Photooxygenation of Aziridines and Some Potential Azomethine Ylides

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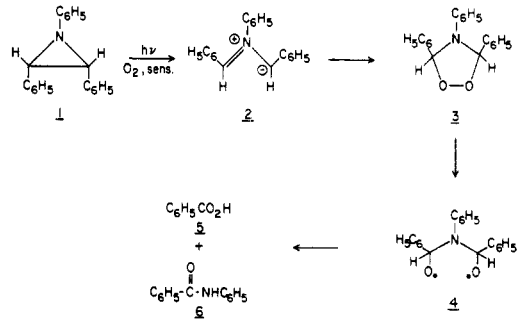
Sensitized photooxygenations of a few bicyclic aziridines and some potential azomethine ylides have been investigated. The photooxygenation of 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine (**7**) gave a 51% yield of 2-cyclohexyl-3-hydroxy-3-phenylphthalimidine (**12**). The photooxygenation of *endo*-2,4,6-triphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene (**13**), on the other hand, gave a mixture of products consisting of benzaldehyde (**16**, 5%), benzoic acid (**5**, 16%), and benzamide (**19**, 7%). Other substrates that we have examined include 2,3-dihydro-5,6-diphenylpyrazine (**22**), *cis*-2,4,5-triphenylimidazoline (**33a**), and 4-benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyloxazoline (**42**). The photooxygenation of **22**, for example, gave a 22% yield of 1,3-dibenzoylurea (**32**), whereas **33a**, under analogous conditions, gave a mixture of products consisting of 2,5,5-triphenylimidazolin-4-one (**40**, 7%), dibenzamide (**36**, 8%), and benzamide (**19**, 21%). The photooxygenation of **42** gave a mixture of products consisting of benzoic acid (**5**, 52%) and *N*-cyclohexylbenzamide (**45**, 19%), whereas the direct photolysis of **42** under nitrogen atmosphere gave a 65% yield of 3,5,6-triphenyl-2*H*-pyran-2-one (**50**). Reasonable mechanisms have been suggested for the formation of the different products in these reactions.

Although numerous examples of 1,3-dipolar additions of different substrates with various dipolarophiles are reported in the literature, there are only a few reported cases of the use of singlet oxygen as dipolarophile in such addition reactions. Thus, it has been observed by Higley and Murray[3] that diazoalkanes, when photooxygenated with singlet oxygen in the presence of aldehydes, give rise to ozonides. It has been suggested that diazoalkanes in these reactions combine with singlet oxygen to give the corresponding dioxadiaza derivatives, which then undergo subsequent transformation to the corresponding ozonides. Takeshita et al.[4] have examined the reactions of certain pyridinium betaines with singlet oxygen and have found that a variety of products are formed in these cases, depending on the reaction conditions. Foote and Ching[5] have shown that nitrones react with singlet oxygen to give addition products, which may undergo further transformations depending on the nature of the substrates. Thus, it has been shown that 2,4,4-trimethyl-Δ^1-pyrroline *N*-oxide reacts with singlet oxygen in deuteriochloroform solution at −63 °C to give a nearly quantitative yield of a hydroperoxide derivative.

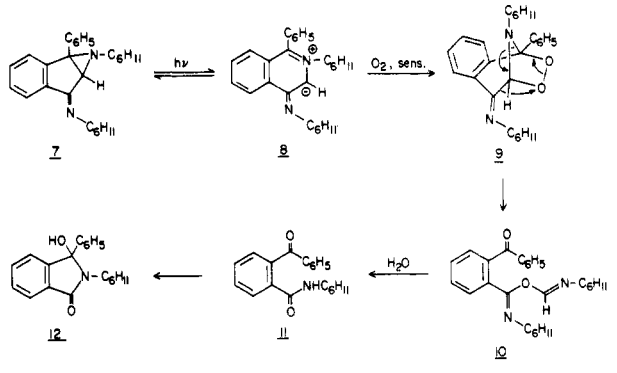
Quite recently we have shown that aziridines undergo photooxygenations to give a variety of products, depending on the nature of the substituents present in the aziridine ring.[6] Thus, it has been shown that 1,2,3-triphenylaziridine (**1**), for example, on photooxygenation gives a mixture of products consisting of benzoic acid (**5**) and benzanilide (**6**). The formation of these products has been rationalized in terms of the reaction of the azomethine ylide (**2**), formed from **1** under photochemical conditions, with singlet oxygen to give the 1,2,4-dioxazolidine intermediate **3**, which then is transformed to the products **5** and **6** through the diradical intermediate **4**, as shown in Scheme I.

The object of the present investigation has been to study the photooxygenations of a few bicyclic aziridines and other similar substrates, which can give rise to azomethine ylides under photochemical conditions. The bicyclic aziridines that we have examined include 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine (**7**) and *endo*-2,4,6-triphenyl-1,3-diazabicyclo[3.4.0]hex-3-ene (**13**).

Scheme I



Scheme II



Results and Discussion

Irradiation of a methanol solution of 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine (**7**), containing a small amount of Rose Bengal, in the presence of oxygen for 0.75 h gave a 51% yield of 2-cyclohexyl-3-hydroxy-3-phenylphthalimidine (**12**) as the only insolable product. The structure of **12** was confirmed by comparison of its spectral data with that of an authenic sample prepared through a reported procedure.[7] The formation of the phthalimidine **12** in the photooxygenation of **7** can be

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(2) This is Document No. NDRL-2016 from the Notre Dame Radiation Laboratory.

(3) D. P. Higley and R. W. Murray, *J. Am. Chem. Soc.*, **96**, 3330 (1974).

(4) H. Takeshita, A. Mori, and S. Ohta, *Bull. Chem. Soc. Jpn*, **47**, 2437 (1974); see also, Y. Tamura, M. Akita, H. Kiyokawa, L. C. Chen, and H. Ishibashi, *Tetrahedron Lett.*, 1751 (1978).

(5) C. S. Foote and T. Y. Ching, *Tetrahedron Lett.*, 2771 (1975).

(6) V. Bhat and M. V. George, *Tetrahedron Lett.*, 4133 (1977).

(7) P. Truitt, L. R. Brammer, and L. T. Creagh, *J. Med. Chem.*, 8, 731 (1965).

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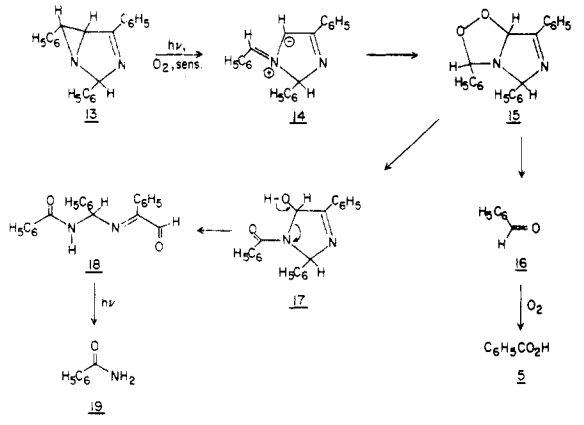
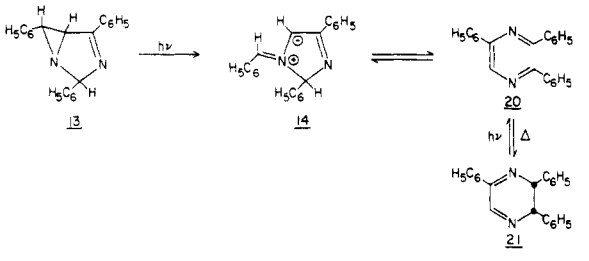
Scheme III



Scheme IV



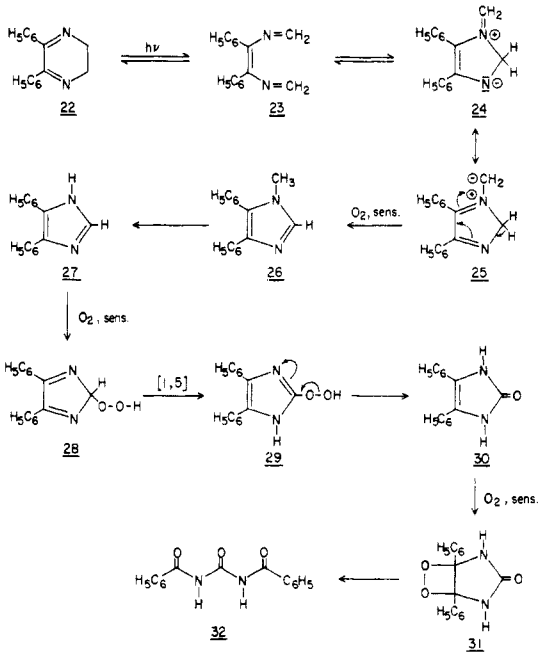
rationalized in terms of a pathway suggested by Padwa and Vega[8] and shown in Scheme II. It may be pointed out here that Padwa and Vega had reported that the photolysis of **7** in the presence of oxygen leads to a 10% yield of 2-benzoyl-*N*-cyclohexylbenzamide (**11**), formed through the hydrolysis of the intermediate **10** under the reaction conditions. However, we have observed that under our conditions the cyclic form **12** is isolated.[9]

The photooxygenation of *endo*-2,4,6-triphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene (**13**), on the other hand, gave rise to a mixture of products consisting of benzaldehyde (**16**, 5%), benzoic acid (**5**, 16%), and benzamide (**19**, 7%). The formation of these products can be rationalized in terms of the pathway shown in Scheme III. Padwa and Glazer[10] have shown that a bicyclic aziridine such as **13** undergoes photochemical ring opening to give the dipolar intermediate **14**, which in turn is converted to the enediimine intermediate **20** and can also be obtained by the photochemical ring opening of the corresponding 2,3-dihydropyrazine derivative **21** (Scheme IV).

Further, it has been observed that the formation of the dipolar intermediate **14** from **13** is more favored in a solvent like methanol, whereas in aprotic solvents like benzene, the formation of the enediimine isomer **20** is preferred. It would be reasonable to assume that the dipolar intermediate **14** formed from **13** will undergo further reaction with singlet oxygen to give the peroxy intermediate **15**, which in turn can undergo further fragmentation as shown in Scheme III to give benzaldehyde (**16**) and benzamide (**19**). The formation of benzoic acid from **13** may be rationalized in terms of the further oxidation of benzaldehyde, formed in this reaction.

With a view to ascertaining whether an enediimine intermediate like **20** is involved in the photooxygenation of **13**, we thought it worthwhile to examine the photooxygenation of a representative dihydropyrazine, namely 2,3-dihydro-5,6-diphenylpyrazine (**22**). Photooxygenation

Scheme V

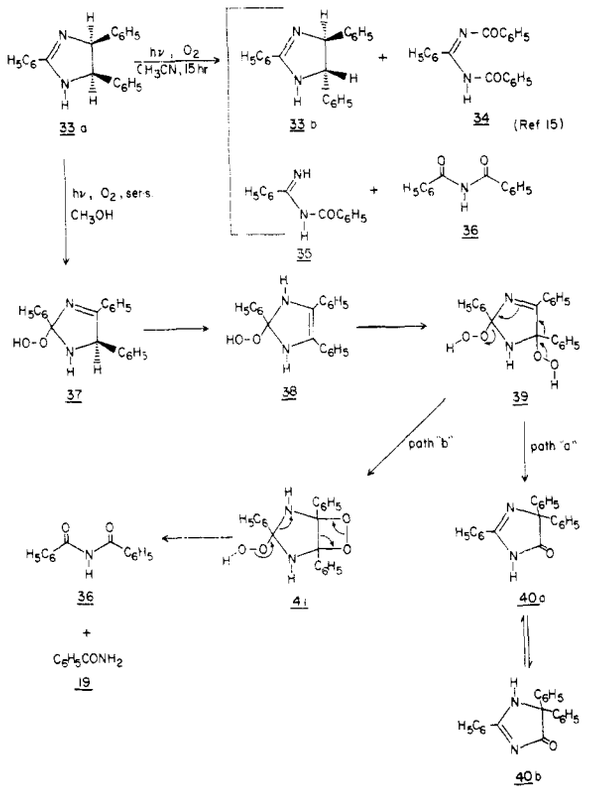


of a solution of **22** in a mixture of benzene and methanol and in the presence of small amounts of Rose Bengal gave a 22% yield of 1,3-dibenzoylurea (**32**) as the sole product. A probable pathway for the formation of **32** from **22** and involving intermediates like **26**, **27**, and **30** is shown in Scheme V. The formation of 1-methyl-4,5-diphenylimidazole (**26**) as an intermediate in the reaction of **22** is similar to the phototransformations of dihydropyrazines to the corresponding imidazole derivatives.[11] It would be reasonable to assume that **26** will undergo photooxygenation in the presence of singlet oxygen to give the demethylated derivative **27**. It is pertinent to note that several examples of such demethylation reactions are reported in the literature.[12-14] The imidazole **27** can subsequently undergo an ene-type of reaction with singlet oxygen to give the hydroperoxy intermediate **28**, which can then be transformed to the imidazolone derivative **30**. In the presence of singlet oxygen, the imidazolone **30** would be expected to undergo further transformation to the peroxy derivative **31**, which could then give rise to 1,3-dibenzoylurea (**32**) (Scheme V). In this connection, it may be pointed out that the imidazolones of the type **30** are known to undergo ready cleavage in the presence of singlet oxygen to give the corresponding tricarbonyl derivatives.[15]

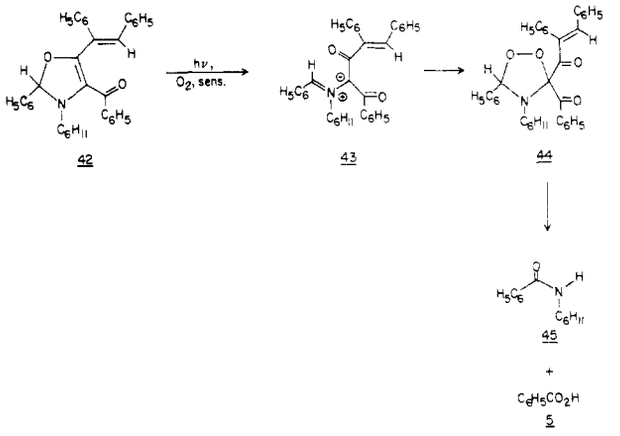
If 1-methyl-4,5-diphenylimidazole (**26**) and 4,5-diphenylimidazole (**27**) are involved as intermediates in the transformation of **22** to **32**, as shown in Scheme V, then it would be reasonable to assume that the photooxygenations of both **26** and **27** under analogous conditions should lead to 1,3-dibenzoylurea (**32**). To test this possibility. we have examined the photooxygenations of both **26** and **27** in separate experiments. Photooxygenation of **26** for 0.5 h in a mixture of benzene and methanol and using Rose Bengal as sensitizer gave a 23% yield of **32**. Similarly, the photooxygenation of **27** under identical conditions gave a 53% yield of **32**. The formation of **32** in the photo-

(8) A. Padwa and E. Vega, *J. Org. Chem.*, **40**, 175 (1975).
(9) W. Graf, E. Girod, E. Schmid, and W. G. Stoll, *Helv. Chim. Acta*, **42**, 1085 (1959).
(10) A. Padwa and E. Glazer, *J. Am. Chem. Soc.*, **94**, 7788 (1972).
(11) P. Beak and J. L. Miesel, *J. Am. Chem. Soc.*, **89**, 2375 (1967).
(12) M. H. Fisch, J. C. Gramain, and J. Olesen, *Chem. Commun.*, 13 (1970).
(13) M. H. Fisch, J. C. Gramain, and J. Olesen, *Chem. Commun.*, 663 (1971).
(14) J. H. E. Lindner, H. J. Kuhn, and K. Gollnick, *Tetrahedron Lett.*, 1705 (1972).
(15) H. H. Wasserman, *Ann. N.Y. Acad. Sci.*, **171**, 108 (1970).

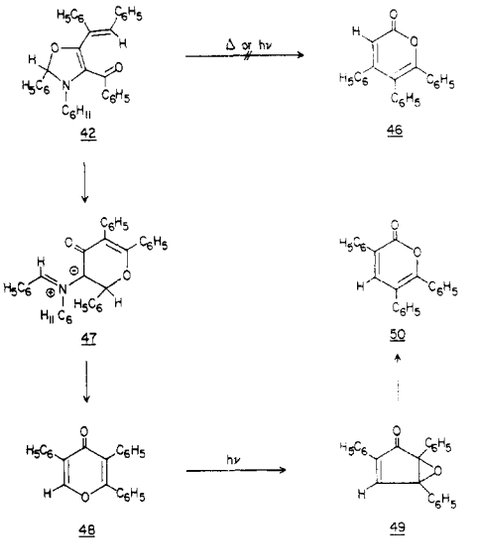
Scheme VI



Scheme VII



Scheme VIII



oxygenations of both **26** and **27** is in support of the mechanism that has been suggested for the transformation of **22** to **32** (Scheme V).

In continuation of our studies, we have examined the photooxygenation of a few substrates which would be expected to give rise to azomethine ylide intermediates under photochemical conditions. In this connection, we have examined the photooxygenations of both *cis*-2,4,5-triphenylimidazoline (**33a**) and 4-benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (**42**). It has been shown by Matsuura and Ito that both *cis*- and *trans*-2,4,5-triphenylimidazolines (**33a** and **33b**), on photolysis in either acetonitrile or benzene solution, give rise to a photostationary mixture of products consisting of **33a** and **33b** in each case.[16,17] These authors have suggested that the initial steps in the phototransformation of either **33a** or **33b** involves the formation of a common azomethine ylide, which then recyclizes to give the mixture of isomers consisting of both **33a** and **33b** in each case. In the course of the present studies, we have observed that the photooxygenation of *cis*-2,4,5-triphenylimidazoline (**33a**) in a mixture of methanol and benzene gave a mixture of products consisting of 2,5,5-triphenylimidazolin-4-one (**40**, 7%), dibenzamide (**36**, 8%), and benzamide (**19**, 21%). The formation of these different products in the photooxygenation of **33a** can be rationalized in terms of the reaction pathway shown in Scheme VI. It has been assumed that **33a** undergoes an "ene-type" of reaction with singlet oxygen to give the hydroperoxy intermediate **37**, which can be subsequently transformed to the bis(hydroperoxy) intermediate **39** through further reaction with singlet oxygen. The intermediate **39** can undergo a fragmentation accompanied by a rearrangement involving a phenyl group migration as per path a shown in Scheme VI to give the imidazolone **40**, which can exist in equilibrium between its tautomeric forms **40a** and **40b**. An alternative mode of transformation is through path b, which involves the formation of the intermediate **41**, which can undergo fragmentation to dibenzamide **36** and benzamide (**19**), as shown in Scheme VI. It is interesting to note that the unsensitized photooxygenation of imidazoline **33a** in acetonitrile has been reported to give a mixture of products consisting of the *trans*-imidazoline **33b**, *N*,*N*′-dibenzoylbenzamidine (**34**), *N*-benzoylbenzamidine (**35**), and dibenzamide (**36**). It is thus apparent that the reaction of **33a** with singlet oxygen under sensitized conditions gives rise to different products, as compared to those derived from the photooxidation of **33a** under sensitized conditions.

The dye-sensitized photooxygenation of an oxazoline, such as 4-benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (**42**), gave rise to a mixture of products consisting of *N*-cyclohexylbenzamide (**45**, 19%) and benzoic acid (**5**, 52%). The formation of both **45** and **5** in this reaction may be rationalized in terms of the pathway shown in Scheme VII and involving intermediates such as **43** and **44**. Lown and co-workers[18] had earlier reported that the oxazoline **42** undergoes transformation both under direct, unsensitized irradiation and thermal conditions to give poor yields of a yellow solid, which they had tentatively characterized as 3,4,5-triphenyl-2*H*-pyran-2-one (**46**) (Scheme VIII). We felt that the for-

(16) T. Matsuura and Y. Ito, *Chem. Lett.*, 431 (1972).
(17) T. Matsuura and Y. Ito, *Bull. Chem. Soc. Jpn.*, 48, 3669 (1975).
(18) J. W. Lown, R. K. Smalley, G. Dallas, and J. W. Maloney, *Can. J. Chem.*, 48, 103 (1970).

mation of the α-pyrone **46** from **42** would be rather difficult to rationalize in terms of straightforward mechanistic reasonings and hence felt that the structure of **46** may need further confirmation. With this view, we have reexamined both the photolysis and thermolysis of the oxazoline **42**. Irradiation of a benzene solution of **42** for 2.5 h gave a 65% yield of a bright yellow solid, mp 147–148 °C and exhibiting the spectral characteristics of **46**, as reported by the earlier workers.[18] The mass spectrum of this product, however, was quite revealing in that it showed a peak at *m/e* 105, characteristic of 2*H*-pyran-2-ones, having a phenyl substituent at the C_6 position.[19-21] On the basis of the mass spectral data and other spectral evidences, we reasoned that the 2*H*-pyran-2-one obtained from **42** is correctly represented as 3,5,6-triphenyl-2*H*-pyran-2-one (**50**) and not **46**, as suggested by earlier workers. Further confirmation of the structure of **50** was, however, derived by its comparison with an authentic sample of 3,5,6-triphenyl-2*H*-pyran-2-one (**50**), prepared by a reported procedure.[22]

It has been observed that the thermolysis of the oxazoline **42** by refluxing it in toluene for 48 h also gives rise to 3,5,6-triphenyl-2*H*-pyran-2-one (**50**) although formed in poor yields (6%).

A reasonable pathway for the formation of the pyrone **50** from the oxazoline **42** under photochemical conditions may involve the 4*H*-pyran-4-one **48** as an intermediate, which could then undergo further transformation to **50** as shown in Scheme VIII. It may be pointed out here that 4*H*-pyran-4-ones, in general, are known to undergo facile phototransformations, leading to the corresponding 2*H*-pyran-2-ones.[23]

Experimental Section

All melting points are uncorrected and were determined on a Mel-Temp melting point apparatus. The IR spectra were recorded on Perkin-Elmer, Model 137 and Model 521 infrared spectrometers. NMR traces were recorded on a Varian A-60 NMR spectrometer using tetramethylsilane as internal standard. The mass spectra were recorded on a Hitachi RMU-6E, single focusing mass spectrometer. All photooxygenation experiments were carried out using a Hanovia 450-W, medium pressure, mercury lamp in a quartz-jacketed immersion well.

Starting Materials. 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine (**7**)[24] (mp 159–160 °C), *endo*-2,-4,6-triphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene (**13**)[10] (mp 143–144 °C), 2,3-dihydro-5,6-diphenylpyrazine (**22**)[25] (mp 162–163 °C), 1-methyl-4,5-diphenylimidazole (**26**)[26] (mp 147 °C), 4,5-diphenylimidazole (**27**)[27] (mp 227 °C), *cis*-2,4,5-triphenylimidazoline (**33a**)[28] (mp 136 °C), and 4-benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (**42**)[29](mp 162–163 °C) were prepared by reported procedures. Benzene, acetone, and methanol used were purified and dried before use, employing standard procedures. Petroleum ether used was the fraction, bp 60–80 °C.

Photooxygenation of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine (7). To a benzene solution of 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]-aziridine (**7**, 1.0 g, 2.6 mmol, in 400 mL) was added a solution of Rose Bengal (0.03 g) in methanol (10 mL). The solution was bubbled with oxygen gas for 15 min and then irradiated for 0.75 h, under a slow stream of oxygen bubbling. The photooxygenation experiment was repeated once more so as to photolyze in all 2.0 g (5.2 mmol) of **7** and the product mixtures were combined together. Removal of the solvent under reduced pressure gave a viscous residue which was chromtographed over silica gel. Elution of the column with a mixture (1:19) of ethyl acetate and benzene gave 0.41 g (51%) of 2-cyclohexyl-3-hydroxy-3-phenylphthalimidine (**12**), mp 224–226 °C. There was no depression in its melting point when mixed with an authentic sample.[7]

Further elution of the column with a mixture (1:19) of ethyl acetate and benzene gave 0.11 g (16%) of benzoic acid (**5**), mp 121–122 °C (mixture melting point).

Continued elution of the column with the same solvent mixture gave 0.05 g (7%) of benzamide (**19**), mp 127–128 °C (mixture melting point).

Photooxygenation of 2,3-Dihydro-5,6-diphenylpyrazine (22). A solution containing 2,3-dihydro-5,6-diphenylpyrazine (**22**, 1.0 g, 4.25 mmol) in benzene (450 mL) was presaturated with oxygen gas and then irradiated for 0.5 h under oxygen bubbling. The photooxygenation was repeated again under identical conditions and the product mixtures were combined together. Removal of the solvent under reduced pressure gave a viscous material, which was chromatographed over silica gel. Elution with a mixture (1:4) of ethyl acetate and benzene gave 0.5 g (22%) of 1,3-dibenzoylurea (**32**), mp 216–217 °C. There was no depression in the melting point of **32** when mixed with an authentic sample.[30]

Photooxygenation of 1-Methyl-4,5-diphenylimidazole (26). A solution of **26** (0.40 g, 1.7 mmol) in benzene (200 mL) was mixed with a solution of Rose Bengal (0.05 g) in methanol (10 mL) and the mixture was irradiated for 0.5 h under a slow stream of oxygen bubbling. Removal of the solvent under vacuum gave a red residual solid, which on fractional crystallization from acetone yielded 0.11 g (23%) of 1,3-dibenzoylurea (**32**), mp 216–217 °C (mixture melting point).

Photooxygenation of 4,5-Diphenylimidazole (27). A solution containing 4,5-diphenylimidazole (0.45 g, 2 mmol) in benzene (200 mL) and Rose Bengal (0.01 g) in methanol (10 mL) was irradiated under oxygen bubbling for 0.5 h. Removal of the solvent under vacuum gave a residual mass, which on fractional crystallization from acetone gave 0.3 g (53%) of 1,3-dibenzoylurea, mp 216–218 °C (mixture melting point).

Photooxygenation of *cis*-2,4,5-Triphenylimidazoline (33a). A solution of *cis*-2,4,5-triphenylimidazoline (**33a**) (0.90 g, 3 mmol) in benzene (450 mL) and Rose Bengal (0.05 g) in methanol (10 mL) was irradiated for 4 h under a slow stream of oxygen bubbling. Removal of the solvent under vacuum gave a residue which was chromatographed over silica gel. Elution with a mixture (1:1) of benzene and petroleum ether gave 0.13 g (7%) of 2,5,5-triphenylimidazolin-4-one (**40**), mp 223–224 °C. There was no depression in the melting point of **40** when mixed with an authentic sample.[31]

Further elution of the column with benzene gave 0.11 g (8%) of dibenzamide (**36**), mp 153–154 °C (mixture melting point).

Subsequent elution of the column with a mixture (19:1) of benzene and ethyl acetate gave 0.15 g (21%) of benzamide (**19**), mp 127–128 °C (mixture melting point).

Photooxygenation of 4-Benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (42). A solution of 4-benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (**42**, 0.80 g, 1.56 mmol) in benzene (450 mL) was mixed with a solution of Rose Bengal (0.02 g) in methanol (10 mL). After bubbling the solution with oxygen for 10 min, it was irradiated for 20 min under oxygen bubbling. The photooxygenation was repeated again to photolyze in all 1.6 g (3.12 mmol) of the oxazoline **42**. Removal of the solvent under vacuum gave an oily residue which was dissolved in chloroform (50 mL) and then extracted with a saturated solution of sodium bicarbonate (50 mL). The

(19) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San Francisco, Calif., 1967, p 208.
(20) Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds", Wiley-Interscience, New York, 1974, p 139.
(21) M. M. Bursey, L. Dusold, and A. Padwa, *Tetrahedron Lett.*, 2649 (1967).
(22) E. F. Ullman, *J. Am. Chem. Soc.*, **85**, 3529 (1963).
(23) For some examples of the photoisomerization of 4*H*-pyran-4-ones to 2*H*-pyran-2-ones, see (a) N. Isibe, M. Odani, and M. Sunami, *Chem. Commun.*, 1034 (1971); (b) N. Ishibe, M. Sunami, and M. Odani, *J. Am. Chem. Soc.*, **95**, 468 (1973).
(24) N. H. Cromwell and M. C. McMaster, *J. Org. Chem.*, **32**, 2145 (1967).
(25) L. H. Amundsen, *J. Chem. Educ.*, **16**, 567 (1939).
(26) A. Pinner, *Ber. Dtsch. Chem. Ges.*, **35**, 4131 (1902).
(27) D. Davidson, M. Weiss, and M. Jelling, *J. Org. Chem.*, **3**, 319 (1938).
(28) O. F. Williams and J. C. Bailor, Jr., *J. Am. Chem. Soc.*, **81**, 4464 (1959).
(29) J. W. Lown, R. K. Smalley, G. Dallas, and J. W. Maloney, *Can. J. Chem.*, **48**, 89 (1970).
(30) R. H. Terss and M. E. McWen, *J. Am. Chem. Soc.*, **76**, 580 (1954).
(31) G. Rio and A. Ranjon, *Bull. Soc. Chim. Fr.*, 543 (1958).

aqueous layer was neutralized with dilute hydrochloric acid to give 0.5 g (52%) of benzoic acid (**5**), mp 121–122 °C (mixture melting point). The chloroform extract was dried over anhydrous sodium sulfate and the solvent was removed under vacuum to give a viscous residue which was chromatographed over silica gel. Elution with benzene gave 0.12 g (19%) of *N*-cyclohexylbenzamide (**45**), mp 147 °C (mixture melting point).

Photolysis of 4-Benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (42). A solution of **42** (1.0 g, 2 mmol) in benzene (600 mL) was flushed with oxygen-free nitrogen gas for 0.5 h and then it was irradiated for 2.5 h. Removal of the solvent under vacuum gave an oily residue which was chromatographed over silica gel. Elution with a mixture (4:1) of petroleum ether and benzene gave 0.41 g (65%) of 3,5,6-triphenyl-2*H*-pyran-2-one (**50**), mp 147–148 °C. There was no depression in the melting point of **50** when mixed with an authentic sample.[22]

Thermolysis of 4-Benzoyl-3-cyclohexyl-5-(*cis*-1,2-diphenylvinyl)-2-phenyl-4-oxazoline (42). A solution of **42** (0.50 g, 1 mmol) in toluene (40 mL) was heated under reflux for 48 h. Removal of the solvent under vacuum gave a viscous material which on treatment with benzene gave 15 mg of a benzene-insoluble material, mp 282–284 °C, which has not been characterized.

The mother liquor, after concentration, was chromatographed over alumina. Elution with a mixture (1:1) of benzene and petroleum ether gave 30 mg of an unidentified product, mp 179–181 °C, after recrystallization from benzene.

Further elution of the column with benzene gave 20 mg (6%) of 3,5,6-triphenyl-2*H*-pyran-2-one (**50**), mp 147–148 °C, after recrystallization from methanol. There was no depression in the melting point of this product when mixed with an authentic sample of **50**.[22]

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Thiophene Systems. 2. Synthesis and Chemistry of Some 4-Alkoxy-3-substituted Thiophene Derivatives[1]

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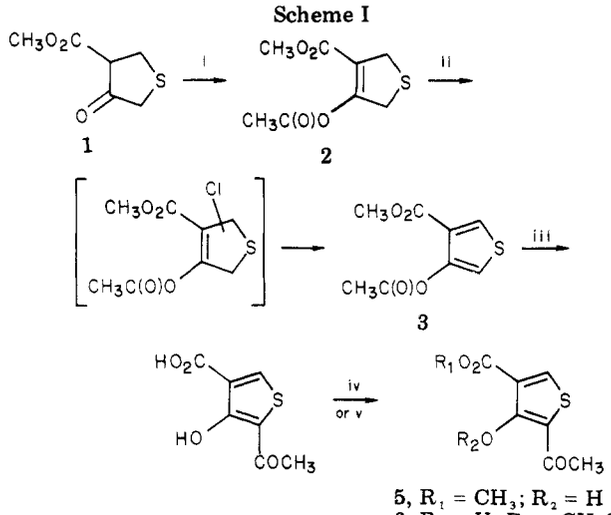
Several 4-alkoxy-, 4-hydroxy- and 3-amino-disubstituted thiophenes were prepared as potential intermediates for the preparation of novel thieno[3,4]tricyclic systems. The 4-alkoxy-3-substituted thiophenes **8a,b** were prepared by acid-catalyzed alcohol exchange of 4-hydroxythiophene **7**. Base stable thiophenes **8a,b** were converted to acids **10a,b**, amides **11a,b**, and hydrazide **12**. Electrophilic substitution reactions with **10b** occurred exclusively to give 5-substituted derivatives. Hydrazide **12** was converted via azide **17** to stable, electron-rich 4-ethoxy-3-thiopheneamine (**23**). 4-Alkoxythiophene derivatives **10a,b** and **19** were converted to 4-hydroxy derivatives with boron tribromide. Intermediate and final compounds were examined for potential tautomerism.

During the course of an investigation into the synthesis of thieno[3,4-*b*][1,5]benzodiazepines[1] and other novel thieno[3,4-*b*]-fused tricyclic compounds, it became necessary to synthesize 4-alkoxy- and 3-amino-substituted thiophenes as potential intermediates. Such thiophenes without substitution in the 2 and 5 positions are not well described in the literature and appear to be relatively unstable and/or difficult to prepare.[2,3]

The ready availability of methyl tetrahydro-4-oxo-3-thiophenecarboxylate[4] (**1**) allowed straightforward preparation of the thiophene system with the desired 3,4 substitution. Reaction of **1** with isopropenyl acetate led to enol acetate **2** which was oxidized by the action of sulfuryl chloride to acetoxy ester **3** via the unisolated chlorosulfide and thermal elimination of hydrogen chloride (Scheme I). The use of sulfuryl chloride for this type of

Scheme I



5, $R_1 = CH_3$; $R_2 = H$
6, $R_1 = H$; $R_2 = CH_3CO$

i. ⟩—OAc/*p*-TSA; ii. SO_2Cl_2 at −20 °C, then reflux; iii. LiI/NaCN/DMF; iv. CH_2N_2; v. Ac_2O/H_2SO_4

α chlorination of sulfides is extremely advantageous since the gaseous byproducts of this reaction are easily removed. Acetate **3** appeared to be an ideal precursor for the 4-hydroxy-3-carboxythiophenes of interest; however, at-

(1) For paper 1 in this series see: Press, J. B.; Hofmann, C. M.; Eudy, N. H.; Fanshawe, W. J.; Day, I. P.; Greenblatt, E. N.; Safir, S. R. *J. Med. Chem.* **1979**, *22*, 725.
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