  $6\alpha$  and  $6\beta$ -nitrocholest-4-ene- $3\beta$ -ol (23) was treated with acetic anhydride (1 ml) and pyridine (3 ml) overnight at room temperature. The solution was taken up into ether, extracted with water then twice with dilute hydrochloric acid solution. After drying over magnesium sulfate and evaporation of the ether, an oil (0.075 g, 75%) was obtained with identical infrared and nmr spectra as the mixture of  $6\alpha$  and  $6\beta$ -nitrocholest-4-ene- $3\beta$ -ol acetate from the above irradiations.

#### Thermal isomerization of 6-nitrocholest-5-ene- $3\beta$ -ol acetate

A sample of 6-nitrocholest-5-ene- $3\beta$ -ol acetate in a sealed tube was heated for 2.5 hours at  $175^\circ$ . The product mixture contained only two minor components (thin layer chromatography) and had infrared and nmr spectra identical in every respect with those of the  $6\alpha$  and  $6\beta$ -nitrocholest-4-ene- $3\beta$ -ol acetate mixtures from the photochemical and synthetic reactions.

#### Dark reactions

A solution of 6-nitrocholest-5-ene- $3\beta$ -ol acetate in acetone does not show any change on thin layer chromatography after several days in the dark. The infrared spectrum

likewise shows no reaction.

Oxime exchange of cholest-4-ene-3,6-dione-3-oxime

A solution of cholest-4-ene-3,6-dione-3-oxime (0.013 g) in 37% formaldehyde (0.5 ml) and 95% ethanol (1 ml) containing one drop of 10% hydrochloric acid was refluxed for 10 hours. The solvents were removed under reduced pressure and the product taken up into methanol (1 ml) and again evaporated to dryness. The light tan oil was taken up into methanol (0.5 ml) and 5 drops of water added. The solution was cooled and the product collected by filtration yielding fine yellow plates mp 121-124°; mixed mp 122-124.5°. The infrared spectrum was identical with an authentic sample of cholest-4-ene-3,6-dione (22).

Cholest-4-ene-3-one-6 $\beta$ -ol oxime

A solution of cholest-4-ene-3-one-6 $\beta$ -ol (22) (0.335 g, 0.84 m mole) in methanol (10 ml) containing hydroxylamine hydrochloride (0.0695 g, 1.0 m mole) and pyridine (0.1 ml) was refluxed for 0.5 hours. The product was filtered and washed with methanol yielding cholest-4-ene-3-one-6 $\beta$ -ol oxime (0.220 g, 63%) mp 230-247°d. Recrystallization from ethyl acetate yielded white crystals (0.145 g) which sublime at 235° and melt from 242-248°d. An additional recrystallization afforded an analytical sample mp 242-248°d; infrared (KBr), 3.03, 6.13(w), 6.17(w), 9.84, and 12.03  $\mu$ ; nmr

(pyridine),  $\delta$ -4.58 (O-C-H), 6.39 (olefinic-H).

Anal. Calcd. for  $C_{27}H_{45}NO_2$ : C, 78.02; H, 10.91; N, 3.37. Found: C, 77.92; H, 10.87; N, 3.16.

A diacetate was prepared by dissolving cholest-4-ene-3-one-6 $\beta$ -ol oxime (0.250 g, 0.6 m mole) in acetic anhydride (1 ml) and pyridine (2 ml) at room temperature. White crystals mp 135.5-138 $^{\circ}$ ;  $\lambda_{max}$  (95% EtOH), 242 m $\mu$  ( $\epsilon$  28,200); infrared (CCl<sub>4</sub>), 5.63 and 5.74 $\mu$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 2.00, 2.17 (O-Ac), 5.48 (H-C-OAc), and 6.30 (olefinic-H) were obtained.

Anal. Calcd. for  $C_{31}H_{51}NO_4$ : C, 74.21; H, 10.25; N, 2.73. Found: C, 74.23; H, 9.80; N, 2.71.

#### Cholest-4-ene-3-one-6 $\alpha$ -ol oxime

A slurry of cholest-4-ene-3-one-6 $\beta$ -ol oxime (1.54 g, 3.7 m mole) in absolute ethanol (50 ml) containing a trace of hydrochloric acid was refluxed for 12 hours. The solvent was evaporated on a rotary evaporator and the crystalline product was recrystallized from methanol-cyclohexane as white needles mp 169-172 $^{\circ}$ ;  $\lambda_{max}$  (95% EtOH), 241.8 m $\mu$  ( $\epsilon$  24,700); infrared (KBr), 2.95, 6.17(w), and 10.32 $\mu$ ; nmr (CCl<sub>4</sub>),  $\delta$ 2.96 (1H), 3.27 (t, 2H), 3.70 (1H), 5.84 (1H), and 9.85 (1H).

Anal. Calcd. for  $C_{27}H_{45}NO_2$ : C, 78.02; H, 10.91; N, 3.37. Found: C, 78.13; H, 10.92; N, 3.28.

A monoacetate was prepared as above. White prisms mp

151-154°;  $\lambda_{\max}$  (95% EtOH), 238.3  $\mu\text{m}$  ( $\epsilon$ 24,700); infrared (CCl<sub>4</sub>), 5.68, 6.13(w)  $\mu\text{m}$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 3.20 (complex multiplet), 3.76 (H-C-OH), and 6.10 (olefinic H).

Anal. Calcd. for C<sub>29</sub>H<sub>49</sub>NO<sub>3</sub>: C, 76.10; H, 10.35; N, 3.06. Found: C, 76.27; H, 10.33; N, 2.98.

Cholest-4-ene-3-one-6 $\beta$ -ol acetate oxime

A solution of cholest-4-ene-3-one-6 $\beta$ -ol acetate (1.0 g, 2.26 m mole) and hydroxylamine hydrochloride (0.47 g, 6.75 m mole) and pyridine (2 ml) in methanol (10 ml) was refluxed for 3 hours. The reaction mixture was worked up in the usual manner yielding a crude oxime (0.95 g, 95%) mp 143-159°. The product was recrystallized from methanol. An analytical sample had mp 159-162°;  $\lambda_{\max}$  (95% EtOH), 234.5  $\mu\text{m}$  ( $\epsilon$ 5,800); infrared (CHCl<sub>3</sub>), 2.78, 3.12, and 5.80  $\mu\text{m}$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 2.03 (O-Ac), 5.43 (H-C-OAc), 6.12 (olefinic H), and 10.7 (oxime H).

Anal. Calcd. for C<sub>29</sub>H<sub>49</sub>NO<sub>3</sub>: C, 76.10; H, 10.35; N, 3.06. Found: C, 76.31; H, 10.45; N, 3.16.

A diacetate was prepared with mp 135-137.5° which was identical in every respect with the diacetate from cholest-4-ene-3-one-6 $\beta$ -ol oxime.

Anal. Calcd. for C<sub>31</sub>H<sub>51</sub>NO<sub>4</sub>: C, 74.21; H, 10.25; N, 2.79. Found: C, 74.13; H, 9.94; N, 2.84.

Cholest-4-ene-3,6-dione-3-oxime

A solution of cholest-4-ene-3-one-6 $\beta$ -ol oxime mp 242-



248°d (0.285 g, 0.68 m mole) in pyridine (2 ml) was treated with an excess of chromium trioxide-pyridine complex and let stand overnight (60). The solution was poured into dilute hydrochloric acid (100 ml) and extracted with two portions of chloroform (50 ml). The organic layers were combined and extracted once with dilute hydrochloric acid (40 ml) and dried over magnesium sulfate. The solvent was evaporated yielding a dark brown mass which was taken up into ethyl acetate and filtered. The filtrate was treated five times with decolorizing carbon and the solvent evaporated. the crude material was three times recrystallized from methanol-ethyl acetate yielding white crystals mp 220-223°; mixed mp with photoproduct was 220-223°. The infrared spectra of both compounds are superimposable.

#### 6-Nitrocholesta-3,5-diene

A solution of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate (2.00 g, 4.0 m mole) in benzene (100 ml) was absorbed onto Woelm grade I neutral alumina (100 g) and let stand for 20 hours. The product was eluted with benzene yielding 6-nitrocholesta-3,5-diene as a yellow oil which was purified by chromatography on alumina. The yield was 1.31 g, 71%;  $\lambda_{\max}$  (95% EtOH), 221.5 m $\mu$  ( $\epsilon$ 1,600), 304 m $\mu$  ( $\epsilon$ 370); infrared (CHCl<sub>3</sub>), 6.13, 9.15, and 10.35 $\mu$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 6.01 and 6.52 (2 olefinic H). All attempts to crystallize this material

failed. However, mp 72-73° is reported (29).

Irradiation of 6-nitrocholesta-3,5-diene in acetone

A solution of 6-nitrocholesta-3,5-diene (0.27 g, 0.64 m mole) in acetone (200 ml) was irradiated under nitrogen with the 550 watt Hanovia mercury arc lamp as an external light source. A Pyrex filter was used during the 3.5 hour irradiation. The solvent was removed on the rotary evaporator and the solid material recrystallized from ethyl acetate yielding cholest-4-ene-3,6-dione-3-oxime (0.218 g, 81%) mp 220-223°. An Infrared spectrum was identical with that of a synthetic sample.

Irradiation of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate in acetone in the presence of oxygen

A solution of 6-nitrocholest-5-ene-3 $\beta$ -ol acetate (0.65 g, 1.37 m mole) in acetone (200 ml) in a Pyrex immersion well vessel was irradiated with a 550 watt Hanovia Type-A lamp for 2 hours. The solvent was removed under reduced pressure. The crude oil was chromatographed on a 3.0 x 25 cm silica gel column in Skelly-B. Fractions eluted with Skelly-B-Benzene 5:1 contained cholest-4-ene-6-one-3 $\beta$ -ol acetate (0.16 g, 26%). It was recrystallized from methanol; mp 108-112°. The infrared spectrum was identical with an authentic sample. Further fractions were combined and crystallized from methanol yielding crystals mp 160-182° (0.098 g, 15%). A further crystallization from methanol gave crystals

mp 161-179° which gave a single spot on thin layer chromatography. The crystals probably are 5 $\alpha$  and 5 $\beta$ -nitrocholestane-6-one-3 $\beta$ -ol acetate; infrared (CCl<sub>4</sub>), 5.69 (sharp), 5.74 (sharp), 6.55(w), 6.81, 7.00(w), 7.29, 7.43, 8.15, 9.35 $\mu$ ;  $\lambda_{\max}$  (95% EtOH), 244 m $\mu$  (shoulder,  $\epsilon$ 8,300). 360 m $\mu$  (tail  $\epsilon$ 370).

Anal. Calcd. for C<sub>29</sub>H<sub>47</sub>NO<sub>5</sub>: C, 71.13; H, 9.68; N, 2.86. Found: C, 71.46; H, 9.54; N, 3.00.

It was carefully determined that no 6-nitrocholest-4-ene-3 $\beta$ -ol acetate of cholest-4-ene-3,6-dione-3-oxime could be detected by thin layer chromatography, infrared analysis or by isolation from the above reaction mixture.

#### Irradiation of 6 $\beta$ -nitrocholest-4-ene-3 $\beta$ -ol acetate

A solution of 6 $\beta$ -nitrocholest-4-ene-3 $\beta$ -ol acetate (0.160 g, 0.33 m mole) in acetone (250 ml) was irradiated with a Hanovia 550 watt mercury arc lamp in a Pyrex immersion well vessel. A steady stream of oxygen was maintained during the irradiation (48 hours). The solvent was removed under reduced pressure yielding unreacted starting material (0.160 g) according to thin layer chromatography and infrared analysis.

#### Irradiation of 6-nitrocholesta 3,5-diene in the presence of oxygen

A solution of 6-nitrocholesta-3,5-diene (0.48 g, 1.16 m mole) in acetone (200 ml) was irradiated with light from a 550 watt Hanovia Type-A lamp in a Pyrex immersion well

vessel for 8 hours. A steady stream of oxygen was maintained during the irradiation. The solvent was removed under reduced pressure and the yellow oil chromatographed on silica gel in benzene. No well defined compound could be isolated though many were present by thin layer chromatography. No cholest-4-ene-3,6-dione-3-oxime could be detected by infrared analysis, thin layer chromatography, or isolation.

Attempted reaction of 6-nitrocholesta-3,5-diene with oxygen in the dark

A solution of 6-nitrocholesta-3,5-diene (0.400 g, 1.0 m mole) in hexane (50 ml) was subjected to a steady stream of oxygen for 2 days in the dark. The oil obtained on evaporation of the solvent was identical with starting material by thin layer chromatography and by infrared analysis.

Experimental for the Pyrolysis of  $\beta$ -Lactones

Erythro-3-bromo-2-methylbutanoic acid

Hydrogen bromide was added to tiglic acid by the established procedure (61). A slurry of tiglic acid (24.3 g, 0.243 mole) in 47% hydrobromic acid (200 ml) was saturated with hydrogen bromide gas at ice bath temperature. The mixture was let stand for 3 days at room temperature then resaturated with hydrogen bromide. After 12 days, the last crystal of tiglic acid dissolved. After 14 days, the erythro

adduct crystallized from solution. The aqueous solution was extracted twice with chloroform. The chloroform was then washed thoroughly with water and then with saturated salt solution. After drying over magnesium sulfate, the solvent was removed yielding a yellow crystalline solid which was readily recrystallized from hot Skelly-B as white crystals (19.86 g, 45%) mp 63.5-64.5<sup>o</sup>; lit. (61) mp 63-64<sup>o</sup>; nmr (CCl<sub>4</sub>),  $\delta$  1.34 (d, 3H), 1.75 (d, 3H), 2.67 (five lines, 1H), 4.42 (five lines, 1H).

Trans-3-hydroxy-2-methylbutanoic acid lactone

Trans-3-hydroxy-2-methylbutanoic acid lactone was prepared essentially by the described method (61). A suspension of erythro-3-bromo-2-methylbutanoic acid (4.00 g, 0.0222 mole) in water (8 ml) in a round bottom flask with magnetic stirrer was treated with most of a suspension of anhydrous sodium carbonate (2.35 g, 0.0223 mole) in water (5 ml). After the acid dissolved, there was a delay of a minute before the sodium salt precipitated. Chloroform (15 ml) was added and the solution rapidly stirred at a temperature less than 30<sup>o</sup>. After 2 hours, the chloroform was removed by first filtering the salts with suction then separating the chloroform layer in a separatory funnel. The chloroform was washed with dilute aqueous sodium bicarbonate and dried over magnesium sulfate. The original aqueous layer, fresh chloroform, and the filtered salts were returned to the

reaction flask where the process was repeated after 4 and after 9 hours. The chloroform was removed by distillation at 50°. The remaining colorless oil (0.57 g, 26%) was pure trans-3-hydroxy-2-methylbutanoic acid lactone; infrared (CHCl<sub>3</sub>), 5.50(s), 8.90(m), 9.84(w)μ; nmr (CHCl<sub>3</sub>), δ 1.36 (d, 3H, J-7.4), 1.54 (d, 3H, J-6.1), 3.22 (12 lines, 1H, J-4.0, 7.4), 4.35 (8 lines, 1H, J-4.0, 6.1).

#### Addition of hydrogen bromide to angelic acid

A literature preparation of the hydrogen bromide adduct with angelic acid was undertaken with different results (32). Angelic acid (2.65 g, 0.0265 mole) in chloroform (100 ml) was saturated with hydrogen bromide gas. After 9 days, nmr analysis showed the presence of adducts and unreacted tiglic acid. After a total of 11 days, the solvent was removed under reduced pressure yielding a yellow oil. This material was taken up into pentane and cooled over Dry Ice. A slightly yellow solid was separated by decanting the solvent. It was recrystallized from pentane at 0°. White crystals of erythro-3-bromo-2-methylbutanoic acid (2.84 g, 59%) mp 60-63° were obtained. A portion of the remaining non-crystalline reaction mixture (2.81 g) was extracted with 3 portions of sodium bicarbonate solution. The neutral fraction weighed 0.652 g. The acid fraction (1.539 g) contained erythro and threo adduct and was used below without further purification.

Cis and trans-3-hydroxy-2-methylbutanoic acid lactone

The mixture of erythro and threo-3-bromo-2-methylbutanoic acids (1.539 g, 0.0085 mole) prepared above was taken up into chloroform (4 ml) and treated with water (5 ml). Enough solid anhydrous sodium bicarbonate was added to make the solution basic to pH paper. After 2 hours and again after 4.5 hours, the chloroform was removed as before. The combined extracts were washed with dilute sodium bicarbonate solution, water, and dried over magnesium sulfate. The chloroform was removed under reduced pressure yielding a pungent smelling colorless liquid; infrared ( $\text{CHCl}_3$ ), 5.50, 6.90, 7.23, 7.36, 7.62, 7.80, 9.82  $\mu$  (all sharp); nmr ( $\text{CCl}_4$ ), for trans-lactone,  $\delta$ 1.35 (d), 1.53 (d), 3.17 (m), 4.28 (m); for cis lactone,  $\delta$ 1.23 (d, J-7.5), 1.43 (d, J-6.3), 3.69 (m, J-7.5), 4.70 (m, J-6.3). Trans lactone predominated slightly.

Addition of hydrogen bromide to tiglic and angelic acids

A solution of tiglic acid (8.7 g, 0.087 mole) in chloroform (300 ml) containing powdered anhydrous magnesium sulfate (3 g) was treated with hydrogen bromide gas at 12 hour intervals for 3 days and everyday thereafter for a total of 8 days. Nmr analysis revealed the slow formation of a mixture of adducts with erythro-3-bromo-2-methylbutanoic acid in considerable excess. A dibromo-adduct was also observed. Tiglic acid but not angelic acid could be

observed during the course of the reaction.

The same reaction was carried out with angelic acid (1.0 g, 10 m mole) in chloroform (300 ml). After 3 days, nmr analysis showed that all angelic acid had been converted to tiglic acid before much adduct had formed. After 10 days, the nmr spectrum of the reaction mixture was very similar to that above except that there was slightly less erythro hydrogen bromide adduct.

Low temperature reaction of hydrogen bromide with angelic acid

A solution of angelic acid (3.35 g, 0.34 mole) mp 41-42° in chloroform (80 ml) cooled in an ice bath, was saturated with hydrogen bromide gas. The flask was tightly stoppered and set in a refrigerator at -20°. After 2 days, nmr analysis showed that all angelic acid had been isomerized to tiglic acid. In addition there was a small amount of a dibromo-adduct with the expected methyl triplet and methine quartet (same J. value). After 6 days, erythro-3-bromo-2-methylbutanoic acid had begun to form.

Reaction of erythro-3-bromo-2-methylbutanoic acid with silver oxide (31)

To a solution of erythro-3-bromo-2-methylbutanoic acid (0.50 g, 2.8 m mole) and ground silica gel (0.25 g) in dry ether (25 ml) was added in small portion over a period of 2.5 hours, silver oxide (0.318 g, 1.88 m mole) prepared



by the method of Westfahl and Grèsham (62). The solution was rapidly stirred at 21° during the addition, then at room temperature for a total of 12 hours. Infrared analysis showed the absence of  $\beta$ -lactone. The silver salts were filtered and washed twice with ether. The filtrate was stripped of solvent leaving a mixture of 80% tiglic acid (0.208 g). The mixture was dissolved in hot pentane from which pure tiglic acid (0.142 g, 51%) mp 63-65° was obtained. An infrared spectrum was identical with an authentic sample.

#### Pyrolysis of trans-3-hydroxy-2-methylbutanoic acid lactone

In a capillary tube sealed at one end, was added trans-3-hydroxy-2-methylbutanoic acid lactone (10  $\mu$ l). The tube was frozen in Dry Ice and sealed before it was placed in an oil bath at 210° for 2 hours. At that time, all liquid had evaporated. The tube was cooled with Dry Ice then broken under a small quantity of carbon tetrachloride. The nmr and infrared spectra of the carbon tetrachloride solution showed only the presence of trans-2-butene by comparison with an authentic sample.

The pyrolysis was repeated with two tubes containing trans lactone (0.01925 g, 0.1923 m mole) at 210° for 3.5 hours. The tubes were broken with a magnetic stirring bar in a flask through which a continuous sweep of purified nitrogen was maintained. The carbon dioxide was collected in two interconnected tubes containing 0.1M barium hydroxide

solution. The precipitated barium carbonate was collected by filtration, washed with acetone and weighed. The calculated yield of carbon dioxide was 91.0%.

Pyrolysis of a mixture of cis and trans-3-hydroxy-2-methylbutanoic acid lactones

A mixture of cis and trans-3-hydroxy-2-methylbutanoic acid lactone (43±6% cis lactone by nmr analysis) was heated at 210° exactly as above except that the tubes were cooled with liquid nitrogen before analysis of the contents. The infrared spectrum showed only cis and trans-2-butene. These hydrocarbons were further analyzed by gas chromatography through a 12 ft silver nitrate-propylene glycol column. The flow rate was 22 ml/min of helium with a column temperature of 23°. The average areas of four runs corresponded to 46±5% cis-2-butene and 54±5% trans-2-butene.

In addition, the decomposition of the lactone mixture was carried out as above and the carbon dioxide collected. The yield was 87.1% in this case.

Experimental for the photochemistry of  
unsaturated acids, amides and anilides

Irradiation of tiglic acid

A solution of tiglic acid (5.0 g, 0.05 mole) mp 76.5-77.5° in anhydrous ethyl ether (425 ml) was irradiated with an internal water cooled mercury arc lamp (Hanovia

Type-A, 550 watt) with a quartz filter. The solution was purged with purified nitrogen for 15 minutes before irradiation. The solution was then irradiated for 4 hours and the solvent removed under reduced pressure. The reaction was repeated five times yielding a yellow oil (23.90 g). The oil was distilled under reduced pressure (20 mm) with fractions collected at 5° intervals from 45° to 75°. Infrared analysis (CCl<sub>4</sub> solution) revealed the presence of β-lactones at 5.45μ and 2-methyl-3-butenic acid at 5.87μ. The fraction bp 75-96° was 2-methyl-3-butenic acid (12.78 g, 51%). The lactone containing fractions were combined and diluted with ether. The ether solution was washed once with dilute sodium bicarbonate solution and once with saturated sodium chloride solution. The ether was dried over magnesium sulfate and evaporated under reduced pressure. The residue was redistilled at 20 mm pressure. The fraction boiling between 60 and 71° was diluted with carbon tetrachloride and carefully extracted with a very dilute solution of aqueous sodium bicarbonate. The carbon tetrachloride was dried over sodium sulfate and evaporated under reduced pressure yielding a mixture of lactones in approximately equal amounts (0.05 g, 0.2%); infrared (CCl<sub>4</sub>), 5.46μ; nmr (CCl<sub>4</sub>), for cis-3-hydroxy-2-methylbutanoic acid lactone, δ1.20 (d), 1.34 (d), 3.71 (m), 4.60 (m); for trans-3-hydroxy-2-methyl-butanoic acid lactone, δ1.28 (d), 1.44 (d), 3.07 (m), 4.17 (m).

The amide of 2-methyl-3-butenic acid above was prepared by the usual procedure. A sample was sublimed at 16 mm Hg and had mp 97-98°; lit. (63) mp 98°. The nmr and infrared spectra of the acid and amide were consistent with the assigned structure.

#### Irradiation of angelic acid

A solution of angelic acid (4.0 g, 0.04 mole) prepared by the method of House and Rasmusson (64) in anhydrous ether (425 ml) was irradiated in the same manner as tiglic acid. A total of 21 g, 0.21 mole was irradiated. The solvent was evaporated under reduced pressure yielding the crude product (23.71 g). The mixture was distilled at 13 mm Hg. The fraction bp 41-74° was distilled at 13 mm Hg after a single sodium bicarbonate extraction yielding a mixture of cis and trans lactones (0.04 g, 0.2%). The mixture was diluted with carbon tetrachloride and extracted with 1% aqueous sodium bicarbonate solution, but a trace of 2-methyl-3-butenic acid remained; infrared (CCl<sub>4</sub>), 5.46 and 5.85 $\mu$ ; nmr (CCl<sub>4</sub>), for cis-3-hydroxy-2-methylbutanoic acid lactone,  $\delta$ 1.22 (d), 1.41 (d), 3.66 (m), 4.66 (m); for trans-3-hydroxy-2-methylbutanoic acid lactone,  $\delta$ 1.36 (d), 1.53 (d), 3.15 (m), 4.24 (m).

A fraction bp 74-98° from the first distillation was 2-methyl-3-butenic acid (9.22 g, 44%). The infrared spectrum

was identical with that obtained from an authentic sample.

#### Irradiation of trans-crotonic acid

Recrystallized trans-crotonic acid (2.00 g, 0.023 mole) in ethyl ether (395 ml) was purged with a stream of nitrogen for 0.5 hour in a quartz immersion well apparatus. The solution was irradiated with a 550 watt mercury arc lamp (Hanovia Type-A) and the reaction followed by infrared analysis. After 2.5 hours, the carbonyl band shifted from 5.90 to 5.85 $\mu$ . The carbon-carbon double bond shifted from 6.04 to 6.10 $\mu$ . No carbonyl band for a  $\beta$ -lactone was evident at any time. The reaction mixture was separated into an acid fraction (1.54 g) and a neutral fraction (0.19 g) by extraction of the photolyzed solution with sodium bicarbonate solution. The acid fraction was distilled under reduced pressure yielding 3-butenic acid (1.19 g, 60%), bp 90° at 33 mm Hg. The reported (12) bp for 3-butenic acid is 73-74° at 16 mm Hg.

The amide of 3-butenic acid crystallized from hexane-benzene had mp 71-72°; lit. (65) mp 73°. The nmr and infrared spectra of the acid and amide were consistent with the assigned structure.

#### Irradiation of 3-methyl-2-butenic acid

Recrystallized 3-methyl-2-butenic acid (4.00 g, 0.040 mole) in anhydrous ether (410 ml) was irradiated in the

same manner as trans-crotonic acid. After 6 hours, the carbonyl band had shifted from 5.91 to 5.84 $\mu$ . No carbonyl band for a  $\beta$ -lactone was evident at any time. A neutral fraction (0.73 g) and an acid fraction (2.61 g) were obtained as before. Distillation gave 3-methyl-3-butenic acid (2.00 g, 50%) bp 104-106 $^{\circ}$  at 33 mm Hg; lit. (66) bp is 94-96 $^{\circ}$  at 24 mm Hg.

The amide of 3-methyl-3-butenic acid was crystallized from hexane-benzene with mp 118-119 $^{\circ}$ ; lit. (66) mp 120 $^{\circ}$ . The infrared and nmr spectra of the acid and amide were consistent with the desired structure.

#### Irradiation of methacrylic acid

A solution of methacrylic acid (5.0 g, 0.058 mole) in ether (410 ml) was irradiated in the same manner as trans-crotonic acid. After 15 hours, infrared analysis indicated the absence of starting material and  $\beta$ -lactones. A white polymer (0.91 g, 18%) with mp > 200 $^{\circ}$  was obtained by filtration of the irradiation mixture; infrared (KBr), 5.87, 6.85, 7.90, and 8.53 $\mu$ . Evaporation of the ether yielded a polymeric oil (4.27 g, 85%); infrared (CHCl<sub>3</sub>), broad bands at 5.87 and 6.90 $\mu$ .

#### Irradiation of 1-cyclopentenecarboxylic acid in tert-butyl alcohol

Sublimed 1-cyclopentenecarboxylic acid (1.30 g, 0.11

mole) mp  $121^{\circ}$ ; lit. (67) mp  $121^{\circ}$ , in tert-butyl alcohol (220 ml) was purged with nitrogen for 0.5 hours. The solution was irradiated in a quartz tube for a total of 36 hours with an external 200 watt medium pressure mercury arc lamp fixed at a distance of 6 inches. The solvent was removed under reduced pressure yielding a white solid (1.86 g). This was triturated with hot benzene and filtered yielding a crystalline powder (0.53 g, 41%). Recrystallization from 95% ethanol-tert-butyl alcohol yielded colorless crystals of 1-cyclopentenecarboxylic acid dimer mp  $337-8^{\circ}$  (sealed tube); infrared (KBr), 3.5 (broad), 5.93, 7.21, 7.76, 8.02, 8.30, and  $8.43\mu$  (all sharp). An analytical sample was dried at  $100^{\circ}$  for 2 hours.

Anal. Calcd. for  $C_{12}H_{16}O_4$ : C, 64.27; H, 7.19; mole wt, 224. Found: C, 64.15; H, 7.25; mole wt 224 (mass spec).

The benzene soluble fraction above contained several compounds which were not characterized.

Irradiation of tiglic acid in aqueous sodium hydroxide solution

Tiglic acid (2.00 g, 0.02 mole) in 0.4N aqueous sodium hydroxide solution (398 ml) was irradiated for 3 hours in the same manner as trans-crotonic acid. The solution was extracted with ether and found to contain no neutral material. The base was neutralized with hydrochloric acid and then thoroughly extracted with ether. The resulting acidic material

(0.402 g) was treated first with phosphorous pentachloride in benzene, then with anhydrous ammonia. The impure amide was obtained in the usual manner (0.402 g). It was recrystallized from hexane-benzene yielding 2-methyl-3-butenic acid amide (0.370 g, 18%) mp 95-97<sup>o</sup>; infrared (KBr), was identical with an authentic sample.

#### Irradiation of tiglic acid at 2537 Å

A solution of tiglic acid (0.086 g, 0.36 m mole) in anhydrous ether (0.214 g) in a quartz nmr tube under nitrogen was irradiated with 2537 Å light from a 50 watt germicidal lamp. The progress of the reaction was followed by nmr analysis. After 83 hours, the ether was evaporated yielding 2-methyl-3-butenic acid (0.084 g) greater than 95% pure by nmr analysis. The infrared spectrum showed only the pure acid without a trace of  $\beta$ -lactone.

#### Irradiation of tiglic acid in acetone

Tiglic acid (25.0 g, 0.25 mole) in acetone (400 ml) was irradiated in the same manner as trans-crotonic acid. The progress of the reaction was followed by nmr. After 4 days, the photostationary state had been obtained with 51.5% tiglic acid and 48.5% angelic acid by nmr. The solvent was removed under reduced pressure. The light yellow oil was distilled at 15 mm Hg, but a good separation was not obtained due to a fluctuating pressure. However, the



fraction containing the most angelic acid was crystallized from petroleum ether at  $-40^{\circ}$  yielding colorless crystals (3.96 g, 16%) mp  $35-45^{\circ}$ ; lit. (36) mp  $45-45.5^{\circ}$ . The infrared spectrum ( $\text{CCl}_4$ ) was identical with an authentic sample.

Irradiation of tiglic acid in the presence of benzophenone

A solution of tiglic acid (1.02 g, 0.01 mole) and benzophenone (1.82 g, 0.01 mole) in spectrograde cyclohexane (200 ml) was irradiated with an external 200 watt medium pressure mercury arc lamp in a water cooled Pyrex vessel for 44 hours. The solution had been purged with purified nitrogen. The reaction was followed by infrared and nmr analysis. White crystals of benzopinacol (0.84 g) mp  $177-9^{\circ}$  were removed by filtration. The solvent was removed under reduced pressure yielding a yellow-white mass of crystals (3.87 g). This material was separated into a neutral fraction and an acid fraction. Recrystallization of the neutral fraction afforded an additional amount of benzopinacol (0.43 g), mp  $177-9^{\circ}$  from benzene-cyclohexane. The total yield of benzopinacol was 68%. The infrared spectrum was identical with an authentic sample.

The acid fraction (2.35 g) appeared to be a mixture of diastereomeric adducts of cyclohexane with tiglic acid and was not characterized further. A small amount of angelic acid was discernible in the nmr spectrum, however.

Irradiation of 2-methyl-3-butenic acid in ether

A solution of 2-methyl-3-butenic acid (0.98 g, 9.8 m mole) in ethyl ether (220 ml) in a quartz immersion well vessel was irradiated in the same manner as trans-crotonic acid. Infrared analysis after 8 hours showed the absence of any carbonyl or carbon-carbon double bond. Nmr analysis of the reaction mixture indicated only the presence of polymers.

Irradiation of 2-methyl-3-butenic acid in toluene

A solution of 2-methyl-3-butenic acid (2.00 g, 0.02 mole) in toluene (50 ml) was purged with nitrogen for 0.5 hours in a quartz tube and then irradiated with 2537 Å light from a 50 watt germicidal lamp. Infrared and nmr analysis of the reaction mixture revealed only toluene and the unchanged acid. The mixture was extracted with dilute sodium hydroxide in the usual manner. 2-Methyl-3-butenic acid (1.919 g, 96%) was recovered.

Dark reactions

Tiglic acid (0.50 g, 5 m mole) in nitrogen purged ether (200 ml) was let stand in the dark for two days. Infrared analysis showed no carbonyl absorption for  $\beta$ -lactones, but only the presence of unreacted starting material. The solvent was removed under reduced pressure. The white solid had the same mp as tiglic acid (0.499 g, 100%).

The above reaction was repeated with angelic acid (0.50 g, 0.5 m mole). There was no reaction after 2 days. The recovered material (0.47 g, 94%) mp 38-42° had an identical infrared spectrum with angelic acid.

#### Irradiation of methacrylic acid amide

A solution of methacrylic acid amide (2.40 g, 0.028 mole), recrystallized from Skelly-B-benzene, in diethyl ether (130 ml) in a quartz vessel was irradiated with 2537 Å light from a Rayonet photochemical reactor for 4 days. A water soluble polymeric precipitate was collected (1.48 g, 67%) by filtration and washed with ether. It had mp > greater than 200°; infrared (KBr), broad bands at 2.97, 6.04, 6.25, 6.80 7.25 and 8.32 $\mu$ . The ether solution was evaporated yielding a white crystalline mass which was taken up into benzene, filtered, then diluted with hot Skelly-B. After cooling, two crops of crystals (0.71 g, 30%) were collected with mp 101-109°. The infrared spectrum was identical with that of the starting amide (KBr).

The reaction was repeated with methanol as the solvent (110 ml). Polymer (0.57 g, 23%) and starting material mp 110-111.5° (1.019 g, 48%) were recovered after 4 days irradiation.

#### Irradiation of tiglic acid amide

Tiglic acid amide (0.50 g, 5 m mole) prepared from

tiglic acid in the usual manner (68) [ $\lambda_{\text{max}}$  (cyclohexane), 199  $\text{m}\mu$  ( $\epsilon$ 13,100)], was dissolved in ether (425 ml). The solution was purged with nitrogen then irradiated in a quartz immersion well vessel with a 550 watt Hanovia Type-A lamp. After 5 hours, the carbon-carbon double bond intensity had decreased to one-third its original value. The amide bands at 5.95 and 6.31 $\mu$  were not affected. The irradiation was stopped after 8 hours. The solvent was evaporated under reduced pressure. The crude yellow oil (0.48 g) was taken up into pentane. White crystals (0.261 g, 52%) of 2-methyl-3-butenic acid amide were obtained which were recrystallized from hexane-benzene; mp 95-97 $^{\circ}$ ; lit. (63) mp 98 $^{\circ}$ . The infrared and nmr spectra were identical with those of an authentic sample.

Irradiation of trans-crotonic acid anilide in absence of acetic acid

A solution of trans-crotonic acid anilide (2.50 g, 0.155 mole) mp 115-6 $^{\circ}$  (69),  $\lambda_{\text{max}}$  (cyclohexane), 265  $\text{m}\mu$  ( $\epsilon$ 18,900), shoulder at 205  $\text{m}\mu$  ( $\epsilon$ 37,500), in nitrogen purged ether (400 ml) was irradiated with a 550 watt Hanovia Type-A lamp in a Pyrex immersion well vessel. The progress of the reaction was followed by TLC. Little change was apparent after 21 hours. The reaction mixture was separated into an acidic fraction (0.06 g, 2.4%) of photoanilide rearrangement products, and a neutral fraction (3.04 g). The neutral fraction was chromatographed on silical gel in benzene.

Fractions 1-7 (200 ml) eluted with benzene were cis-crotonic acid anilide (0.81 g, 32%). Recrystallization from hexane-acetone gave white crystals mp 100-102°; lit, (48) mp 102°;  $\lambda_{\text{max}}$  (cyclohexane), 265 m $\mu$  ( $\epsilon$ 12,400), shoulder at 205 m $\mu$  ( $\epsilon$ 25,700); nmr (CDCl<sub>3</sub>),  $\delta$ 2.11 (d, 3H), 5.84 (d, 1H) 6.15 (quartet, 1H), 6.9-7.7 (aromatic, 5H) and 8.0 (s, N-H).

Fractions 8-15 eluted with benzene-chloroform 1:1 were trans-crotonic acid anilide (1.13 g, 45%). Recrystallization from acetone-hexane afforded crystals mp 113-116°; mixed mp 113-116° and identical infrared spectrum with starting material. No significant fractions were subsequently eluted.

Irradiation of trans-crotonic acid anilide in the presence of acetic acid

A solution of trans-crotonic acid anilide (1.62 g, 0.01 mole) in ethyl ether (325 ml) containing acetic acid (1 g) in a Pyrex immersion well vessel was irradiated with a 550 watt mercury arc lamp (Hanovia Type-A). The progress of the reaction was followed by TLC. The reaction was filtered from a precipitate every 24 hours. After 5 days, the ether solution was extracted thoroughly with dilute aqueous sodium hydroxide, water, dilute hydrochloric acid and water. It was dried over magnesium sulfate and evaporated yielding a yellow oil (0.970 g). This material was chromatographed on silica gel in benzene. Fractions 3-5 (200 ml) eluted with benzene were a mixture of cis and trans-crotonic acid

anilides. Fractions 7-9 eluted with 25% chloroform in benzene contained 4-methyldihydrocarbestyryl (0.41 g, 25%) mp 92-101°. A sample was sublimed at 114° at 0.33 mm Hg yielding colorless prisms mp 100-102°; infrared (KBr), 6.10 and 6.30 $\mu$ ; nmr (CCl<sub>4</sub>),  $\delta$  1.31 (d, 3H), 2.37 (d, 1H), 2.53 (d, 1H), 3.0 (m, 1H), 10.4 (s, 1H). The reported melting point is 98° (49). The mass spectrum has intense ions at m/e 118, 128, 146, and 161(M<sup>+</sup>).

#### Irradiation of cis-crotonic acid anilide

A solution of cis-crotonic acid anilide (0.250 g, 1.50 m mole) in ether (50 ml) containing acetic acid (1 g) in a quartz tube, was purged with nitrogen for 0.5 hours. The solution was irradiated with the 50 watt 2537 Å lamp for a total time of 32 hours. The reaction progress was followed by thin layer chromatography. The yellow ether solution was extracted thoroughly with aqueous sodium hydroxide, water, dilute hydrochloric acid, water, and then dried over magnesium sulfate. The solution was decolorized with carbon. The solvent was removed under reduced pressure yielding yellow crystals (0.038 g, 15%). This compound was recrystallized from hexane-acetone yielding crystals (0.017 g) mp 99-101°. The infrared (KBr), was identical with starting material. A small amount of trans-crotonic acid anilide could be seen in the nmr spectrum of the reaction mixture

but it could not be characterized.

Irradiation of methacrylic acid  
anilide in the presence of acetic acid

A solution of methacrylic acid anilide (70) (1.05 g, 6.5 m mole) mp 84.5-85°,  $\lambda_{\text{max}}$  (cyclohexane), 260 m $\mu$  ( $\epsilon$ 9,600), shoulder at 205 m $\mu$  ( $\epsilon$ 21,800), in ethyl ether (325 ml) containing a small amount of acetic acid (1 g) was irradiated in a Pyrex immersion well vessel with a 550 watt mercury arc lamp. The reaction was followed by thin layer chromatography. After 9 hours, the solution was thoroughly extracted with dilute sodium hydroxide solution, water, dilute hydrochloric acid solution, then again with water. The ether was dried over magnesium sulfate and removed under reduced pressure yielding a yellow crystalline mass (1.007 g). This material was taken up into hot hexane and cooled. The hexane insoluble material was crystallized from hexane-acetone. Several crops of starting material were collected (0.410 g, 39%) mp 84-84.5°. The hexane soluble fraction was repeatedly crystallized from hot hexane. Colorless prisms mp 131° of 3-methyldihydrocarbostyryl (0.525 g, 50%) were obtained; infrared (KBr), 6.04 and 6.18 $\mu$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 1.26 (d, 3H), 2.7 (m, 3H), 9.7 (s, 1H). The mass spectrum had major ions at m/e 92, 118, and 161(M<sup>+</sup>). The reported (50) mp is 131°.

Irradiation of methacrylic acid anilide  
in the absence of acetic acid

A solution of methacrylic acid anilide (0.50 g, 3.1 m mole) in ethyl ether (50 ml) was irradiated with a 50 watt germicidal lamp in a quartz vessel and the reaction followed by thin layer chromatography. A photostationary state was reached after 23 hours. The reaction mixture was separated into an acidic fraction (0.051 g, 10%) of photoanilide rearrangement products and a neutral fraction (0.46 g). This fraction was recrystallized from hexane yielding starting methacrylic acid anilide (0.41 g, 82%) mp 82-85°. The infrared spectrum was found to be identical with that of starting material.

Irradiation of tiglic acid anilide  
in the absence of acetic acid

A solution of tiglic acid anilide (2.500 g, 0.25 mole) with  $\lambda_{\max}$  (cyclohexane), 257 m $\mu$  ( $\epsilon$ 11,500) and shoulder at 205 m $\mu$  ( $\epsilon$ 22,900) and mp 76.5-77.5° (71) in ethyl ether (425 ml) was irradiated with a 550 watt Hanovia Type-A lamp for 9 hours. A Pyrex immersion well vessel was used. An acidic fraction of photoanilide rearrangement products was separated (0.047 g, 1.9%). The neutral fraction (2.34 g) was chromatographed on silica gel in benzene. Fractions eluted with benzene, were combined (0.46 g, 19%) and recrystallized from ether-hexane yielding white crystals of angelic



anilide mp 126-128<sup>o</sup>;  $\lambda_{\max}$  (cyclohexane), 249.5  $\mu\mu$  ( $\epsilon$ 12,000), shoulder at 200  $\mu\mu$  ( $\epsilon$ 23,600). The reported melting point is 126<sup>o</sup> (71). The infrared spectrum was identical with that of an authentic sample.

Fractions eluted with benzene-cholorform 75:25, were a mixture of diastereomers of 3,4-dimethyldihydrocarbostyryl (1.34 g, 54%). A sample was sublimed at 115<sup>o</sup> at 0.03 mm Hg yielding white crystals mp 116.5-117.5<sup>o</sup>; infrared (KBr), 6.10 and 6.29 $\mu$ ; nmr (CDCl<sub>3</sub>),  $\delta$ 1.09 (d, 3H), 1.21 (d, 3H), 2.8 (m, 2H), 7.0 (m, 4H), 10.5 (s, 1H);  $\lambda_{\max}$  (cyclohexane), 247  $\mu\mu$  ( $\epsilon$ 13,400), 201.5  $\mu\mu$  ( $\epsilon$ 39,500). The mass spectrum showed major ions at m/e 132, 160, and 175(M<sup>r</sup>). An authentic sample was prepared (47) mp 116.5-117.5<sup>o</sup>, with identical infrared spectrum with the photoproduct.

Irradiation of tiglic acid anilide  
in the presence of acetic acid

A solution of tiglic acid anilide (1.057 g, 0.01057 mole) in ethyl ether (425 ml) containing acetic acid (1 ml) was irradiated for 6 hours in exactly the same manner as in the absence of acetic acid. The neutral portion of the reaction mixture (0.921 g) was triturated with hexane. The hexane insoluble portion was recrystallized from acetone-hexane yielding angelic acid anilide (0.168 g, 16%) mp 126-128<sup>o</sup>. The infrared spectrum was identical with that of an authentic sample. The hexane soluble fraction was

recrystallized from hexane..Several crops were collected (0.614 g, 58%) of 3,4-dimethyldihydrocarbostyryl. A sample sublimed at 120° at 0.13 mm Hg had mp 116.5-117.5° and an identical infrared spectrum with an authentic sample.

#### Irradiation of N-deuterotiglic acid anilide

N-Deuterotiglic acid anilide was prepared by shaking a solution of tiglic acid anilide in chloroform with deuterium oxide for 24 hours (95% N-deuterated by nmr).

A solution of N-deuterotiglic acid anilide (1.20 g, 0.012 mole) in ethyl ether (150 ml) in an internally cooled Pyrex vessel was irradiated externally with a 200 watt medium pressure mercury arc lamp for 40 hours. The reaction mixture was worked up in the same manner as before. All N-deuterium was therefore washed out. The isolated angelic acid anilide, mp 129-130° from acetone-hexane, did not contain any deuterium as expected by nmr and analysis of the mass spectrum. The mass spectrum had intense ions at m/e 55, 83, 93, and 175(M<sup>+</sup>).

The 3,4-dimethyldihydrocarbostyryl fraction was not sublimed, but repeatedly recrystallized from Skelly-B; mp 118-120° was obtained. Nmr analysis revealed the incorporation of 14% deuterium in the 3 or 4 position. The mass spectrum showed 15% d<sub>1</sub>, or 15% deuterium in the 3 or 4 position. The deuterium is entirely in the 3 position since it

was washed out by sodium methoxide catalysed exchange with methanol (nmr).

Irradiation of tiglic acid 2,4,6-trideuteroanilide

2,4,6-Trideuteroaniline was prepared by the method of Ronayne et. al. (72) with 93% deuteration at the ortho position (nmr). The mass spectrum had 1.1%  $d_0$ , 2.3%  $d_1$ , 14.2%  $d_2$ , 82.5%  $d_3$ , or a total of 92.8% deuterium in each ortho position.

A solution of tiglic acid 2,4,6-trideuteroanilide (1.600 g, 0.016 mole) mp 77-78<sup>o</sup> (from cyclohexane) in ethyl ether (325 ml) was irradiated with the 550 watt mercury vapor lamp (Hanovia Type-A) in a water cooled Pyrex immersion well vessel. After an 8.5 hour irradiation period, the solvent was removed under reduced pressure yielding a yellow oil (1.74 g). The oil was triturated with hot Skelly-B. The insoluble portion was decolorized with carbon in ether. The ether was evaporated yielding angelic acid 2,4,6-trideuteroanilide (0.390 g, 24%). Two recrystallizations from acetone-hexane raised the melting point to 128<sup>o</sup>. Nmr and mass spectrometry showed absolutely no migration of deuterium had occurred during the cis, trans isomerization.

The Skelly-B soluble fraction was recrystallized several times from pentane-ether yielding off white crystals mp 115-117<sup>o</sup> of the deuterated 3,4-dimethyldihydrocarbostyryl (1.120 g, 70%). Nmr analysis showed 52% deuteration of the

3 or 4 position. The mass spectra had 1.4%  $d_0$ , 7.3%  $d_1$ , 53.7%  $d_2$ , and 37.6%  $d_3$ . The difference between the per cent  $d_3$  in the starting anilide and the per cent  $d_3$  in the 3,4-dimethyldihydrocarbostyryl normalized to 100% indicates the maximum loss of 54.5% deuterium during the reaction; or 45.5% of the migrating deuterium must remain in the 3 position. Base catalysed exchange showed that all deuterium must be in the 3 position and not in the 4 position.

#### Irradiation of trans-cinnamic acid anilide

A solution of trans-cinnamic acid anilide (2.00 g, 9 m mole) mp 150.5-152.5° (73) with  $\lambda_{\max}$  (cyclohexane), 284 m $\mu$  ( $\epsilon$ 29,700), 219 m $\mu$  ( $\epsilon$  32,600), in ethyl ether (425 ml), was irradiated with a 550 watt Hanovia Type-A lamp for 7 hours. Nmr analysis showed only the presence of cis-cinnamic acid anilide. After 2 days, only a small amount of photo-anilide rearrangement products were formed in addition. A Pyrex immersion well was used.

After 7 hours irradiation, the ether solvent was removed and the yellow oil triturated with hot cyclohexane. The cyclohexane was removed under reduced pressure yielding crystals of cis-cinnamic acid anilide (0.81 g, 41%). Two recrystallizations from cyclohexane gave white needles mp 98-99°; infrared (KBr), 2.95(w), 6.07, 6.16, 6.67, and 6.95 $\mu$ ;  $\lambda_{\max}$  (cyclohexane), 228 m $\mu$  ( $\epsilon$ 16,800), shoulder at 266 m $\mu$  ( $\epsilon$ 10,100); nmr (CDCl<sub>3</sub>),  $\delta$ 6.02 (d, 1H), 6.82 (d, 1H), 7.3

(aromatic 10 H plus N-H).

Anal. Calcd. for  $C_{15}H_{13}NO$ : C, 80.69; H, 5.87; N, 6.27. Found: C, 80.68; H, 5.78; N, 6.26.

If the above irradiation was carried out in the presence of acetic acid (1 g) for a period of 8 days, only cis-cinnamic acid anilide and polymer are formed (nmr, TLC).

#### Irradiation of $\alpha$ -phenylacrylic acid anilide

A solution of  $\alpha$ -phenylacrylic acid anilide (74) (2.80 g, 0.0125 mole) with  $\lambda_{max}$  (cyclohexane), 256  $m\mu$  ( $\epsilon$  11,100) and shoulder at 230  $m\mu$  ( $\epsilon$  12,800) and acetic acid (1.5 g) in ethyl ether (425 ml) was irradiated with a 550 watt mercury arc lamp (Hanovia Type-A) in a quartz immersion well vessel. The reaction progress was followed by TLC. After 24 hours, the quartz well was cleaned of polymer. After 48 hours, the reaction mixture was thoroughly washed with aqueous sodium hydroxide, water, dilute hydrochloric acid (recovered acidic material; 0.06 g, 2%) and again with water. The ether was dried after decolorization with carbon. The ether was removed yielding a yellow solid (1.28 g). Two recrystallizations from carbon tetrachloride gave yellow crystals mp 134-135<sup>o</sup> (0.55 g, 20%) identical with starting material by TLC and infrared spectrum comparison. According to TLC, the mother liquors contained more  $\alpha$ -phenylacrylic acid and 3 compounds. One may be a hydrocarbostyryl derivative.

3-Deutero-4-hydro-3,4-dimethylcarbostyryl

A solution of 3,4-dimethyldihydrocarbostyryl (0.150 g, 0.85 m mole) in deuterioethanol (25 ml) containing sodium (0.075 g) was placed on the steam bath in a stoppered flask for 4 hours. At that time, the mixture was poured into water (150 ml) and thoroughly extracted with chloroform. The chloroform extracts were combined and washed with dilute hydrochloric acid and water. The organic solvent was dried over magnesium sulfate then decolorized with carbon. The solvent was evaporated and the crystalline material obtained was twice sublimed at  $115^{\circ}$  and 0.13 mm Hg yielding colorless crystals homogeneous on thin layer chromatography and with mp  $105-110^{\circ}$ . A mixture of the diastereomers was obtained. Nmr analysis showed 85% incorporation of deuterium in the 3 position. The mass spectrum had 91.1%  $d_1$  and intense ions at m/e 133, 161, and  $176(M^+)$ .

Irradiation of 3-deutero-4-hydro-3,4-dimethylcarbostyryl

A solution of 3-deutero-4-hydro-3,4-dimethylcarbostyryl (0.0833 g) in ether (0.5338 g) in a quartz nmr tube was irradiated with 2537 Å light from a 50 watt germicidal lamp for 8 hours. The ether was removed first with a stream of nitrogen, then in a drying pistol. The recovered starting material (0.0825 g, 99%) mp  $104-110^{\circ}$  had 86% deuterium in the 3 position and no deuterium on the nitrogen atom.

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