Photochemistry of β-Iodoacrylamides

R. Marshall Wilson* and Thomas J. Commons

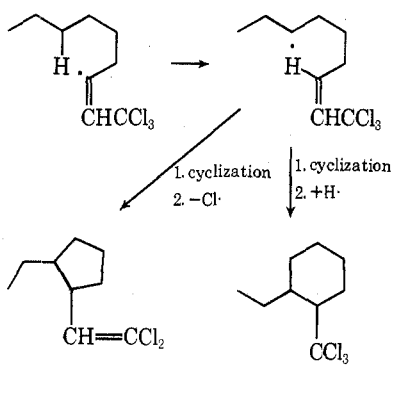
Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221

Received February 13, 1975

The irradiation of *N*-alkyl-β-iodoacrylamides at 253.7 nm affords the dealkylated acrylamides. In the case of amides derived from acyclic amines such as *N,N*-dibutyl-*cis*-β-iodoacrylamide (**3**) two fragments are found, the dealkylated amide, *N*-butylacrylamide (**4**), and a carbonyl compound, butanal. The β-iodoacrylamides of cyclic amines yield ring-cleaved ketoacrylamides which may be recyclized under anhydrous acidic conditions to yield novel acrylyl enamides; thus *N*-(*trans*-β-iodoacrylyl)-2,6-dimethylpiperidine (**5**) is photolytically cleaved to form 6-acrylamidoheptan-2-one (**6**), which may be recyclized with *p*-toluenesulfonic acid to *N*-acrylyl-2,6-dimethyl-Δ^2-piperideine (**8**). The unsymmetrical amine (±)-sedridine (**13**) forms a much more complex mixture of products upon irradiation of the *cis*-β-iodoacrylamide derivative in methanol. Cleavage of the more highly substituted carbon–nitrogen ring bond leads to formation of 8-acrylamido-2-octen-4-one (**16**) and 8-acrylamido-2-methoxyoctan-4-one (**15**). In sharp contrast, oxidation of the less highly substituted carbon–nitrogen ring bond does not lead to ring cleavage, but instead affords the unusually stable acrylenamide **17**. These reactions are thought to proceed through vinyl radicals which readily abstract hydrogen atoms situated α to the amide nitrogen atom. The resulting α amido radicals proceed to labile intermediates which are subsequently hydrolyzed to the products. This overall process provides a novel means of selectively degrading secondary amines as well as ready access to unusual enamide derivatives.

In view of the extensive examination of aryl halide photochemistry,[1] it is surprising that very little is known about the related photochemistry of vinyl halides. It does appear that the primary photochemical reaction of vinyl iodides is the homolytic cleavage of the carbon–iodine bond to form vinyl radicals,[2] and that once formed these vinyl radicals are powerful hydrogen abstracting species.[2,3] Of particular interest are several reported examples in which thermally generated vinyl radicals have been observed to undergo intramolecular hydrogen abstraction reactions (Scheme I) followed by ring formation in limited yields.[3b,4]

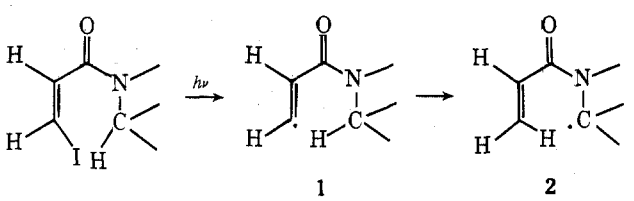
Scheme I



One might expect vinyl radicals to be particularly well suited for hydrogen abstraction reactions by virtue of the sp^2 hybridization of the unpaired electron. In this configuration the unpaired electron would be more electrophilic than either an sp^3 or p hybridized species, and the abstraction of a hydrogen atom from either an sp^3 methylene or methinyl group should be an exothermic process by about 10–15 kcal/mol.[5] Therefore, it would seem that in appropriately designed molecules intramolecular vinyl radical hydrogen abstraction might become the dominant mode of reaction.

The acrylamido vinyl radical (**1**) illustrated in Scheme II would seem to provide such a system. Therefore, we have investigated the photochemistry of β-iodoacrylamides in order to determine the ultimate fate of the vinyl radicals in this system, and to explore the synthetic possibilities of this method of remote functionalization which at least in a general sense is very reminiscent of the synthetically most useful Hofmann–Löffler–Fretag[6] and Barton reactions.[7]

Scheme II

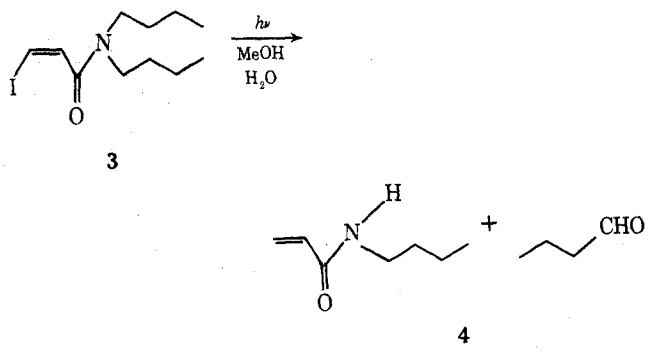


Results and Discussion

In the following examples the starting β-iodoacrylamides were formed from the appropriate amine and either *cis*- or *trans*-β-iodoacrylyl chloride. These acrylyl chlorides were prepared by treatment of propiolic acid with 47% hydrogen iodide[8] followed by generation of the acid chloride with oxalyl chloride. The cis isomer is the exclusive product obtained when the acid chloride is prepared at room temperature. However, the cis isomer is isomerized to the trans isomer when exposed to traces of iodine. When *cis*-β-iodoacrylyl chloride is heated, iodine is released and isomerization occurs to the extent that after heating for 27 hr at 80° the trans:cis ratio is 92:8. This isomerization provides a facile preparation of the *trans*-β-iodoacrylyl chloride. Since the photochemistry of the acrylamides does not seem to be influenced by the stereochemistry of the β-iodoacrylamide moiety (vide infra), the decision as to which acid chloride isomer to use in the synthesis of a particular amide was based entirely upon the ease of preparation and characterization of that amide.

The simplest system studied was *N,N*-dibutyl-*cis*-β-iodoacrylamide (**3**). Irradiation of this material at 253.7 nm in methanol solution led to a surprisingly clean reaction in which the only products were *N*-butylacrylamide (**4**), 65% yield, and butanal, which was isolated as its 2,4-DNP derivative, 62% yield (Scheme III). The structures of these products are in accord with what might be expected from the general mechanistic considerations outlined in Scheme II. The vinyl iodide moiety has been reduced while at the same time the amine moiety has been oxidized. In this particular example the exact nature of the oxidized amine moiety could not be determined as any intermediates are apparently very labile with respect to hydrolysis to the ob-

Scheme III



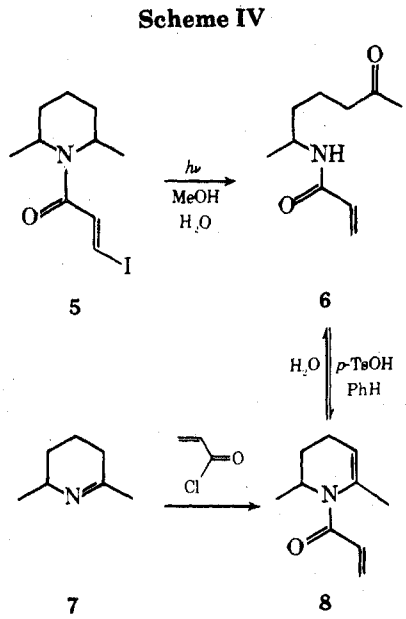
3 4

served products. The source of the water involved in this and subsequent hydrolyses may be the solvent, as no special precautions were taken to dry the methanol. Alternatively, it was observed that thin layer chromatographic analyses of these crude reaction mixtures were frequently complicated by the presence of significant amounts of iodine. Upon removal of the iodine by extraction with aqueous thiosulfate, one could obtain thin layer chromatograms that exhibited well-defined hydrolysis product spots. Therefore, it may be that the hydrolysis also is occurring during the aqueous extraction steps frequently employed in the isolation of the products.

N-(*trans*-β-Iodoacrylyl)-2,6-dimethylpiperidine (**5**) was examined rather than the *cis*-β-iodoacryl isomer, since the cis isomer could only be prepared in low yields. The difficulty in forming the cis isomer can probably be attributed to the steric congestion between the cis iodo group and the two ring methyl groups. When **5** was irradiated with 253.7-nm light, isomerization of the trans to the cis isomer could be observed during the early stages of the reaction. Upon completion of the reaction a single product **6** was obtained in 77% yield.

The structure of **6** was confirmed both spectroscopically: [O=CNH- ν_{max} (KBr) 3235, 1655 (s), and 1625 cm^{-1} (s); O=CCH$_3$ ν_{max} (KBr) 1705 cm^{-1}; δ ($CDCl_3$) singlet 2.13 ppm (3 H); CH_2=CHC=O δ ($CDCl_3$) doublet of doublets (J = 4 and 8 Hz) 5.64 ppm (1 H), doublet (J = 8 Hz) 6.18 (1 H), doublet (J = 4 Hz) 6.21 (1 H)] and by comparison with material prepared by an alternate route (Scheme IV). Acylation[9] of Δ^1-piperideine (**7**)[10] with acrylyl chloride afforded the enamide **8** [>NC(CH$_3$)=CH- δ ($CDCl_3$) singlet 2.02 ppm (3 H), broad 4.97 (1 H); CH_2=CHC=O δ ($CDCl_3$) doublet of doublets (J = 4 and 8 Hz) 5.56 ppm (1 H), complex 6.0–6.5 (2 H)] which was extremely sensitive to moisture and hydrolyzed to **6** upon standing overnight in solution exposed to the atmosphere. The reverse reaction from **6** to **8** could be readily effected by simply heating **6** in benzene solution containing *p*-toluenesulfonic acid. The possibility that **8** might be an intermediate in the photochemical formation of **6** was considered. However, here again, perhaps owing to the presence of iodine and the extreme sensitivity of **8** to moisture, **8** could not be observed in the crude photolysis mixture.

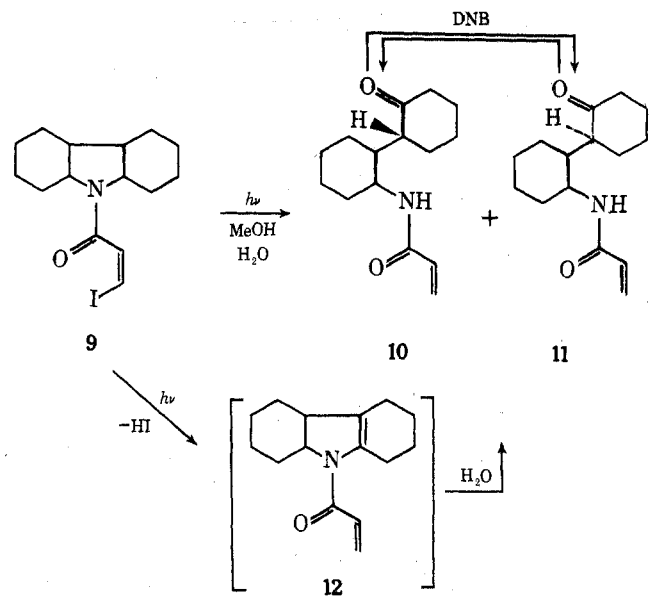
Scheme IV



5 6 7 8

The photolysis of *N*-(*cis*-β-iodoacrylyl)decahydrocarbazole (**9**) was complicated by the formation of epimeric products **10** (26% yield) and **11** (12% yield) (Scheme V).

Scheme V



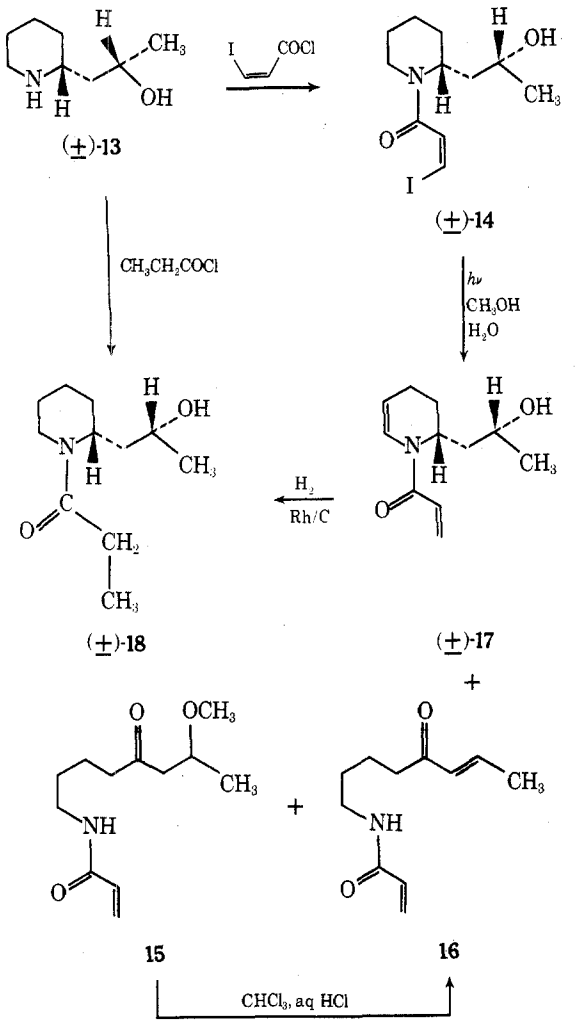
9 10 11 12

The stereochemistry of these substances is uncertain, but their epimeric relationship to each other was established by their interconversion upon treatment with the base 1,5-diazabicyclo[3.4.0]nonene-5 (DBN). Here again the possibility exists that these epimers arise from the hydrolysis of the enamide **12**. However, it is also possible that epimerization occurs following the generation of the ketones **10** and **11**. Whatever the case may be, it is clear that epimeric products should be anticipated in this reaction when the carbon atom β to the amide nitrogen in the starting material is an asymmetric center.

The unsymmetrically substituted amine (±)-sedridine (**13**) was prepared by a modification of known procedures (see Experimental Section),[11] and its *cis*-β-iodoacrylamide **14** photolyzed.[12] A complex reaction mixture resulted (Scheme VI) which after extensive chromatography afforded the ring-cleaved ketones **15** (21%) and **16** (5%) and the enamide **17** (25%).[13]

The structures of the ketones **15** and **16** were assigned on the basis of spectroscopic data [for **15** -CH_2C(=O)CH_2-$CH(OCH_3)CH_3$ ν_{max} (neat) 1705 cm^{-1}, δ ($CDCl_3$) doublet (J = 6 Hz) 1.17 ppm (3 H), complex 2.33–2.77 (4 H), singlet 3.33 (3 H), and triplet of quartets (J = 6 and 6 Hz) 3.82 (1 H); CH_2=CHC(=O)NH- ν_{max} (neat) 3260, 1655 (s), and 1625 cm^{-1} (s), δ ($CDCl_3$) doublet of doublets (J = 6 and 6 Hz) 5.60 ppm (1 H), two doublets (J = 6 and 6 Hz) both at 6.27 (1 H each); for **16** -CH_2C(=O)CH=$CHCH_3$ ν_{max} (KBr) 1690 cm^{-1}, δ ($CDCl_3$) doublet of doublets (J = 6 and 2 Hz) 1.90 ppm (3 H), broad triplet 2.60 (2 H), doublet of

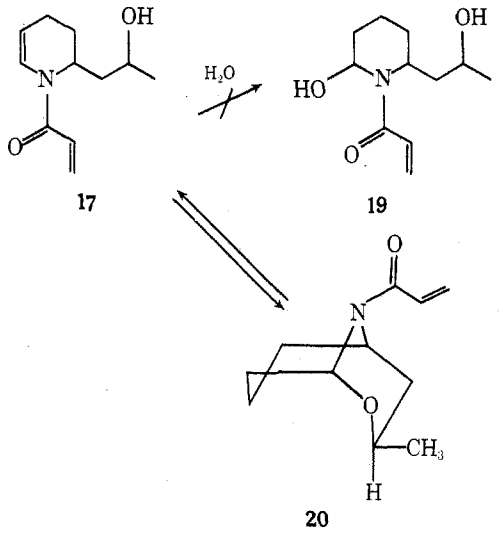
Scheme VI



quartets (J = 6 and 16 Hz) 6.85 (1 H); CH_2=CHC(=O)NH- ν_{max} (KBr) 3230, 1650 (s), and 1625 (s) cm^{-1}, δ ($CDCl_3$) doublet of doublets (J = 8 and 4 Hz) 5.57 ppm (1 H), complex 5.90–6.50 (4 H) includes the α proton of the α,β-unsaturated ketone moiety, m/e 195 (M^+)] as well as the conversion of **15** to **16** upon treatment with aqueous acid (Scheme VI). The assignment of structure to the enamide **17** presented a greater problem, since this material was inert to acidic hydrolysis conditions that would normally be expected to cleave an enamide linkage. The presence of an enamide system in **17** was most conspicuous in the ultraviolet absorption spectrum, λ_{max} (EtOH) 278 nm (ε 1340). The unrearranged carbon skeleton of **17** was demonstrated by catalytic hydrogenation to form a single amide **18** which could also be prepared by treatment of (±)-sedridine (**13**) with propionyl chloride. Furthermore, the observation of only the sedridine-derived amide **18** upon catalytic hydrogenation strongly suggested that the formation of the enamide system had not altered the asymmetric ring carbon atom present in the starting material. The structure **17** was also in accord with the rather complex NMR spectrum, which displayed signals at δ 4.6 ppm broad singlet (-OH), 5.2–4.6 multiplet (-NCH- and -CH=CHN<), 5.83 doublet of doublets (J = 9.0 and 4.0 Hz, >NCOCH=CH_2), 7.3–6.2 multiplet (>NCOCH=CH_2 and -CH=CHN<).

A possible explanation for the failure of enamide **17** to undergo hydrolytic ring cleavage is provided in Scheme VII. The usual hydrolysis of enamide systems requires the addition of water to the enamide carbon–carbon double

Scheme VII

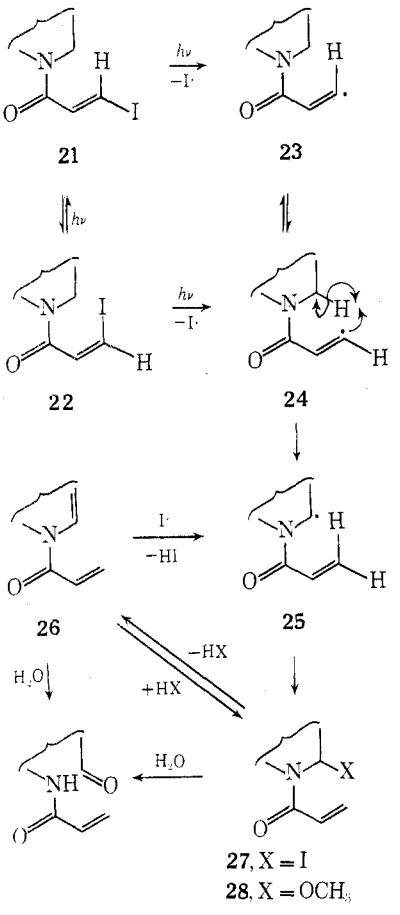


bond (**19**). This type of addition of an external nucleophile might be blocked in **17** by the more facile internal addition of the alcohol moiety to afford **20**. In support of this hypothesis it has been possible in large-scale reactions to isolate small quantities of an unstable oil which upon standing is rapidly transformed into **17**. While it was very difficult to obtain this substance free of contamination by **17**, it was possible to obtain simple spectroscopic data which were in accord with the proposed structure **20**. The infrared spectrum of the unstable material did not display significant absorption in the 3500-cm^{-1} region. In the NMR spectrum the signals associated with the vinyl protons remained unchanged relative to those in the spectrum of **17**. A new one-proton signal appears at δ 5.6 ppm which might be assigned to the -OCHNCO- proton of **20**, and two signals appear as a complex pattern between δ 5.1 and 4.2 ppm which might be attributed to the >CCHNCO- and the >CHO- protons of **20**. Finally, the signals assigned to the -OH and the -CH=CHNCO- protons in the spectrum of **17** are absent in the spectrum of the unstable substance.

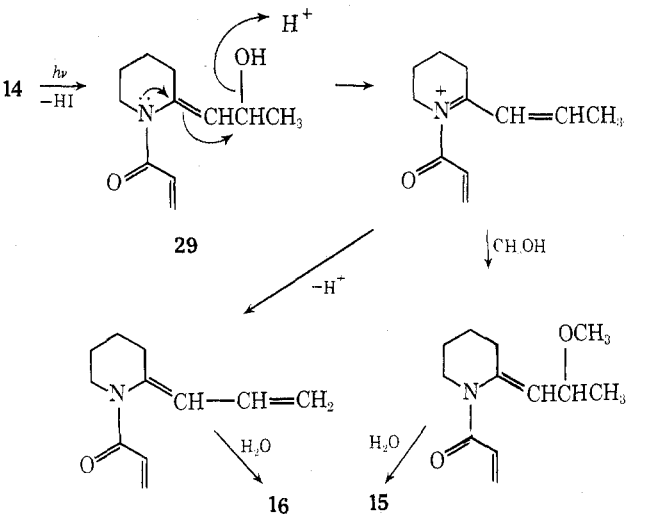
From these data, it must be concluded that the photodegradation of unsymmetrical amines by this method results in the oxidation of either methinyl or methylene groups α to the nitrogen atom. It is of interest to compare the relative reactivities of the methinyl and the methylene hydrogens in **14** with the relative reactivities of the same type of hydrogens in intermolecular vinyl radical hydrogen abstraction reactions. Since abstraction of the methinyl ring hydrogen atom in **14** ultimately gives rise to ring-cleavage products **15** and **16**, and abstraction of a methylene ring hydrogen atom gives rise to the enamide **17**, the relative reactivities of methinyl vs. methylene hydrogens observed here would be (**15** + **16**:**17**/2) 2.1:1. This value compares very well with the relative reactivities determined from intermolecular vinyl radical hydrogen abstractions, 2.2:1.[3a]

On the basis of the examples described above it would seem possible to draw the following conclusions regarding the mechanism of this novel remote functionalization of β-iodoacrylamides. In each of these cases the primary photochemical event is certainly the homolytic cleavage of the carbon–iodine bond (Scheme VIII). In order for the resulting vinyl radical to abstract one of the hydrogen atoms α to the amide nitrogen atom, the radical must assume a cis stereochemistry with respect to the amide carbonyl (**24**). As indicated previously, this reaction does not seem to be influenced by the geometry of the iodine atom in the starting material. Both the trans (**21**) and the cis (**22**) isomers ex-

Scheme VIII



Scheme IX



hibit the same photochemistry. This is at least in part due to the rapid equilibration of these isomers during the early stages of the irradiation. Cis–trans interconversion was easily observed by thin layer chromatography in each case, and in the case of **5** both cis and trans isomers have been recovered from partially photolyzed reaction mixtures. Furthermore, if the trans β-iodoamide **21** undergoes photolytic cleavage to the vinyl radical with the improper geometry (**23**), α hydrogen abstraction could still take place through a rapid prior inversion to the vinyl radical of the appropriate geometry (**24**).[14]

The course of the reaction following the formation of the α amido radical **25** is not entirely clear. There is considerable evidence that an enamide intermediate (**26**) is involved. Such an intermediate would normally not be isolable under the irradiation conditions where moist methanol was used as a solvent. Under these conditions the enamide **8** was rapidly hydrolyzed to the keto amide **6.** However, the unusual enamide **17** could be isolated owing to its stability toward hydrolysis. Further indirect evidence for an enamide intermediate was observed with amide **9,** which was substituted at the carbon atom β to the nitrogen. Epimerization at the β carbon accompanied dealkylation of **9** as would be expected if the dealkylation occurred through the hydrolysis of the enamide **12.** Also the ring-cleaved products **15** and **16** afforded by the sedridine amide **14** indicated the intermediacy of enamide **29** (Scheme IX). In neither **15** nor **16** was the hydroxyl group retained. This hydroxyl group would be expected to be labilized by the formation of enamide **29,** and should undergo a facile exchange with methanol in the presence of HI. The dehydration of **29** might account for the formation of **16,** although **16** might also arise following ring cleavage to **15** through the loss of methanol.

It is interesting that in no instance were the 1,3-acyl migration products,[15] which are characteristic of enamide photochemistry, observed. This may be due to the rapid reactions of the enamides with the hydroxylic solvents, methanol and water. Indeed, reactions conducted in hydrocarbon solvents led to polymeric mixtures from which no discrete products could be isolated. As implied in Scheme IX, methanol might very well react with protonated enamides to mask the enamide as an α amido ether **28** (Scheme VIII). Alternatively, an α amido iodide **27** might intervene and undergo exchange with methanol to form **28.** Any of these rather complex sequences of events outlined in Scheme VIII would serve to reduce the enamide concentration to the point where the enamide was effectively masked against further photochemical reaction, but not against the intramolecular processes mentioned in Scheme IX.

In conclusion it appears that the mechanism of this reaction is fairly well defined up to the point where the α amido radical **25** is formed. From **25** a variety of alternative pathways are possible. However, most of these pathways lead to products which would be sensitive to hydrolysis, and upon hydrolysis would converge to a greatly simplified set of products. Therefore, while further investigation of the chemistry of species related to **25** may lead to the development of other useful reactions such as cyclizations analogous to those illustrated in Scheme I, the present work has clearly outlined the scope of the hydrolytic pathway.

Summary

A new photochemical degradation of secondary amines has been developed which provides entry to unusual acrylamide derivatives and acrylylenamides. Good yields of a single acrylamide may be realized from the β-iodoacrylamides of symmetrically substituted amines, although there is a tendency for alkyl groups β to the amide nitrogen to suffer epimerization during the course of the reaction. Amides of unsymmetrically substituted amines give rise to mixtures of products which are derived from the oxidation of either of the *N*-alkyl groups. This unusual process represents the first deliberate application of sp_2 hybridized vinyl radicals in intramolecular hydrogen abstraction reactions and gives some indication of the promise of vinyl iodide photochemistry.

Experimental Section

Melting points and boiling points are uncorrected; melting points were determined on a Mettler FP-2 hot-stage apparatus with a polarizing microscope. Nuclear magnetic resonance spectra

were recorded with a Varian Associates A-60 or T-60 spectrometer. Chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as an internal standard. Infrared spectra were recorded on a Perkin-Elmer Model 337 or 700 spectrophotometer. Ultraviolet spectra were determined on a Carey Model 14 spectrophotometer. Mass spectra were recorded on a Hitachi RMU 7 spectrometer at 70 eV. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Thick layer chromatography was performed with Brinkmann silica gel $PF_{254+366}$ and column chromatography with Brinkmann silica gel (less than 0.08 mm). All organic extracts were dried over anhydrous magnesium sulfate and all solvents were removed with a rotary evaporator under reduced pressure unless noted otherwise.

Synthesis of *cis*- and *trans*-β-Iodoacrylyl Chloride. Oxalyl chloride (29.0 ml, 0.340 mol) was added dropwise with stirring at room temperature to 24.94 g (0.126 mol) of *cis*-β-iodoacrylic acid, mp 65.1–67.0° (lit.[8] mp 65°). After stirring for 12 hr at room temperature, the reaction mixture was distilled to yield 22.4 g (82%) of *cis*-β-iodoacrylyl chloride: bp 36° (0.08 mm); NMR (neat) δ 7.48 (d, 1 H, J = 8.0 Hz), 8.01 ppm (d, 1 H, J = 8.0 Hz). NMR signals associated with the trans isomer were not detected. Caution must be exercised not to allow the distillation bath temperature go above about 40–50°. At temperatures higher than this iodine is formed and cis–trans isomerization takes place. Isomerization will also take place at room temperature during the course of the reaction if the *cis*-β-iodoacrylic acid is not thoroughly recrystallized so as to remove all traces of iodine.

Pure *cis*-β-iodoacrylyl chloride was stirred for 27 hr at 80°. Analysis of the reaction mixture by NMR indicated that the trans isomer now predominated (trans:cis 92:8). The *trans*-β-iodoacrylyl chloride had NMR (neat) δ 7.05 (d, 1 H, J = 15.0 Hz), 8.38 ppm (d, 1 H, J = 15 Hz). This material was used in subsequent reactions without further purification. An analytical sample that was free of the cis isomer as judged by NMR was obtained by Kugelrohr distillation, bp 40–50° (3 mm). Anal. Calcd for C_3H_2ClIO: C, 16.28; H, 0.94, Cl, 16.46; I, 58.91. Found: C, 16.46; H, 0.93; Cl, 16.45; I, 58.70.

Synthesis of *N,N*-Dibutyl-*cis*-β-iodoacrylamide (3). To a solution of 1.7 ml (10.1 mmol) of dibutylamine and 1.3 ml (9.83 mmol) of collidine in 100 ml of benzene was added dropwise with stirring at room temperature 2.16 g (9.98 mmol) of *cis*-β-iodoacrylyl chloride in 10 ml of benzene. After 2 hr the collidinium hydrochloride was removed by filtration, and the benzene filtrate was evaporated to dryness to afford a dark oil which was purified by column chromatography on silica gel. The major impurity was the trans isomer (349.5 mg, 11.3%). The cis isomer **3** was obtained as an oil which following a Kugelrohr distillation afforded 2.45 g (79.5%) of **3** as a colorless liquid: bp 90–98° (0.05 mm); ir (neat) 1640 cm^{-1}; NMR ($CDCl_3$) δ 0.53–1.90 (complex, 14 H), 3.21 and 3.38 (two overlapping triplets, 4 H, J = 10 and 7 Hz), 6.78 (d, 1 H, J = 8.0 Hz), 7.13 (d, 1 H, J = 8.0 Hz).

Anal. Calcd for $C_{11}H_{20}NOI$: C, 42.73; H, 6.52; N, 4.53; I, 41.04. Found: C, 42.71; H, 6.70; N, 4.74; I. 41.25.

Irradiation of *N,N*-Dibutyl-*cis*-β-iodoacrylamide (3). A solution of 182.1 mg (0.589 mmol) of **3** in 5 ml of methanol in a Vycor tube was irradiated with 253.7-nm light (Rayonet photochemical reactor) under an atmosphere of nitrogen for 22 hr. The crude reaction mixture was treated with 10 ml of 2,4-DNP solution (246.7 mg of 2,4-DNP, 13 drops of concentrated hydrochloric acid diluted to 25 ml with methanol) and warmed on a steam bath. Removal of the solvent and recrystallization from methanol yielded two crops of the 2,4-DNP derivative of butanal. Treatment of the mother liquors with sodium thiosulfate to remove the iodine followed by preparative thick layer chromatography of the mother liquor residue afforded a third crop of the 2,4-DNP derivative of butanal for a combined yield of 91.6 mg (62%). This material was identical as judged by thin layer chromatography and NMR with an authentic sample prepared from butanal and 2,4-DNP solution.

Isolation of the major band from the thick layer chromatography of the aforementioned mother liquors afforded an oil which following a Kugelrohr distillation [92–98° (0.005 mm)] provided a pure sample of *N*-butylacrylamide (**4**): 49.0 mg (65%); ir (neat) 3250, 3050, 2945, 2905 (sh), 2850, 1650, and 1625 cm^{-1}; NMR ($CDCl_3$) δ 0.57–1.83 (m, 7 H), 3.23 and 3.38 (two overlapping triplets, 2 H, J = 6 and 7 Hz), 5.55 (d of d, 1 H, J = 7.0 and 5.0 Hz), 6.36 (d, 1 H, J = 5 Hz), 6.39 (d, 1 H, J = 7 Hz), 7.60 ppm (broad, 1 H). This material was identical as judged by thin layer chromatography, ir, and NMR with an authentic sample prepared from acrylyl chloride and *N*-butylamine purified by conventional distillation, bp 84.0–85.5° (0.1 mm) [lit.[16] bp 88–92° (0.01 mm)].

Synthesis of *N*-(*trans*-β-Iodoacrylyl-2,6-dimethylpiperidine (5). A solution of 2,6-dimethylpiperidine (4.6 ml, 33.13 mmol) in 25 ml of benzene was added dropwise over 20 min to an ice-cold solution of 1.25 g (5.78 mmol) of *trans*-β-iodoacrylyl chloride in 100 ml of benzene. The reaction mixture was stirred for 1 hr at room temperature, the piperidinium salt was removed by filtration, and the filtrate was evaporated to dryness to afford a dark brown oil that was purified by column chromatography on silica gel eluting with chloroform. The major fraction was a light brown oil which crystallized upon standing (1.32 g, 78%). Recrystallization from methylene chloride–ligroin gave the amide **5** (1.11 g, 66%) as a colorless solid: mp 69.0–69.4°; ir (KBr) 1620 and 1565 cm^{-1}; NMR ($CDCl_3$) δ 1.31 (d, 6 H, J = 7.0 Hz), 1.63 (m, 6 H), 4.42 (m, 2 H), 7.18 (d, 1 H, J = 14.0 Hz), 7.57 ppm (d, 1 H, J = 14.0 Hz); λ_{max} (95% EtOH) 249 nm (ε 11,500); *m/e* 293 (M^+).

Anal. Calcd for $C_{10}H_{16}NOI$: C, 40.97; H, 5.50; N, 4.78; I, 43.29. Found: C, 40.99; H, 5.53; N, 4.83; I, 43.17.

Photolysis of *N*-(*trans*-β-Iodoacrylyl)-2,6-dimethylpiperidine (5). A solution of 749.1 mg (2.56 mmol) of **5** in 40 ml of methanol in a Vycor tube was irradiated with 253.7-nm light (Rayonet photochemical reactor) for 15 hr. Evaporation of the solvent followed by column chromatography of the residue on silica gel eluting with chloroform provided a light brown oil which crystallized upon standing. Recrystallization from ether afforded the ring-cleaved keto amide **6** (359.1 mg, 77%) as a colorless solid: mp 38.0–39.1°; ir (KBr) 3235, 3030, 2910, 1705, 1655, 1625, and 1545 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, 3 H, J = 7.0 Hz), 1.53 (m, 4 H), 2.13 (s, 3 H), 2.43 (m, 2 H), 4.03 (m, 1 H), 5.64 (d of d, 1 H, J = 4.0 and 8.0 Hz), 5.76 (broad, 1 H), 6.18 (d, 1 H, J = 8 Hz), 6.21 ppm (d, 1 H, J = 4 Hz); λ_{max} (95% EtOH) 225 nm (ε 5040); *m/e* 183 (M^+).

Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.42; H, 9.36; N, 7.62.

Synthesis of *N*-(1-Methyl-5-oxohexyl)acrylamide (6). Acrylyl chloride[9] (660 mg, 7.29 mmol) was added dropwise with stirring to an ice-cold solution of 610 mg (5.5 mmol) of 2,6-dimethyl-Δ^1-piperideine (**7**)[10] and 727.9 mg (7.19 mmol) of triethylamine in 25 ml of benzene. After stirring at room temperature for 40 min, the salt was removed by filtration and the filtrate was evaporated to dryness to afford a dark brown oil. Purification by column chromatography on silica gel yielded the enamide **8** as an unstable, light brown oil: NMR ($CDCl_3$) δ 1.15 (d, 3 H, J = 7.0 Hz), 1.40–2.40 (complex, 4 H), 2.02 (s, 3 H), 4.43 (m, 1 H), 4.97 (m, 1 H), 5.56 (d of d, 1 H, J = 4.0 and 8.0 Hz), 6.0–6.5 ppm (complex, 2 H). Upon standing exposed to the atmosphere overnight or treatment with hydrochloric acid in moist ether for 3 hr, **8** was completely hydrolyzed to the ring-cleaved amide **6** (0.370 g, 37% based on **7**): mp 39.7–40.9°, undepressed mixture melting point with the photoproduct of **5** and identical ir, NMR, and TLC behavior.

The reverse reaction from **6** to **8** may be realized by refluxing **6** in benzene solution containing a trace of *p*-toluenesuflonic acid.

Synthesis of *N*-(*cis*-β-Iodoacrylyl)dodecahydrocarbazole (9). To a solution of 1.94 g (10.9 mmol) of dodecahydrocarbazole and 1.5 ml (11.3 mmol) collidine in 100 ml of benzene was added dropwise with stirring at room temperature 2.49 g (11.5 mmol) of *cis*-β-iodoacrylyl chloride. After stirring for 2.5 hr the collidinium hydrochloride was removed by filtration and the filtrate was evaporated to dryness to afford a dark brown oil that was purified by column chromatography on silica gel eluting with chloroform. The major fraction was an oil which crystallized upon standing and yielded the pure amide **9** upon recrystallization from methylene chloride–ligroin: 3.23 g, 83%; mp 102.8–103.0°; ir (KBr) 1645 and 1595 cm^{-1}; NMR ($CDCl_3$) δ 0.60–2.63 (complex, 17 H), 2.63–3.40 (complex, 2 H), 3.40–4.43 (complex, 7 H), 7.03 ppm (AB, 2 H, J = 8.0 Hz); λ_{max} (95% EtOH) 222 nm (ε 7570); *m/e* 359 (M^+).

Anal. Calcd for $C_{25}H_{22}NOI$: C, 50.15; H, 6.17; N, 3.90; I, 35.32. Found: C, 50.16; H, 6.09; N, 3.89; I, 35.38.

Photolysis of *N*-(*cis*-β-Iodoacrylyl)dodecahydrocarbazole (9). A solution of 1.09 g (3.04 mmol) of **9** in 40 ml of methanol in a Vycor tube was irradiated under a nitrogen atmosphere with 253.7-nm light (Rayonet photochemical reactor) for 55 hr. Evaporation of the solvent afforded an oil composed of two very similar components (TLC). These components were separated by multiple elutions on thick layer chromatography plates. The faster moving band afforded an oil which crystallized upon standing (196.9 mg, 27% based on recovered starting material). Recrystallization from ether provided colorless crystals of the ring-cleaved amide **10**: mp 99.2–101.3°; ir (KBr) 3255, 1710, 1660, and 1625 cm^{-1}; NMR ($CDCl_3$) δ 0.53–2.77 (complex, 18 H), 3.53 (m, 1 H), 5.55 (two overlapping d of d, 1 H, J = 4.0 and 9.0 Hz), 6.08 (d, 1 H, J = 9.0 Hz), 6.15 (d, 1 H, J = 4.0 Hz), 6.30 ppm (broad, 1 H); λ_{max} (95% EtOH) 229 nm (ε 5520); *m/e* 249 (M^+).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.27; H, 9.22; N, 5.64.

The slower moving band afforded a solid (87.5 mg, 12% based on recovered starting material) which following recrystallization from methylene chloride–ligroin afforded colorless crystals of the epimeric ring-cleaved amide **11**: mp 116.8–118.1°; ir (KBr) 3235, 1705, 1650, and 1620 cm^{-1}; NMR ($CDCl_3$) δ 0.57–2.70 (complex, 18 H), 3.70 (m, 1 H), 5.62 (two overlapping d of d, 1 H, J = 4.0 and 8.0 Hz), 5.60 (broad, 1 H), 6.17 (d, 1 H, J = 9.0 Hz), 6.21 ppm (d, 1 H, J = 4.0 Hz); λ_{max} (95% EtOH) 228 nm (ϵ 5260); m/e 249 (M^+).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.30; H, 9.24; N, 5.61.

Treatment of either **10** or **11** with 1,5-diazabicyclo[3.4.0]nonene-5 (DBN) in benzene at room temperature afforded an equilibrium mixture of **10** and **11** in which **11** was the major component.

Modified Synthesis of (±)-Sedridine (13) and (±)-Allosedridine.[11] A solution of 10.56 (77.1 mmol) of 1-(2-pyridyl)propan-2-ol[11a] and 3.80 g of 5% rhodium on carbon in 25 ml of absolute ethanol was shaken in a hydrogen atmosphere (50 psi) at 40–50° for 28 hr. Removal of the catalyst by filtration and evaporation of the solvent afforded an oil which crystallized upon standing (9.11 g, 84%). This mixture of the diasteromers, (±)-sedridine and (±)-allosedridine, was used in the next step without further purification.

To a stirred solution of the aforementioned diastereomer mixture (365.8 mg, 2.55 mmol) and collidine (340 μl, 2.57 mmol) in 20 ml of chloroform was added dropwise at room temperature 370 μl (2.60 mmol) of benzyl chloroformate in 10 ml of chloroform. After 24 hr the reaction mixture was extracted with 10% hydrochloric acid. The organic layer was dried and evaporated to dryness to yield an oil that was easily separated into two components by column chromatography on 50 g of silica gel eluting with chloroform. The less polar material (298.1 mg, 45%) was recrystallized from ether to yield the carbobenzoxy derivative of (±)-sedridine as colorless crystals: mp 32.6–34.4°; ir 3420 and 1670 cm^{-1}; NMR ($CDCl_3$) δ 1.18 (d, 3 H, J = 6.0 Hz), 1.00–1.88 (complex, 8 H), 1.88–4.77 (complex, 5 H), 5.17 (s, 2 H), 7.33 ppm (s, 5 H). Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.41; H, 8.38; N, 4.98. The more polar material (174.5 mg, 25%), the carbobenzoxy derivative of (±)-allosedridine, was isolated as an oil: ir (neat) 3410 and 1685 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, 3 H, J = 8.0 Hz), 1.27–2.23 (complex, 8 H), 2.43–3.33 (complex, 2 H), 3.47–4.67 (complex, 3 H), 5.12 (s, 2 H), 7.33 ppm (s, 5 H).

A solution of the crystalline carbobenzoxy derivative (2.3859 g, 8.60 mmol) and 900 mg of 10% palladium on carbon in 25 ml of absolute ethanol was stirred under 1 atm of hydrogen at room temperature for 15 hr. Following removal of the catalyst by filtration and evaporation of the filtrate to dryness, the residue was recrystallized from ether to give (±)-sedridine (**13**) (1.07 g, 87%) as a colorless solid, mp 73.0–75.0° (lit.[11b,c] mp 75.0°). In a similar fashion the oily carbobenzoxy derivative was converted to (±)-allosedridine (81%), which following recrystallization from ether had mp 69.7–70.3° (lit.[11b,c] mp 70–71°).

Synthesis of *N*-(*cis*-β-Iodoacrylyl)sedridine (14). To an ice-cold solution of 438.3 mg (3.06 mmol) of sedridine (**13**) and 400 μl (3.02 mmol) of collidine in 50 ml of benzene was added dropwise with stirring 660 mg (3.05 mmol) of *cis*-β-iodoacrylyl chloride in 10 ml of benzene. The mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was extracted with 10% hydrochloric acid, and the organic layer was dried and evaporated to dryness to afford a light brown oil that was purified by column chromatography on silica gel. Recrystallization from ether of the material from the most polar band afforded the amide **14** (673.4 mg, 69%) as colorless crystals: mp 51.1–52.0°; ir (KBr) 3390, 1600, and 1590 cm^{-1}; NMR ($CDCl_3$) δ 1.18 (d, 3 H, J = 6.0 Hz), 1.38–2.42 (complex, 8 H), 2.75–3.38 (m, 1 H), 3.42–4.00 (complex, 2 H), 4.00–4.55 (m, 1 H), 6.85 (d, 1 H, J = 9.0 Hz), 7.20 ppm (d, 1 H, J = 9.0 Hz).

Anal. Calcd for $C_{11}H_{18}NO_2I$: C, 40.88; H, 5.61; N, 4.33; I, 39.27. Found: C, 40.79; H, 5.51; N, 4.29; I, 39.11.

Photolysis of *N*-(*cis*-β-Iodoacrylyl)sedridine (14). A solution of 2.625 g (8.12 mmol) of **14** in 400 ml of methanol in a quartz flask was irradiated under a nitrogen atmosphere with 253.7-nm light (Rayonet photochemical reactor) for 26.5 hr. The solvent was removed under reduced pressure, and the residual oil was redissolved in chloroform and extracted with aqueous sodium thiosulfate. The organic layer was dried and evaporated to dryness. The residue was purified initially by column chromatography on silica gel eluting with carbon tetrachloride–chloroform. The fractions from the column chromatography were further purified by thick layer chromatography where necessary. The following materials were obtained in order of their elution from the column.

A. Bicyclic Amide 20. This material was separated from the following material, **17**, by extensive thick layer chromatography and was isolated as a light yellow oil (57.4 mg, 4%). Upon standing for several days it was converted to **17**. Nevertheless, it was possible to obtain limited spectroscopic data with a sample contaminated with only a minor amount of **17**: ir (neat) 1650 and 1620 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, 3 H, J = 6.0 Hz), 1.43–2.43 (complex, 8 H), 4.17–5.17 (complex, 2 H), 5.58 (m, 1 H), 5.72 (d of d, 1 H, J = 4.0 and 9.0 Hz), 6.41 (d, 1 H, J = 4.0 Hz), 6.55 ppm (d, 1 H, J = 9.0 Hz).

B. Enamide 17. Recrystallization from ether afforded enamide **17** (341 mg, 21%, including the additional material obtained from the conversion of **20**, 25%) as colorless crystals: mp 64.7–65.0°; ir (KBr) 3375, 1640, and 1600 cm^{-1}; NMR ($CDCl_3$) δ 1.17 (d, 3 H, J = 6.0 Hz), 1.00–2.43 (m, 6 H), 3.23–3.87 (m, 1 H), 4.23–5.40 (complex, 3 H), 5.83 (d of d, 1 H, J = 4.0 and 9.0 Hz), 6.50 (d, 1 H, J = 4.0 Hz), 6.63 (d, 1 H, J = 9.0 Hz), 6.66 ppm (br d, 1 H, J = 8.0 Hz); λ_{max} (95% EtOH) 278 nm (ϵ 7340); m/e 195 (M^+).

Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.51, H, 8.52; N, 7.19.

C. The Acetylene. An acetylenic compound[13] was obtained as a yellow oil (307.6 mg, 19%) contaminated with small amounts of the starting material which could not be removed even after extensive thick layer chromatography: ir (neat) 3370, 2080, and 1600 cm^{-1} (broad); NMR ($CDCl_3$) δ 1.23 (d, 3 H, J = 6.0 Hz), 1.07–2.43 (complex, 8 H), 3.00–4.12 (complex, 3 H), 3.37 (s, 1 H), 4.05–4.60 (complex, 1 H), 4.60–5.20 ppm ((complex, 1 H).

D. α,β-Unsaturated Ketone 16. Recrystallization from ether afforded the ketone **16** (36.0 mg, 5%) as colorless needles: mp 86.2–86.3°; ir (KBr) 3230, 3050, 2910, 1690, 1650, 1625, and 1560 cm^{-1}; NMR ($CDCl_3$) δ 1.33–1.77 (complex, 4 H), 1.90 (d of d, 3 H, J = 6.0 and 2.0 Hz), 2.27–2.89 (m, 2 H), 3.03–3.53 (m, 2 H), 5.57 (d of d, 1 H, J = 8.0 and 4.0 Hz), 5.90–6.50 (complex, 4 H), 6.85 (d of q, 1 H, J = 6.0 and 16.0 Hz); m/e 195 (M^+).

Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.63: H, 8.72; N, 7.08.

E. Methoxy Ketone 15. Recrystallization of **15** in an ice bath using ether with a trace of methylene chloride to eliminate clouding of the solution before crystallization began provided **15** (411.6 mg, 22%) as a colorless powder: mp 26.8–27.4°; ir (neat) 3260, 1705, 1655, 1625, and 1545 cm^{-1}; NMR ($CDCl_3$) δ 1.17 (d, 3 H, J = 6.0 Hz), 1.40–1.90 (m, 4 H), 2.33–2.77 (m, 4 H), 3.03–3.50 (m, 2 H), 3.33 (s, 3 H), 3.82 (t of q, 1 H, J = 6.0 and 6.0 Hz), 5.60 (d of d, 1 H, J = 6.0 and 6.0 Hz), 6.27 (two d, 2 H, J = 6.0 Hz), 6.90–7.40 ppm (broad, 1 H).

Anal. Calcd for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31; N, 6.16. Found: C, 63.45; H, 9.45; N, 6.24.

The methoxy ketone **15** is converted to the α,β-unsaturated ketone **16** in nearly quantitative yield upon dissolving in a moist chlorform solution of hydrochloric acid and refluxing for 65 hr.

Synthesis of *N*-Propionyl Sedridine (18). To a solution of 177.5 mg (1.24 mmol) of (±)-sedridine (**13**) and 180 μl (1.29 mmol) of triethylamine in 10 ml of benzene was added dropwise with stirring at room temperature 110 μl (1.27 mmol) of propionyl chloride in 10 ml of benzene. The reaction mixture was extracted with 10% aqueous hydrochloric acid after 1.5 hr. The organic layer was dried and evaporated to dryness to provide a light yellow oil which was purified by a Kugelrohr distillation. The fraction collected between 129 and 135° (0.25 mm), 196.6 mg (80%), was the pure amide **18**: ir ($CHCl_3$) 3370 and 1605 cm^{-1}; NMR ($CDCl_3$) δ 1.14 (t, 3 H, J = 8.0 Hz), 1.18 (d, 3 H, J = 5.0 Hz), 1.40–2.20 (complex, 8 H), 2.49 (q, 2 H, J = 6.0 Hz), 2.66–4.50 (complex, 4 H), 4.70–5.10 ppm (complex, 1 H).

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 10.62; N, 7.03. Found: C, 66.11; H, 10.98; N, 7.14.

The enamide **17** (8.7 mg, 0.045 mmol) and 98.5 mg of 5% rhodium on carbon in 5 ml of absolute ethanol were stirred under one atmosphere of hydrogen for 12.5 hr. The catalyst was removed by filtration and the filtrate was evaporated to dryness to afford a light yellow oil in quantitative yield. The oil was homogeneous by TLC and was identical with **18** prepared by the aforementioned procedure as judged by TLC, ir, and NMR comparison.

Acknowledgment. We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (GM-17267) for their generous support of this work.

Registry No.—**3**, 55711-80-3; **4**, 2565-18-6; **5**, 55711-81-4; **6**, 55711-82-5; **7**, 823-20-1; **8**, 55711-83-6; **9**, 55711-84-7; **10**, 55711-85-8; **13**, 41447-10-3; **13** carbobenzoxy derivative 55711-86-9; **14**, 55711-87-0; **15**, 55711-88-1; **16**, 55711-89-2; **17**, 55711-90-5; **18**, 55711-91-6; **20**, 55711-92-7; *cis*-β-iodoacrylyl chloride, 55711-93-8; *trans*-β-iodoacrylyl chloride, 55711-94-9; oxalyl chloride, 79-37-8; *cis*-β-iodoacrylic acid, 6214-35-3; dibutylamine, 111-92-2; 2,6-dimethylpiperidine, 504-03-0; acrylyl chloride, 814-68-6; dodecahydrocarbazole, 6326-88-1; 1,5-diazabicyclo[3.4.0]nonene-5, 3001-72-7; (±)-allosedridine, 26623-96-1; (±)-allosedridine carbobenzoxy derivative, 55711-95-0; 1-(2-pyridyl)-propan-2-ol 5307-19-7; benzyl chloroformate, 501-53-1; propionyl chloride, 79-03-8.

References and Notes

(1) (a) T. Kametani and K. Fukumoto, *Acc. Chem. Res.*, **5**, 212 (1972); (b) A. Gilbert, "Photochemistry", Vol. 2, Burlington House, London, 1971, pp 514–520; (c) Vol. 3, 1972, pp 601–607.
(2) R. C. Neuman, Jr., and G. D. Holmes, *J. Org. Chem.*, **33**, 4317 (1968), and references cited therein.
(3) (a) P. G. Webb and J. A. Kampmeier, *J. Am. Chem. Soc.*, **93**, 3730 (1971); (b) R. M. Kopchik and J. A. Kampmeier, *ibid.*, **90**, 6733 (1968), and references cited therein.
(4) E. I. Heiba and R. M. Dessau, *J. Am. Chem. Soc.*, **89**, 3772 (1967).
(5) R. C. Weast, Ed., "Handbook of Chemistry and Physics", 53rd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1973.
(6) M. E. Wolff, *Chem. Rev.*, **63**, 55 (1963).
(7) M. Akhtar, *Adv. Photochem.*, **2**, 263 (1964).
(8) F. Stolz, *Ber.*, **19**, 536 (1886).
(9) G. H. Stempel, Jr., R. P. Cross, and R. P. Mariella, *J. Am. Chem. Soc.*, **72**, 2299 (1950).
(10) M. F. Grundon and B. E. Reynolds, *J. Chem. Soc.*, 3898 (1963); 2445 (1964).
(11) (a) L. A. Walter, "Organic Syntheses", Collect. Vol. III, Wiley, New York, N.Y. 1955, p 757; (b) H. C. Beyerman, J. Eenshuistra, W. Eveleens, and A. Zweistra, *Recl. Trav. Chim. Pays-Bas*, **78**, 43 (1959); (c) H. C. Beyerman, L. Maat, A. Van Veen, and A. Zweistra, *Recl. Trav. Chim. Pays-Bas*, **84**, 1367 (1965).
(12) The photochemistry of the diastereomeric β-iodoacrylamide of (±)-allosedridine was also examined and found to be qualitatively the same as that of the sedridine derivative.
(13) An acetylenic product was also isolated in this reaction (19%). It most probably arises from the simple loss of hydrogen iodide from the acrylate moiety of **14**. While this product accounted for an appreciable amount of the starting material consumed in this reaction, similar products were not detected in any of the aforementioned photolyses.
(14) N. Wada, K. Tokumaru, and O. Simamura, *Bull. Chem. Soc. Jpn.*, **44**, 1112 (1971); M. J. S. Dewar and M. Shanshal, *J. Am. Chem. Soc.*, **91**, 3654 (1969); W. G. Bentrude, *Annu. Rev. Phys. Chem.*, **18**, 283 (1967).
(15) N. C. Yang and G. R. Lenz, *Tetrahedron Lett.*, 4897 (1967); R. W. Hoffmann and K. R. Eicken, *ibid.*, 1759 (1968).
(16) E. F. Jordan, Jr., G. R. Riser, W. E. Parker, and A. N. Wrigley, *J. Polym. Sci., Part A-2*, **4**, 975 (1966).

Optically Active Amines. XX.[1,2] Application of the Salicylidenimino Chirality Rule to Cyclic Terpene Amines[3]

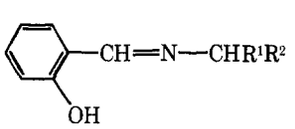
Howard E. Smith,* [4a] Elizabeth P. Burrows,[4a] Eddie H. Massey,[4a,5] and Fu-Ming Chen[4b]

Departments of Chemistry, Vanderbilt University, Nashville, Tennessee 37235, and Tennessee State University, Nashville, Tennessee 37203

Received May 9, 1975

The signs of the Cotton effects near 255 and 315 nm observed in the circular dichroism spectra of the *N*-salicylidene derivatives of a group of cyclic terpene amines (menthane, thujane, and fenchane ring systems) correlate with the absolute configurations of the amines. The Cotton effects are generated by the coupled oscillator mechanism, and their signs are determined by the chirality (right-handed screw for positive chirality) of the vicinal carbon–carbon bonds and the attachment bond of the salicylidenimino chromophore.

Application of the salicylidenimino chirality rule to the establishment of the absolute configuration of *N*-salicylidene (Schiff base) derivatives (1) of chiral α- and β-arylalk-

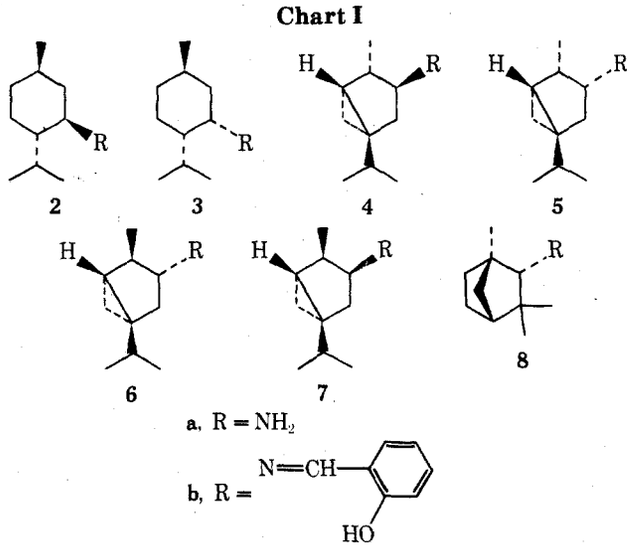


1

ylamines has been extensively documented.[1,6] The rule correlates the absolute configuration of these derivatives with their optical rotatory dispersion[7] (ORD) and circular dichroism[6] (CD) spectra. The magnitudes of the rotational strengths for the observed Cotton effects near 255 and 315 nm and the general features of the spectra indicate that the dominant mechanism operative in generation of the Cotton effects is electric transition moment dipole–dipole coupling of the aryl group with the salicylidenimino chromophore.[6] Positive chirality (right-handed screw) results in positive Cotton effects at 255 and 315 nm.

For the *N*-salicylidene derivatives of chiral alkylamines corresponding but less intense Cotton effects are observed.[8–11] As an extension of this work, we now report the CD spectra of the *N*-salicylidene derivatives of a group of cyclic terpene amines (**2a–8a**) (Chart I and Table I). In these spectra the signs of the observed Cotton effects near 255 and 315 nm, considered to be generated by the coupled oscillator mechanism,[15] correlate with the absolute configuration of the amine moiety.

Chart I



Results and Discussion

Configuration and Preferred Conformation. The absolute configurations of the *N*-salicylidene derivatives **2b–8b** follow from those of the respective amines. Both