Photoisomerization of Selected Oxiranes. Intermediacy of Carbonyl Ylides[1]

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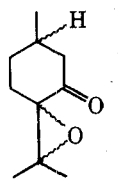
Received May 10, 1976

Several α-cyano β-arylglycidates were synthesized and their trans–cis photoisomerizations were studied. At elevated temperature (110 °C), a clean reaction occurred, providing a synthetically useful route to cis isomers. The isomerization proceeds via ylides, which may in turn be formed from a triplet excited state of a parent oxirane. The reaction in a matrix (77 K) was also studied and the mechanisms are discussed. A photorearrangement of the ylide was found in the case of a β-methyl-β-phenyl analogue.

While the photoequilibration of cyclopropanes has been studied extensively[2] this aspect of the photochemistry of the analogous oxiranes has been accorded only limited attention.[3,4a,b] Although photoinduced isomerizations of α,β-epoxy ketones, including *trans*-dypnone oxide[4c] and β-pulegone oxide (**1**),[4d] are known, such substrates for the most part have lowest energy n,π* singlet and triplet states.[4a] In such cases it has generally been assumed that cis–trans photoisomerization occurs by initial C–O bond cleavage and that the chemically significant excited state has n,π* character;[3] however, C–C bond cleavage has been invoked to explain the photointerconversion of epimers of epoxy ketone **1**.[4d]



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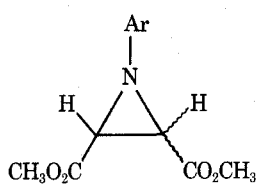

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Aziridines bearing stabilizing substituents such as **2** constitute another class of small-ring compounds known to photointerconvert to their epimers. It has been demonstrated that such substrates, which are thermo- as well as photolabile, equilibrate in the absence of dipolarophiles by way of azomethine ylides formed by thermal or photoinduced C–C bond scission.[5]

The present study was initiated to investigate the photointerconversion of a class of oxiranes known to undergo reversible C–C bond photolysis to carbonyl ylides[6] and to assess the extent to which constraints imposed by orbital symmetry restrictions apply. The isomeric methyl α-cyano-β-phenylglycidates, **3a** and **4a**, respectively, were synthesized from (*E*)- and (*Z*)-methyl α-cyanocinnamate (**5** and **6**), respectively.[7,8] (*E*)-Methyl α-cyanocinnamate (**5**) was prepared by condensation of benzaldehyde with methyl cyanoacetate using potassium fluoride.[7a] The requisite *Z* alkene **6** was obtained from the *E* isomer **5** by irradiation (254 nm)[9] of the latter in benzene in a quartz vessel. The resulting mixture was difficult to resolve by chromatographic methods into the alkenes **5** and **6** and thus conversions to **3a** and **4a** were conducted prior to separation of these precursors.

Epoxidation[8] of the mixture of (*E*)- and (*Z*)-methyl α-cyanocinnamates gave **3a** and **4a**. These trans and cis glycidates **3a** and **4a**, respectively, were separated by silica gel column chromatography and purified by recrystallization. Since the homogeneous *E* alkene precursor, unlike its *Z* counterpart, is available by direct condensation, the oxidation to **3a** in this case may be conducted on pure samples in the manner described for the mixture of **5** and **6**.

The stereochemical relationships assigned to **3a** and **4a** rest on the method of preparation and NMR data. The chemical shifts observed for the methyl protons of the carbomethoxy group of **4a** are shielded relative to those of **3a** as expected from the stereochemical relationship and proximity of the phenyl and carbomethoxy groups in **4a**.[10] Furthermore, the thermal equilibration of the neat epimers **3a** and **4a** (120 °C in benzene) demonstrates that **3a** is the more stable epimer (~7:1 and 5:1, respectively) although complete equilibration was not achieved even after 48 h. This result is in accord with the proposed assignments.

Contrary to expectations, based on the results of previous experience with vicinal diaryl oxides, the oxirane **3a** (0.2 M)[9] undergoes facile photoequilibration (254 nm, 3 h, eight lamps) in benzene to give a 1:1.8–2.0 mixture of **3a** to **4a**, presumably by way of carbonyl ylide intermediates **3b** and **4b**. The epimer ratio is readily determined by NMR analysis based on the differences in spectra. When **4a** is irradiated under the same conditions the ratio of **3a** to **4a** is 1:6.7. Clearly a true photoequilibrium is not established in either case due to the intervention of competing side reactions. Nevertheless this process is of synthetic utility (60% recovery of **3a** and **4a**) and may provide the only convenient route to the less stable epimeric oxirane in many cases. For example, the thermal equilibration described above favors the trans isomer and the requisite cis alkene is unavailable and/or may not be oxidized stereospecifically without interfering side reactions which is also the case for the cis epimer of **10** (see below). To our knowledge the photoequilibration of oxiranes such as **3a** and **4a** was without precedent in what are believed to be π,π* systems prior to the discovery of the reactions under discussion.[3]

A pronounced effect of temperature on the formation of by-products in the photolysis of **3a** and **4a** in benzene or toluene is apparent, which if general may enhance the synthetic utility of oxirane photoisomerization processes. Surprisingly, the complexity of the product mixtures decreases markedly when the photoisomerizations of both **3a** and **4a** are conducted

Scheme I. Summary of Possible Interconversions Contributing to Oxirane Photoisomerizations

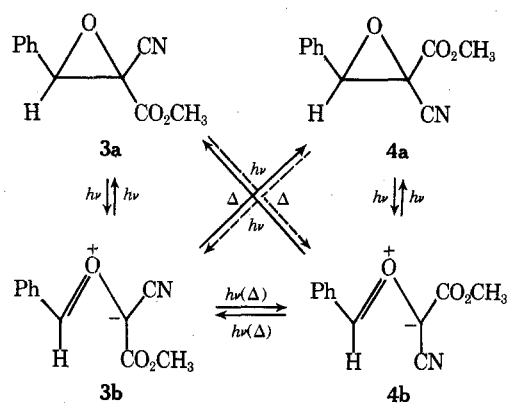


Table I. Effects of Temperature and Light Flux on the Photoequilibration of 3a and 4a [a]

Temp, °C	No. of lamps	Ratio (3a:4a)
140 [b]	16	1:0.37
110 [b]	16	1:1.1
80 [b]	16	1:1.1
40 [b]	16	1:1.3
110 [c]	16	1:2.2 [d]
110 [c]	12	1:1.8
110 [c]	8	1:1.6
110 [c]	4	1:09

[a] Irradiated for 3 h; 0.5 mmol in 5 ml of toluene (0.1 M). [b] Conducted in a decalin bath. [c] Conducted under conditions of reflux. [d] Irradiation for 2.5 h gave essentially the same values.

at 80 °C (benzene at reflux, 6 h). A much cleaner photoequilibration is observed with both the trans and cis glycidates (**3a** and **4a,** 1:2.1 and 1:3.6, respectively) under conditions where these substrates are thermally stable. It is also evident from the isomer ratios that the oxirane isomerization in this case is not thermally induced since the cis rather than trans isomer predominates regardless of whether **3a** or **4a** is photolyzed.

To assess the role of temperature and light flux on the equilibration rate and ratio, a series of experiments were designed to evaluate the effect of variations in these parameters with time (see Table I). Clearly increasing temperature has little effect upon the rate of attainment or position of equilibrium until the temperature is elevated to a point where thermal equlibration begins to compete with the photoprocesses as evidenced by the onset of an increase in the trans isomer **3a** and its ultimate emergence as the dominant epimer, i.e., 140 °C where C–C thermolysis competes with photolysis.

In contrast, variations in light flux as expected have a marked effect upon the rate of photoequilibration. It is apparent from Table I that the photoisomerization of **3a** to **4a** is optimized upon irradiation for 2.5 h with 16 lamps[9] in toluene at reflux. The products **3a** (30%) and **4a** (60%) may be recovered (90%) by preparative TLC and were identified by TLC and NMR. The product ratios reported were verified spectroscopically (NMR) prior to separation.

The results appear to relegate thermal mechanisms for ylide isomerization to a minor role in the photoisomerization process, at least within the limited temperature range studied. Possible alternative explanations may be envisaged for the photointerconversion of **3a** and **4a.** Experiments conducted at lower temperatures (7 °C) indicate that the reaction complexity increases substantially, in fact to the point where photoequilibration data are no longer accessible by NMR spectroscopy.

Strict adherence to the principles of orbital symmetry constraints requires that isomerization is obligatory if disrotatory photoinduced opening of the oxiranes **3a** and **4a** to carbonyl ylides **3b** and **4b** precedes conrotatory thermal cyclization in a two-step photoinitiated process.[11a] The conclusions regarding the modes of cleavage and cyclization are based upon the isoelectronic interrelationships which exist between aziridines and oxiranes. Both are 4n systems, and in this respect are analogous to the cyclopropyl anion which, it is argued, should undergo disrotatory opening in the excited state to the allyl anion.[11b,c]

Evidence has been presented that azomethine ylides generated photolytically may undergo photoisomerization.[5a] Thus the carbonyl ylides formed photochemically at 25 °C may also be photolabile and subject to secondary photoisomerization prior to cyclization, particularly in view of their stability and high absorbance (Scheme I).[6b] In this temperature range as noted ylide thermal equilibration cannot play a significant role.

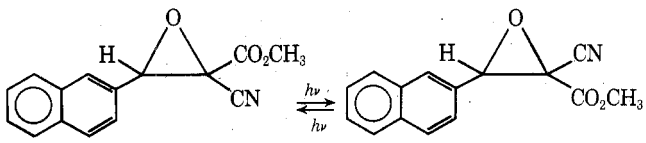
Recent evidence indicates, however, that orbital symmetry restrictions may apply less stringently to oxiranes than aziridines in ground state reactions.[5c,11b,c] Kinetic thermolysis studies of α-cyano-*cis*-stilbene oxide confirm that isomerization in the ground state must occur by dis- as well as conrotatory modes (36 and 64%, respectively).[5c] In this case the conclusion is inescapable that "orbital symmetry rules are violated". On the basis of this departure from symmetry restrictions, it is not unreasonable to conclude that similar deviations from expected behavior could be encountered in excited state processes as well, leading, for example, to photoinduced conrotatory oxirane opening. If indeed such is the case, then photoisomerization could be expected regardless of the recyclization mode. Isomerization could only be avoided in the unlikely event that the individual isomeric carbonyl ylides formed by concurrent con- and disrotatory electrocyclic opening undergo recyclization at precisely those relative rates and modes required to regenerate the initial oxirane in the absence of its epimer.

Several other factors may be significant in determining the photostationary equilibrium composition established between **3a** and **4a,** including the relative differences in oxirane as well as carbonyl ylide absorbtivities in the region of the source emission. The magntudes of the decay constants for **3a** and **4a** are also relevant as are the values for intermediates such as the ylides if photointerconversion in contrast to thermal equilibration plays a dominant role in the photoisomerization process. It is clear from this discussion that a complete mechanistic analysis is beyond the scope of this communication; however, it is not uncommon that the less stable isomer is the major isomer present at equilibrium in solution upon irradiation of alkenes and cyclopropanes[2] as is the case in these oxirane studies; i.e., the less stable isomer predominates.[11d]

Certain mechanistic aspects of the photoequilibration of **3a** and **4a** may be explained, however. The unique role of benzene or toluene as a solvent in the isomerization of **3a** and **4a** prompted us to investigate the possibility that the triplet state may be implicated in the isomerization processes. Quenching studies were conducted on the trans oxirane **3a** (0.1 M) using a series of cyclohexane solutions containing incremental amounts of *trans*-1,3-pentadiene (E_t = 59 kcal mol^{-1})[11d] over a concentration range of 0.2–1.2 M. The solutions were irradiated for 2 h and NMR analyses of the photolysates were conducted. The extent of isomerization to the epimer **4a** was found to be suppressed when the quencher concentration exceeds 0.2 M. In the absence of quencher, however, ~15% conversion has occurred in cyclohexane as solvent, cf. benzene as a solvent. This suggests that a long-lived triplet intermediate might intervene at some stage in the reaction. Unfortunately [3 + 2 → 5] cycloaddition(s) of the ylide to the conjuated diene quencher competes with photoisomerization. This complicates the quenching studies substantially by introducing potentially photolabile by-products which interfere and alter the light absorbed by the oxirane at 254 nm. Sensitization experiments were therefore performed to supplement the dubious quenching results and ensure that the photoisomerization is triplet rather than singlet in character.

Sensitization of the photoequilibration of **3a** and **4a** could not be achieved with common high-energy solvent sensitizers employed, with the possible exception of benzene.[6a] *trans*-Methyl α-cyano-β-(2-naphthyl)glycidate (**7**) was selected for preliminary sensitization studies and was synthesized in high yield (90%) by base-catalyzed *m*-chloroperbenzoic acid oxidation of (*E*)-methyl α-cyano-β-(2-naphthyl)acrylate (**9**).

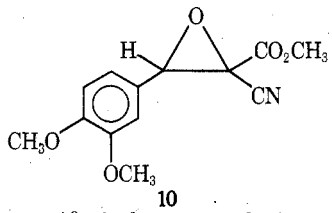
Direct irradiation (350 nm)[9] of a benzene solution of the trans oxirane **7** (6 h) in a Pyrex vessel, in the absence of added sensitizer, induces isomerization to a mixture of trans and cis oxiranes whose composition is 1:2.6, respectively. That the photoisomerization of **7** to **8**, and presumably the photo-



7 **8**

equilibration of **3a** and **4a** as well, may proceed through the triplet state was confirmed by irradiation of **7** in the presence of the sensitizeranthraquinone (62 kcal mol^{-1}) with a visible source.[12a] The results proved similar to those obtained upon direct irradiation of **7** (350 nm)[9] in the absence of a low-energy triplet sensitizer. Benzophenone (60 kcal mol^{-1}) is also effective as a sensitizer (350 nm)[9] for the photoequilibration of **7**. A filter composed of naphthalene (saturated) in benzene as a solvent or a uranyl glass filter was employed to ensure that direct absorption due to tailing at long wavelength in the spectrum of **7** is excluded and that the sensitizer is the sole absorbing species. In fact, insignificant isomerization occurs with the filter until sensitizer is added.

It was found that triplet sensitization also may be extended to *trans*-methyl α-cyano-β-(3,4-dimethoxyphenyl)glycidate (**10**); however, a sensitizer with a higher triplet energy, i.e., acetophenone (74 kcal mol^{-1}), is required in this case. The method employed for the preparation of **7** also proved successful for the synthesis of the substituted trans glycidate **10.**



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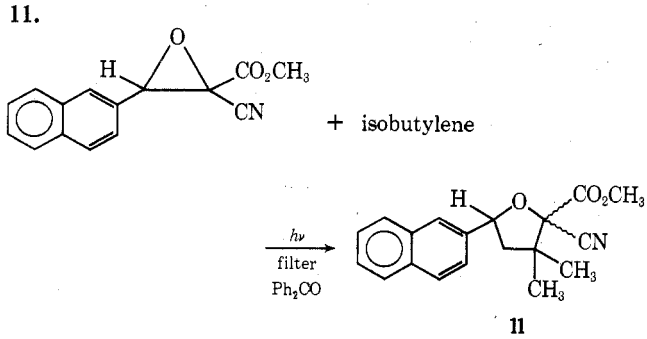
Irradiation (350 nm)[9] of a benzene solution of the trans oxirane **10** (0.2 M) containing acetophenone (0.4 M) for 14 h results in significant interconversion to the cis isomer with the cis/trans ratio approaching 2.0. Acetone proved to be a less effective sensitizer; however, significant amounts (~11%) of the cis isomer are apparent in the NMR spectrum of the photolysate (350 nm, 12 h) when this ketone is used as a solvent sensitizer.

Our contention that the photointerconversion observed for the oxiranes **3a** and **4a** as well as **7** and **8** and the reported [3 + 2]cycloaddition reactions exhibited by these oxiranes probably involve common intermediates, namely carbonyl ylides, was also investigated.[6] A solution of **7** in benzene saturated with isobutylene was irradiated (350 nm)[9] for 5 h with a naphthalene filter. A 20% decrease in the concentration of **7** was observed in a 5-h time span under these conditions. A similar experiment was then performed after addition of benzophenone and essentially complete conversion of the oxirane **7** (>95%, NMR) occurs with formation of the adducts **11.**



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By-products of the type observed with **3a, 4a,** and **7** in benzene are absent in cases where the dipolarophile is present, which suggests that side reactions are slower than cycloaddition. In fact isobutylene is sufficiently active as a dipolarophile in benzene that concomitant cis–trans isomerization is markedly suppressed. Since benzophenone undergoes intersystem crossing with unit efficiency to the triplet state and exerts such a dramatic effect on the conversion of **7** to **11** it is concluded that oxirane ring opening must be triplet in character and the nascent ylide is formed in the triplet excited state. Interception of the intermediate ylides by the dipolarophile is thought to occur in the ground state because of the observe regioselectivity and stereospecificity where dipolarophile cofiguration permits.[6a,13] Regardless of the mechanism of cycloaddition, the results cited for **7** are consistent with initial disrotatory opening of the oxirane in the excited triplet state with formation of a triplet ylide intermediate which is intercepted, after deactivation to the singlet ground state, by the dipolarophile or recyclizes after spin-inversion in a conrotatory fashion with overall net isomerization.[6] Thus common intermediates, carbonyl ylides, are invoked for both the isomerization and cycloaddition processes; however, as noted above for **3a** and **4a,** thermal and/or photoequilibration of the ylide and/or "violations of orbital symmetry" in the course of ring opening may contribute to oxirane isomerization. Furthermore, homolytic C–O bond photocleavage is advanced in the case of certain oxiranes to explain cis–trans isomerization[4] and this process may also contribute to photoequilibration here.

At this time it has not been determined if the reversible isomerization of **3a** and **4a** observed upon direct irradiation occurs in the singlet manifold; however, at least two explanations may be used to rationalize the results of unsensitized reactions in terms of triplet mechanisms. Direct excitation of the oxirane to the singlet state followed by intersystem crossing to the oxirane triplet may occur with subsequent electrocyclic opening to the triplet ylide and recyclization, after spin-inversion and relaxation to the singlet ground state. Alternatively, ring opening may precede intersystem crossing and in this manner the triplet oxirane would be circumvented.

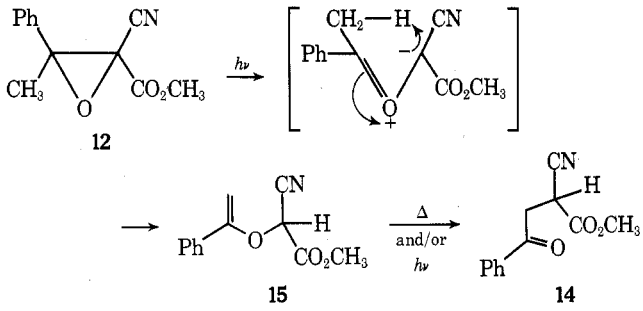
Photochemical experiments were performed at subambient temperature (77 K) to provide further insight into the mechanism by which the isomerization of **3a** to **4a** (and **7** to **8**) occurs. Reversible color formation in matrices at 77 K induced by light is a phenomenon characteristic of a variety of oxiranes including **3a, 4a, 7,** and **10** which has been attributed to C–C bond cleavage with formation of carbonyl ylides (λ_{max} 547 and 535 nm for **3b** and **4b,** respectively).[14]

It is evident from rigid matrix spectral data that the absorbtivities of the colored ylides produced upon irradiation (254 nm)[9] at 77 K are significantly greater than the parent oxirane. Thus ylide formation is restricted to the immediate region of the cell surface exposed to ultraviolet light. The resulting shielding effect must be overcome to increase photoefficiency, and techniques have been devised for maximizing the exposure and utilization of radiation, particularly in matrices, and are discussed elsewhere.[6b]

The behavior exhibited by **3a** at 77 K in an inert matrix upon photolysis utilizing the double-irradiation technique described earlier[6b] contrasts markedly with that observed for **4a,** which undergoes complete conversion to **3a.** Simultaneous illumination of **3a,** on the other hand, at 77 K with both ultraviolet (254 nm)[9] and visible (400–600 nm) sources,[12b] for a period of 3 h and subsequent analysis of the irradiated sample confirms that unlike **4a** no *detectable* photoconversion to the alternate isomer **4a** occurs (NMR, etc.) despite the fact that the colored ylide is obviously formed.

The absence of isomerization after photogeneration and

Scheme II



irradiation of the ylide derived from **3a** is in accord with expectations based on orbital symmetry arguments, if only allowed processes are considered.[11a] Significant thermal processes should be arrested under the matrix conditions and the isomerization of **3a** may be attributed to photoinduced recyclization of a relatively stable ylide which is not without precedent.[15] It remains to be explained why isomerization of **4a** to **3a** is complete under identical conditions. One possible reason for the disparate results obtained in the low-temperature photochemistry observed between **3a** and **4a** is the ionic interaction between the "cationic" center of the ylide and the carbomethoxy group which constrains **3b** from undergoing isomerization in the matrix while providing driving force for the observed photoconversions of **4b** to **3b** and ultimately **3a.** It is reported[16] that β-cyano-β-acetylstyrene oxide as well as other such α,β-epoxy ketones rearrange thermally to afford 1,3-dioxolenes through a mechanism involving C–C bond cleavage and subsequent cyclization of the resulting ylide; however, no such products are isolable in the case of **3a** and additional studies are required to validate or refute our proposal.

Unexpected results were obtained when an attempt was made to extend the photoequilibration process to *trans*- and *cis*-methyl α-cyano-β-methyl-β-phenylglycidate (**12** and **13,** respectively) separated from the oxidation mixture obtained from (*E*)- and (*Z*)-methyl α-cyano-β-methylcinnamate.[8] While both **12** and **13** develop blue colors upon irradiation (254 nm)[9] at 77 K, which attests to ylide formation, neither undergoes photoequilibration in benzene solution (254 nm, 40–80 °C), which is circumvented by an intramolecular photorearrangement. Upon irradiation of **12** and **13** in benzene (254 nm, 12 h), the product is methyl α-cyano-β-benzoylpropionate (**14**). Structural identification of **14** was achieved by independent synthesis.[17] It is believed that the enol ether **15** is implicated in the transformation of **12** (and/or **13**) to **14** and is formed by 1,4-proton transfer from the activated methyl to the carbanionic center of the ylide (Scheme II). Precedent exists for photoinduced 1,3-sigmatropic rearrangements such as **15** to **14.**[18] In addition, it is reported that this reaction may be induced thermally (180 °C).[8] Thus each step in the conversion **12** → **15** → **14** may be thermal in nature. Under milder conditions (120 °C), however, the formation of **15** together with **14** was observed by NMR. It is significant that no thermal equilibration of **12** to **13** is detectable below 120 °C. While isolation of the sensitive enol ether **15** was not attempted, evidence for its presence in solution was obtained by acid hydrolysis to acetophenone[6a] and conversion to **14** at higher temperature (130 °C). The signals for the enol ether **15,** present in the crude pyrolysate obtained from **12,** upon photolysis (254 nm, 40 °C) appear to decrease in intensity which suggests that in this system the conversion of **15** → **14,** as well as the formation of **15,** may also be induced photochemically.[18]

Experimental Section

General. Infrared spectra were determined on Perkin-Elmer Model 337 and 257 infrared spectrophotometers. ^{1}H NMR spectra were obtained on a Varian A-60 or Hitachi Perkin-Elmer R-20B spectrometer with 1% tetramethylsilane as an internal standard. A Hitachi Perkin-Elmer RMU-6E spectrometer was used for mass spectral analyses. Ultraviolet absorption spectra were recorded on a Cary Model 17 spectrophotometer. All melting points were established on a Büchi melting point apparatus and are uncorrected. Silica gel PF_{254} on microscope slides or glass plates was used for thin and thick layer chromatographic separation. Visualization was achieved by exposure of the chromatogram to short-wavelength ultraviolet light (Blak-Ray UVL-21) and/or developed in iodine vapor. A Griffin-Worden pressure vessel (Kontes Glass Co., Vineland, N.J.) was used for pressurized reactions. All combustion analyses for C, H, and N fell within acceptable limits of theoretical values and were performed by Galbraith Laboratories, Inc.

Preparation of (*E*)-Methyl α-Cyanocinnamate (5). The alkene **5** was synthesized (87%) by condensation of benzaldehyde (10.5 g, 0.1 mol) with methyl cyanoacetate (12 g, 0.12 mol) in methanol according to the procedure described by Rand and co-workers[7a] using potassium fluoride (2 g) as a catalyst.

Preparation of (*Z*)-Methyl α-Cyanocinnamate (6). The *E* isomer **5** (4 g, 0.02 mol) was dissolved in benzene (200 ml) and irradiated in a quartz vessel for a period of 12 h with a 254-nm source.[9] The photolysate was concentrated to a mixture containing **5** and **6** (1.5:1.0, respectively) which was not readily resolvable by chromatographic methods and was converted to the desired oxiranes **3a** and **4a** after preliminary purification, but without prior separation.

Photoisomerization of **5** to **6** may also be accomplished in cyclohexane in a Pyrex vessel using a 275-W cosmetic sunlamp as a light source; however, the ratio of **5:6** is only 4:1 after irradiation for 8 h under these conditions. The NMR spectrum, determined on the unseparated alkenes, differs significantly from tlhat reported earlier: NMR (CCl_4) δ 3.84 (s, 3 H, $-OCH_3$), 7.58 (s, 1 H, –CH).[7c]

Synthesis of the Isomeric Methyl α-Cyano-β-phenylglycidates (3a and 4, Respectively). A minor modification of the method of Robert and Pommeret[8] was utilized for the preparation of phenylglycidates **3a** and **4a.** To a solution of 4 g (0.021 mol) of the unresolved mixture of **3a** and **4a** dissolved in 50 ml of acetonitrile containing 4 ml of 1 M sulfuric acid was added dropwise 30 ml of aqueous sodium hypochlorite (household bleach, ~0.75 M) at 5 °C. The mixture obtained was allowed to stir (25 °C, 30 min) and was then diluted with water and the organic components isolated in the usual manner. The separation and purification of the oxiranes **3a** and **4a** were achieved by chromatography on silica gel. Oxirane **4a** (1.2 g) emerges first: mp 57–58 °C [$(C_2H_5)_2O$–C_6H_{14}]; ir (Nujol) 2240 (–CN), 1764 cm^{-1} (–CO); NMR ($CDCl_3$) δ 3.63 (s, 3 H, $-OCH_3$), 4.65 (s, 1 H, –CH); mass spectrum *m/e* 203 (M^+). Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.59. Found: C, 65.17; H, 4.47; N, 6.68. Elution of the isomer **3a** follows (~1.9 g): mp 55–56 °C [$(C_2H_5)_2O$–C_6H_{14}]; ir (Nujol) 2259 (–CN), 1735 cm^{-1} (–CO); NMR ($CDCl_3$) δ 3.91 (s, 3 H, $-OCH_3$), 4.60 (s, 1 H, –CH); mass spectrum *m/e* 203 (M^+). Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.59. Found: C, 64.87; H, 4.40; N, 6.82.

The trans isomer **3a** may be obtained directly from the *E* cinnamate using the method described above (78%) or by base-catalyzed oxidation using *m*-chloroperbenzoic acid (see below). The latter method is not adequate for epoxidation of mixtures of **5** and **6** because stereochemistry is not maintained (**3a:4a,** 4.6:1).

Preparation of (*E*)-Methyl α-Cyano-β-(2-naphthyl)acrylate (9). The acrylate **9** was prepared (93%) by condensation of 2-naphthaldehyde (15.6 g, 0.1 mol) with methyl cyanoacetate (12 g, 0.12 mol) according to the procedure described for **5:** mp 143 °C (CH_2Cl_2–C_6H_{14}); ir (Nujol) 2210 (–CN), 1738 cm^{-1} (–CO); NMR ($CDCl_3$) δ 3.94 (s, 3 H, $-OCH_3$), 8.30 (s, 1 H, –CH); mass spectrum *m/e* 237 (M^+). Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 76.09; H, 4.51; N, 5.87.

Oxidation of 9 to *trans*-Methyl α-Cyano-β-(2-naphthyl)glycidate (7). To a suspension of 2.4 g (0.01 mol) of α-cyanoacrylate **9** in 30 ml of methanol at 0 °C was added 2.1 g (0.012 mol) of 85% *m*-chloroperbenzoic acid and 2 ml of 1 N sodium methoxide. The mixture was then stirred at room temperature for 1 h at which time the alkene **9,** monitored by TLC, was consumed. Sufficient sodium bicarbonate was added and the reaction mixture was worked up in the conventional manner. The glycidate **7** was obtained in high yield after recrystallization of the crude product from a methylene chloride–hexane mixture (90%): mp 98–99 °C; ir (Nujol) 2250 (–CN), 1755 cm^{-1} (–CO); NMR ($CDCl_3$) δ 3.83 (s, 3 H, $-OCH_3$), 4.61 (s, 1 H, –CH); mass spectrum *m/e* 253 (M^+). Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.38; N, 5.53. Found: C, 70.90; H, 4.48; N, 5.47. The NMR spectrum of the cis glycidate formed upon photolysis of **8** is consistent with the assigned structure[10]: δ 3.53 (s, 3 H, $-OCH_3$) and 4.76 (s, 1 H, –CH).

Preparation of *trans*-Methyl α-Cyano-β-(3,4-dimethoxy-

phenyl)glycidate (10). The method described for the preparation of **7** also proved useful for the conversion of (*E*)-methyl α-cyano-β-(3,4-dimethoxycinnamate) to **10** (87%): mp 118 °C (CH_2Cl_2–C_6H_{14}); ir (Nujol) 2280 (–CN, weak), 1770 cm^{-1} (–CO); NMR ($CDCl_3$) δ 3.84 (br s, 6 H, $ArOCH_3$), 3.88 (s, 3 H, $-OCH_3$), 4.41 (s, 1 H, –CH); mass spectrum *m/e* 263 (M^+). Anal. Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32 Found: C, 59.44; H, 4.89; N, 5.27. The requisite cinnamate was prepared (94%) by condensation of veratraldehyde with methyl cyanoacetate according to the procedure described earlier for the synthesis of the *E* cinnamate **5:** mp 123 °C (CH_2Cl_2–C_6H_{14}); ir (Nujol) 2210 (–CN), 1737 cm^{-1} (–CO); NMR ($CDCl_3$) δ 3.92 (br s, 6 H, $ArOCH_3$), 3.90 (s, 3 H, $-OCH_3$), 8.08 (s, 1 H, –CH); mass spectrum *m/e* 247 (M^+). Anal. Calcd for $C_{13}H_{13}NO_5$: C, 63.15; H, 5.30; N, 5.66. Found: C, 63.35; H, 5.23; N, 5.60.

The NMR of the cis dimethoxyglycidate formed upon sensitized photoequilibration of **10** is consistent with the assigned structure:[10] NMR ($CDCl_3$) δ 3.40 (s, 3 H, $-OCH_3$), 3.70 (br s, 6 H, $ArOCH_3$), 4.62 (s, 1 H, –CH).

Irradiation of the Trans Cyanonaphthylglycidate 7 in Isobutylene–Benzene Solution. A solution of **7** in benzene (0.03 M) saturated with isobutylene was irradiated for 5 h at 40 °C using a 350-nm source.[9] A filter was introduced consisting of a saturated solution of naphthalene in benzene or a uranyl glass sleeve. Both were sufficiently opaque to reduce direct absorption by **7** to an insignificant level. Upon addition of benzophenone (0.05 M) as a sensitizer, however, essentially complete conversion (>95%) to the adduct(s) **11** occurs as evidenced by NMR data. NMR ($CDCl_3$, major isomer) δ 1.08 (s, 3 H, CH_3–), 1.52 (s, 3 H, CH_3–), ~2.2 (m, 2 H, $-CH_2$–), 3.80 (s, 3 H, OCH_3), and ~5.4 (m, 1 H, –CH); ($CDCl_3$, minor isomer) 1.17 (s, 3 H, CH_3–), 1.49 (s, 3 H, CH_3–), ~2.2 (m, 2 H, $-CH_2$–), 3.80 (s, 3 H, OCH_3), and ~5.4 (m, 1 H, CH).

Preparation of the Isomeric Methyl α-Cyano-β-methyl-β-phenylglycidates (12 and 13). A mixture of (*E*)- and (*Z*)-methyl β-methylcinnamates was prepared by the conventional ondensation utilizing ammonium acetate as a catalyst. The isomeric products were isolated by distillation, bp 130–131 °C (0.4 mm) [lit.[19] 150–165 °C (0.9 mm)]. The NMR spectrum is in agreement with reported values.[7c]

A sample of the mixtures of cinnamates (2.1 g, 0.01 mol) was oxidized in the manner described for **3a** and **4a,** and the resulting oxiranes **12** and **13** resolved by column chromatography. The cis oxirane **13** (0.81 g, 3.7 mmol, 37%) eluted first and was obtained as an oil: ir (liquid film) 2260 (–CN), 1776 and 1740 cm^{-1} (–CO); NMR ($CDCl_3$) δ 1.94 (s, 3 H, CH_3) and 3.43 (s, 3 H, OCH_3); mass spectrum *m/e* 217 (M^+). Elution of the trans isomer **12** (1.17 g, 5.4 mmol, 54%) follows: mp 74–75 °C [$(C_2H_5)_2O$–C_6H_{14})]; ir 2260 (–CN), 1738 cm^{-1} (–CO); mass spectrum *m/e* 217 (M^+).

Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.14; H, 5.11; N, 6.37.

Preparation of an Authentic Sample of Methyl α-Cyano-α-benzoylpropionate (14). A solution of 2.0 g (0.01 mol) of phenacyl bromide was added dropwise to 10 ml of a 1 N solution of sodium methoxide containing 1.0 g (0.01 mol) of methyl cyanoacetate. The resulting mixture was allowed to stand for 2 h at room temperature and quenched with water. The organic products were then extracted with ethyl acetate and worked up in the conventional manner.

The crude residual product was purified by chromatography on silica gel and recrystallized from ether–hexane mixtures to give 0.68 g (30%) of the propionate **14:** mp 58–59 °C; ir 2250 (–CN), 1748 (–COOR), 1668 cm^{-1} (PhCO–); NMR ($CDCl_3$) δ 3.78 (s, 3 H, $-OCH_3$) and 3.5–4.2 (m, 3 H, $-CH_2$, –CH–); mass spectrum *m/e* 217 (M^+).

Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.50; H, 5.12; N, 6.41.

Pyrolysis of *trans*-Methyl α-Cyano-β-methyl-β-phenylglycidate (12). A solution of 200 mg of the oxirane **12** was heated in benzene at 120 °C for 12 h. The NMR spectrum of the crude pyrolysate revealed new signals at δ 4.42 (d, 1 H), 4.97 (d, 1 H), and 5.29 (s, 1 H), which are attributed to the enol ether **15** together with peaks of **12** and **14.**

Acknowledgment. The authors are indebted to the National Science Foundation (Grant MPS75-14831) and the Army Research Office, Durham (Grant ARO-D-31-124-73-G4), for support of this work. We also wish to thank Dr. E. Elder and Ms. J. Thompson for aid in the preparation of the manuscript and Mr. Steve Spera for technical assistance.

Registry No.—**3a,** 60239-39-6; **4a,** 60239-40-9; **5,** 14533-86-9; **6,** 14533-85-8; **7,** 60239-41-0; **9,** 60239-42-1; **10,** 60239-43-2; *cis*-**10,** 60239-44-3; *cis*-**11,** 60239-46-5; *trans*-**11,** 60239-45-4; **12,** 0239-47-6; **13,** 60239-48-7; **14,** 22984-73-2; **15,** 60239-49-8; 2-naphthaldehyde, 42007-10-3; methyl cyanoacetate, 105-34-0; isobutylene, 115-11-7; (*E*)-methyl β-methylcinnamate, 3461-50-5; (*Z*)-methyl β-methylcinnamate, 26423-89-2; phenacyl bromide, 70-11-1.

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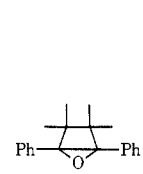
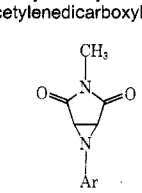


16



17

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The Unusually Mild and Facile Basic Hydrolysis of *N*-Nitroso-2-(methylamino)acetonitrile[1]

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Received April 21, 1976

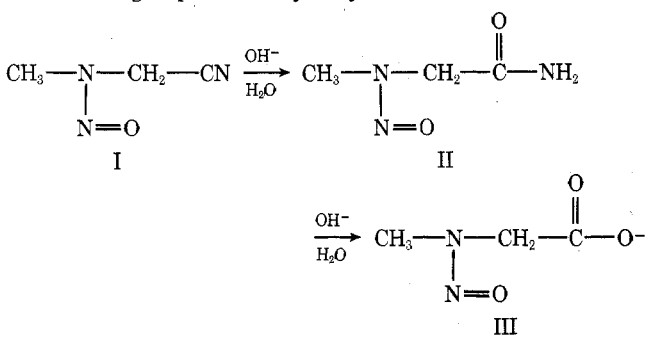
At pH 13 and room temperature, *N*-nitroso-2-(methylamino)acetonitrile (I) undergoes two unusually fast and successive hydrolytic changes that can be detected quantitatively by differential pulse polarography. The final hydrolysis product is *N*-nitrososarcosine (III), via the intermediate amide (II). The kinetics and activation parameters of the transformations have been determined. A mechanism has been proposed to account for these rapid reactions involving anchimeric assistance to the hydrolyses by the appropriately placed nitroso group. Isotopic labeling studies using ^{18}O enriched water and mass spectrometry confirm the proposed mechanism involving exclusive attack on carbon by hydroxide ion.

During the course of electroanalytical studies of a series of *N*-nitrosamines using differential pulse polarography,[2] one *N*-nitrosamine displayed unusual behavior. In aqueous solution at pH 13, *N*-nitroso-2-(methylamino)acetonitrile (I) displayed the anticipated current–potential peak at a negative potential vs. the saturated calomel electrode (SCE) but the expected peak was followed by a second peak, an unusual result for a *N*-nitrosamine.[2] In addition to the second peak, the situation was even more unusual by the observation that the peaks varied in height in some regular way as a function of time. A careful study yielded the results shown in Figure 1 where curves 1–5 are the results of repetitive scans on the same solution recorded over a period of approximately 200 min. Since the peak potential (E_p) of a *N*-nitrosamine is a function of pH and molecular structure, the results suggested that a chemical change was occurring resulting possibly in the formation of nitrosamines different from the original.

In this paper we report the results of an investigation to interpret the observed changes.

As Figure 1 shows, the initial scan yields two peaks at −1.26 and −1.42 V vs. SCE. The second scan taken about 5 min later shows a decrease in the first peak and an increase in the second with the suggestion of a third ill-defined peak at a more negative potential. Curve 5, recorded about 200 min after curve 1, shows that the species giving rise to the peaks at −1.26 and −1.42 V have completely disappeared; the only species left is that giving rise to the ill-defined peak at about −1.8 V.

Although it is well known that nitriles do not undergo basic hydrolysis rapidly at room temperature,[3] the most logical hypothesis to explain the polarographic results seemed to be the following sequence of hydrolytic reactions:



The final product (III) in the suggested sequence is the anion of *N*-nitrososarcosine. To establish the validity of the hydrolysis sequence, *N*-nitrososarcosine was prepared[4] and its properties were compared with those of the final hydrolysis product (III).

Figure 2, curve 1, shows the differential pulse polarogram obtained after acidifying (pH 1) the solution that yielded curve 5, Figure 1. The anodic shift of E_p with lower pH is characteristic of *N*-nitrosamines.[2,5] Curve 2, Figure 2, was obtained after addition of authentic *N*-nitrososarcosine to the solution that yielded curve 1. The increase in peak height without shift in potential strongly suggested that *N*-nitrososarcosine is the electroactive species in Figure 2, curve 1.

Since the polarograms were run on dilute solutions (ca. 10^{-4} M) and product isolation and identification would be difficult, reactions modeled after the polarographic runs were repeated on a preparative scale. The organic product was isolated by evaporation of the water and extraction of the residue with acetone. Evaporation of the acetone yielded a yellow oil which crystallized only after being held at 0 °C overnight. (In some cases the oil did not crystallize.) The crystals had a melting point of 66–67 °C. The melting point and crystallization behavior are those previously reported for nitrososarcosine.[4]

This result confirms the findings of Lijinsky et al. concerning the melting point of this compound as contrasted to the values of 73–74 °C reported by Hammick et al.[6] and 75–77 °C reported by Bergel et al.[7]

To confirm the identity of the hydrolysis product, the NMR, uv, and ir spectra of the final product were obtained; they were identical with those of authentic *N*-nitrososarcosine (Tables I and II). These results show unequivocally that the final product was, in fact, *N*-nitrososarcosine.

The unnitrosated parent amine, 2-(methylamino)acetonitrile, was subjected to the same alkaline reaction conditions as I. No change occurs over a period of 48 h, as would be expected for a simple nitrile. Thus, the *N*-nitroso group in I is clearly having an unusual activating effect on the nitrile group. To understand this effect, the kinetics of the reactions were determined using the rate of decay of the peak currents in the differential pulse polarograms. Both reactions (I → II and II → III) are second order overall, first order in nitrosamine and first order in OH^-. Rate constant data and calculated activation parameters are given in Table III. The most significant