# Studies in the Aziridine Series. Reactions of *trans*-1,3-Dibenzoyl-2-phenylaziridine and Related Systems[1]

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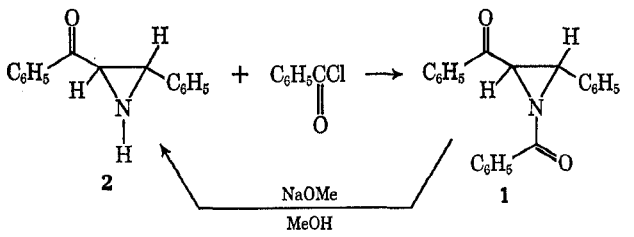
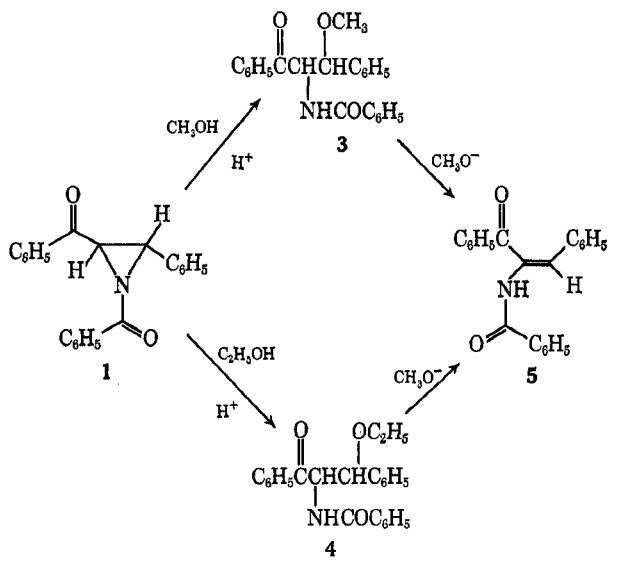
*trans*-1,3-Dibenzoyl-2-phenylaziridine (1) undergoes thermal rearrangement to 1,4-diphenyl-4-benzoyloxy-2-azabutadiene (14) *via* carbon–carbon bond cleavage of the aziridine ring. The inability of an external trapping reagent to trap the 1,3-dipole intermediate suggests that either the isomerization is a concerted process or else the 1,3 dipole rearranges faster than it can be trapped. The reactions of 1 with acid, base, and sodium iodide have also been investigated. The details of each reaction are described and evidence is presented demonstrating the existence of transient intermediates.

The thermal and photochemical behavior of small-membered nitrogen heterocycles has been the subject of recent reports from these laboratories.[3,4] Of specific interest has been the photochemistry of the 2-aroylaziridine system. Investigations of this ring system have shown that the nature and position of the substituents about the ring may produce markedly different chemical effects.[4] In order to accurately assess the electronic effects of substituents attached to the nitrogen atom, the photochemistry of a N-benzoyl substituted aziridine was undertaken.[5] Attempts to prepare and characterize a representative example of this system, *i.e.*, *trans*-1,3-dibenzoyl-2-phenylaziridine (1), led to the discovery of a large number of new ground-state transformations of this ring system. Our interests in the effects of substitution on the stability and chemistry of the aziridine ring motivated our investigation of these new reactions. The present paper describes the results of our studies.

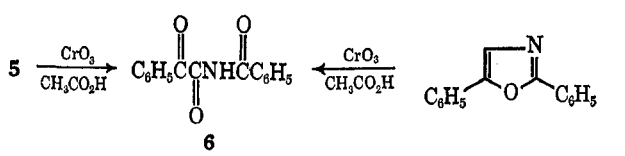
*trans*-1,3-Dibenzoyl-2-phenylaziridine (1) was prepared by the reaction of *trans*-2-phenyl-3-benzoylaziridine (2) with benzoyl chloride in benzene. The assignment of structure 1 was supported by its elemental analysis, spectroscopic data (see Experimental Section), and hydrolysis of the material with sodium methoxide in methanol to 2 and methyl benzoate.




Treatment of 1 with methanol in the presence of a trace amount of acid led to the formation of 2-benzamido-1,3-diphenyl-3-methoxypropanone (3). A similar reaction with ethanol led to 2-benzamido-1,3-diphenyl-3-ethoxypropanone (4). Both of these compounds gave (α-benzamido)-*cis*-benzalacetophenone (5) when treated with base. Structure 5 was established by its elemental analysis, by spectroscopic data, and by

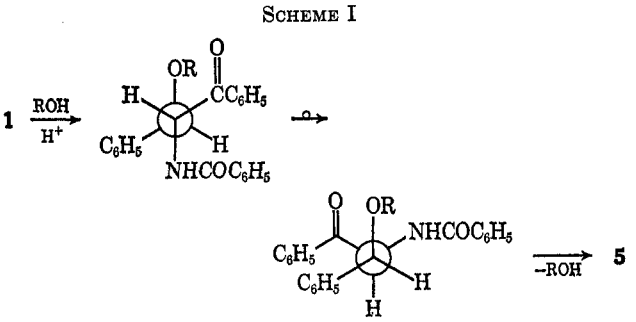



chemical degradation. Chromium trioxide oxidation of 5 in glacial acetic acid gave N-phenylglyoxylbenzamide (6), which could be prepared independently by the chromium trioxide oxidation of 2,5-diphenyloxazole. The oxidation of oxazoles are known to form N-phenylglyoxylbenzamides.[6] The *cis* relationship of the phenyl




and benzoyl groups is to be expected since the acid-catalyzed ring opening of the aziridine ring and the elimination of alcohol should occur in a stereospecific *trans* fashion (see Scheme I). We anticipated that a reaction

SCHEME I




(1) This work was presented in part at the 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969. For a preliminary report, see A. Padwa and W. Eisenhardt, *Chem. Commun.*, 1215 (1969).

(2) Alfred P. Sloan Foundation Fellow, 1968–1970.

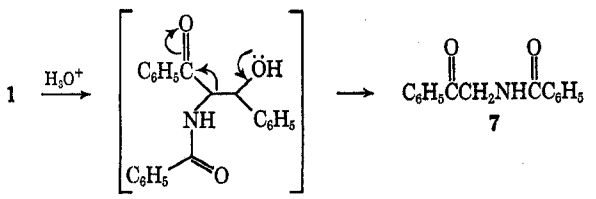
(3) A. Padwa and W. Eisenhardt, *ibid.*, **7**, 380 (1968); A. Padwa, L. Hamilton, and D. Eastman, *J. Org. Chem.*, **33**, 1317 (1968).

(4) A. Padwa and L. Hamilton, *J. Amer. Chem. Soc.*, **89**, 102 (1967); **87**, 1821 (1965). A. Padwa and W. Eisenhardt, *ibid.*, **90**, 2442 (1968).

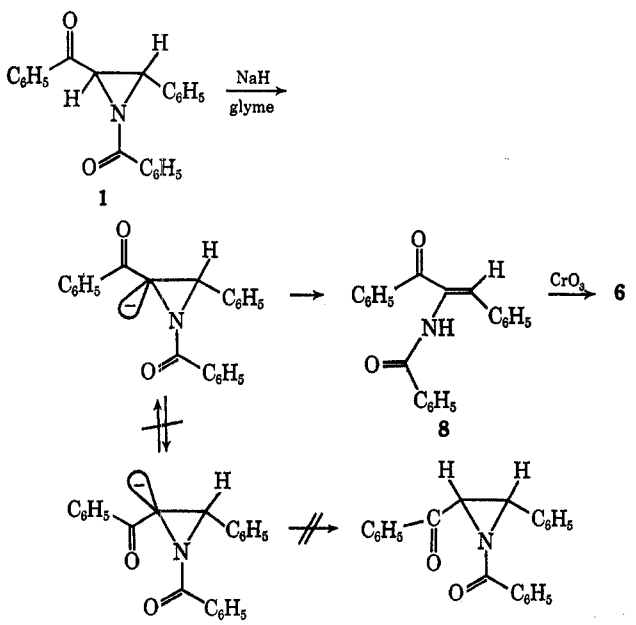
(5) The results of the photochemical studies will be reported at a later date.

(6) E. Fischer, *Ber.*, **29**, 209 (1896).

similar to that described above should occur upon treatment of **1** with aqueous acid. However, the initially produced 2-benzamido-1,3-diphenyl-3-hydroxypropanone underwent further fragmentation under the reaction conditions and gave N-phenacylbenzamide (**7**) and benzaldehyde.

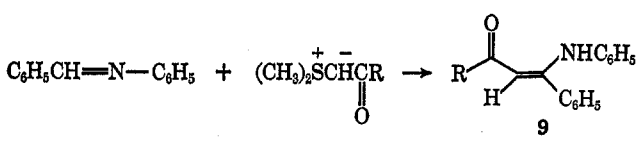


When a solution of **1** was treated with either sodium hydride or potassium *t*-butoxide, the isomeric (α-benzamido)-*trans*-benzalacetophenone (**8**) was isolated in excellent yield. The structure of **8** was confirmed by elemental analysis and by the oxidation of **8** to N-phenylglyoxylbenzamide (**6**). The mass spectra of **5** and **8** were virtually identical, although their nmr and infrared spectra were significantly different.

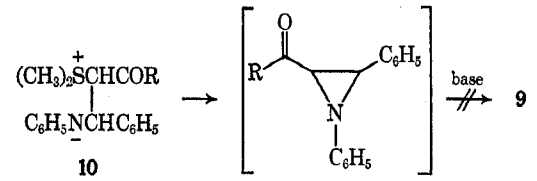


It is interesting to note that the ring opening of **1** to **8** occurred in a stereoselective manner. This implies that the aziridine ring is opened (to give **8**) faster than isomerization to the *cis* isomer. For the sake of completeness, we undertook a brief examination of the stability of **1** toward base isomerization. For short periods of time *trans*-aziridine **1** was recovered unchanged; no isomerization to the thermodynamically more stable *cis*-aziridine was detected.[7] Similarly, **5** was not isomerized to **8** (or **8** to **5**) under the base conditions.

The isolation of **8** from **1** is interesting in view of a recent publication concerning the reaction of benzalaniline with sulfonium ylides.[8] The major product of these reactions were cinnamic acid derivatives **9**. The

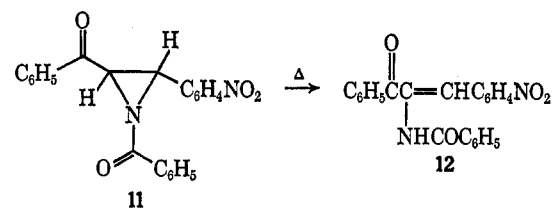


authors suggested that the initially formed betaine (**10**) underwent initial closure to an aziridine which rapidly opened to the observed product (**9**). From our results



it is clear that the base-catalyzed opening of a carbonyl aziridine gives an α-substituted benzalacetophenone derivative rather than the β-substituted isomer. We conclude, therefore, that the reaction of sulfonium ylides with imines does not involve the intermediacy of an aziridine. A similar conclusion has also been independently reached by Deyrup.[9]

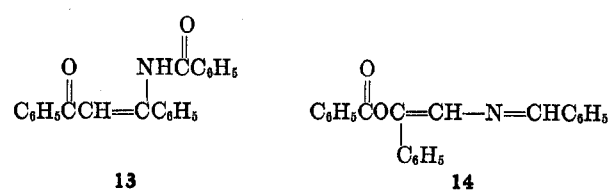
Heating a solution of **1** in benzene produced a single component in high yield (85%) that was shown to be isomeric with starting material. The thermal isomerization of the closely related nitroaziridine system (**11**) has been studied by Heine and Kaplan.[10] They reported that *trans*-1,3-dibenzoyl-2-*p*-nitrophenylaziridine (**11**) rearranged to α-benzamido-*p*-nitrobenzalacetophenone (**12**) when heated in an inert solvent.



It was suggested that the reaction proceeds by transfer of the aziridinyl hydrogen adjacent to the benzoyl group to the amido oxygen with concurrent breaking of the three-membered ring.

The isolation and characterization of *cis*- and *trans*-(α-benzamido)benzalacetophenone (**5** and **8**), however, eliminates this type of structure from further consideration as the thermolysis product of **1**.

Compounds **13** and **14** were also entertained as possible structures for the thermal product.

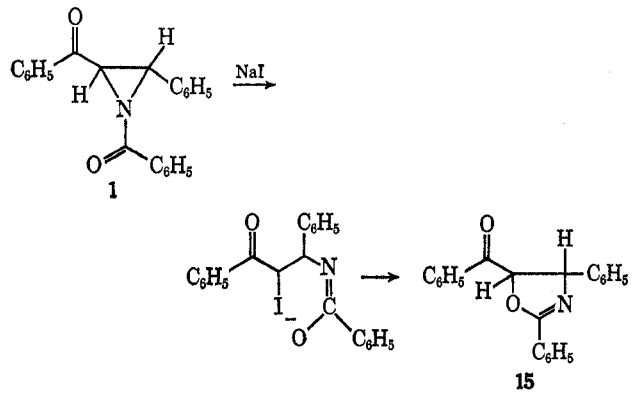


Compound **13** might be expected to arise by transfer of the aziridinyl hydrogen adjacent to the phenyl group to the amino oxygen followed by bond cleavage. This type of hydrogen transfer has been suggested to be important in the photochemistry of certain aroylaziridines[4] and perhaps strengthens the possible formation of compound **13** from the thermal reaction of **1**. Analysis of all the data enables us to reject structure **13** and indicates that structure **14** is the true structure of the thermal product.

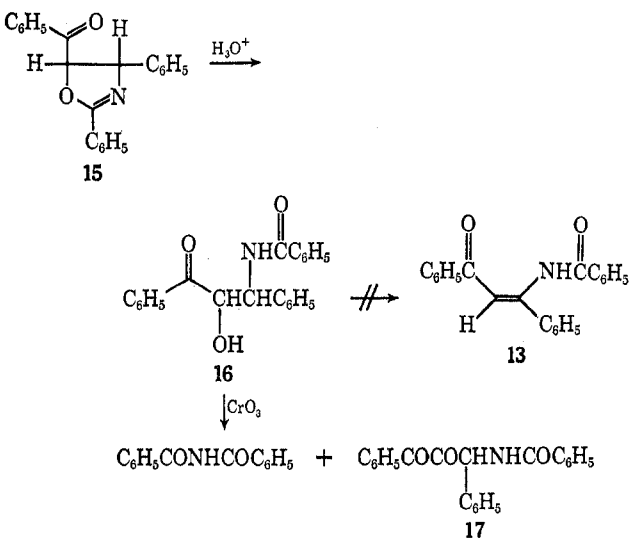
The isomerization of 1-acylaziridines into 2-aryl- or 2-alkyl-2-oxazolines by nucleophiles such as iodide ion

(7) R. E. Lutz and A. B. Turner, *J. Org. Chem.*, **33**, 516 (1968).
(8) A. J. Speziale, C. C. Tung, K. W. Ratts, and A. Yao, *J. Amer. Chem. Soc.*, **87**, 3460 (1965).
(9) J. A. Deyrup, *J. Org. Chem.*, **34**, 2724 (1969).
(10) H. W. Heine and M. S. Kaplan, *ibid.*, **32**, 3069 (1967).

has been extensively investigated in recent years.[11-15] The mechanism proposed for the isomerization involves initial attack by the nucleophile on an aziridinyl carbon to form a N-β-iodoethylbenzamido ion. In a subsequent step the ion cyclizes to the oxazoline and regenerates the iodide ion. When **1** was treated with sodium iodide in refluxing acetone the anticipated *trans*-2,4-diphenyl-5-benzoyl-2-oxazoline (**15**) was isolated.

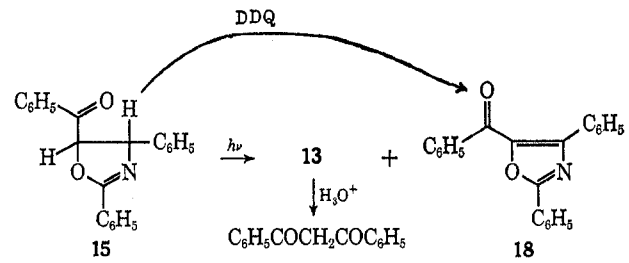



We intended to subject oxazoline **15** to acidic conditions so as to form N-1-phenyl-2-hydroxy-2-benzoylbenzamide (**16**). We hoped that compound **16** would in turn undergo dehydration to produce (β-benzamido)-*trans*-benzalacetophenone (**13**), a compound that was under consideration as the possible thermal rearrangement product of **1**.



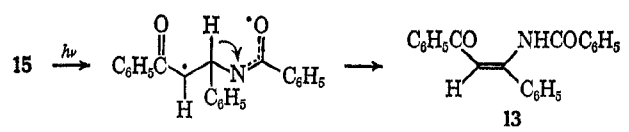

The conversion of **15** to **16** was in fact experimentally realized. Spectroscopic data and the further oxidation of **16** to dibenzamide and N-1-phenyl-1-phenylglyoxyl methylbenzamide (**17**) confirmed its structure. However, all attempts to dehydrate **16** to **13** have failed.

Although the desired β-benzamido-*trans*-benzalacetophenone (**13**) was not available from **16**, it occurred to us that the 5-benzoyl-2-oxazoline system (**15**) might serve as an alternate precursor to **13**. This observation might be achieved by photolytic rearrangement of **15**. In fact, irradiation of **15** in pentane afforded **13** in high yield together with small amounts of 5-benzoyl-2,4-diphenyloxazole (**18**). The structure of **13** was inferred




from its composition, spectral data, and chemical behavior. Specifically, the nmr spectrum ($CDCl_3$) exhibited a singlet at $\tau$ −3.01, a multiplet centered at $\tau$ 2.31, and a singlet at $\tau$ 3.63. The peak areas were in the ratio of 1:15:1. The fact that the chemical shift associated with the proton attached to the nitrogen was markedly deshielded and invariant with concentration strongly suggested that the benzamido group of **13** is *cis* to the benzoyl group. Chemical confirmation for this structure was obtained by hydrolysis of **13** to dibenzoylmethane. Comparison of the physical properties of **13** with those of the thermal product obtained from **1** revealed that the two compounds were basically different. The elucidation of the structure of the minor photoproduct as 5-benzoyl-2,4-diphenyloxazole (**18**) was based on its spectral properties, elemental composition, and an independent synthesis. Compound **18** could be prepared in high yield by the oxidation of **15** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in refluxing benzene.

The formation of **13** from **15** may be visualized as occurring by scission of the O–C bond followed by an unusual but not unprecedented 1,2-hydrogen shift.[16-18]




Having eliminated structures **5**, **8**, and **13** from further consideration, we feel that all of the evidence points strongly to 1,4-diphenyl-4-benzoyloxy-2-azabutadiene (**14**) as the structure of the thermal product of **1**. This assignment is supported by the spectral data, catalytic hydrogenation, and the reactivity of **14** toward sodium methoxide. The nmr spectrum of the thermal product showed multiplets at $\tau$ 1.72 (3 H) and 2.60 (14 H). The three-proton multiplet at $\tau$ 1.72 can be assigned to the *ortho* hydrogens of the imine phenyl ring and the imine hydrogen. The thermal product could be reduced with hydrogen and palladium on charcoal. The product isolated was identified as the

(11) H. W. Heine, M. E. Fetter, and E. M. Nicholsen, *J. Amer. Chem. Soc.*, **81**, 2202 (1959); H. W. Heine, W. G. Kenyon, and E. M. Johnson, *ibid.*, **83**, 2570 (1961); H. W. Heine, D. C. King, and L. A. Portland, *J. Org. Chem.*, **31**, 2662 (1966); H. W. Heine, *Agew. Chem., Int. Ed. Engl.*, **1**, 528 (1962).

(12) M. Lidaks and S. Hillers, *Latv. PSR Zinat. Akad. Vestis*, No. 2, 211 (1961); *Chem. Abstr.*, **58**, 4530 (1963).

(13) F. E. Fanta and E. N. Walsh, *J. Org. Chem.*, **30**, 3574 (1965); **31**, 59 (1966).

(14) R. D. Guthrie and D. Murphy, *J. Chem. Soc.*, 3828 (1965).

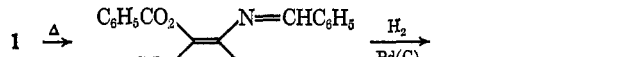
(15) P. Thyrum and A. R. Day, *J. Med. Chem.*, **8**, 107 (1965).

(16) G. W. Griffin, J. Covell, R. C. Petterson, R. M. Dodson, and G. Close, *J. Amer. Chem. Soc.*, **87**, 1410 (1965).

(17) D. I. Schuster and I. S. Krull, *ibid.*, **88**, 3456 (1966).

(18) A. Padwa, D. Crumrine, R. Hartman, and R. Layton, *ibid.*, **89**, 4435 (1967).

benzylphenethylammonium salt of benzoic acid (**19**) on the basis of its spectral data and by an independent synthesis of **19** from benzylphenethylamine and benzoic acid. Treatment of **14** with sodium methoxide gave one major product that was assigned as 2,5-dibenzoyl-3,6-diphenyl-1,4-dihydropyrazine (**20**) on the basis of its analysis and spectral properties and from mechanistic considerations. A reasonable mechanism for the formation of **20** is presented in Scheme II.

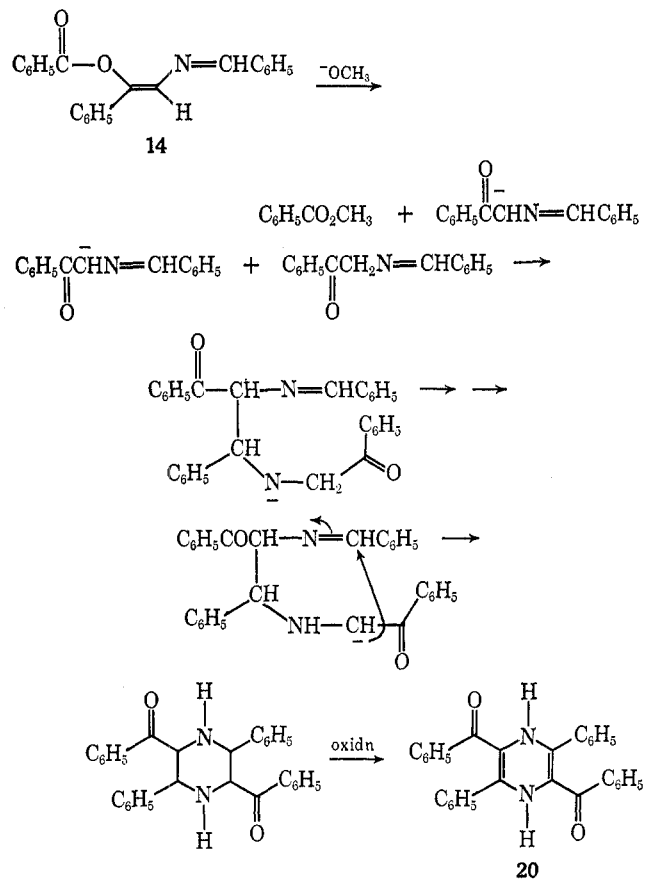


**14**

$[C_6H_5CH_2CH_2NH_2CH_2C_6H_5]^+ C_6H_5CO_2^-$

**19**

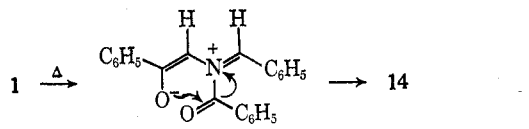
SCHEME II



**20**

In this postulated mechanism, sodium methoxide attacks the ester linkage to give a N-benzoylmethylbenzalimine anion which cyclizes to an intermediate hexahydropyrazine that in turn is air oxidized to the final product.

The mechanism by which **1** isomerizes to **14** and the intermediate or transition state involved in the reaction are of considerable interest. Recent work has demonstrated that appropriately substituted aziridines form adducts with various alkenes and alkynes when heated in inert solvents.[9,19-25] These reactions can be envisaged as occurring by an initial cleavage of the carbon–carbon bond of the aziridine ring to form a 1,3-dipole intermediate which subsequently adds to the unsaturated substrate. The mechanism that we propose for the above rearrangement (**1** → **14**) involves cleavage of the carbon–carbon bond of the aziridine ring to give a 1,3-dipole intermediate which subsequently rearranges to the final product by way of a benzoyl migration. Experiments designed to trap the 1,3-dipole intermediate by heating **1** in the presence of dimethylacetylene dicarboxylate, cyclohexene, or substituted butadienes were unsuccessful. The inability of an external trapping reagent to trap the 1,3-dipole intermediate suggests that either the isomerization is a concerted process or else the 1,3 dipole rearranges faster than it can be trapped. The thermal rearrangement of



dibenzoylaziridine **1** stands in marked contrast to previous work on related 1,3-diaroyl-2-arylaziridines.[10] The fact that a different route occurs in the thermal rearrangement of **1** to **14** suggests that either the nitro group plays an important role in the pyrolytic behavior of these small nitrogen heterocycles or else the structure of the rearranged product in the nitro system has been misassigned.

## Experimental Section[26]

*trans*-**1,3-Dibenzoyl-2-phenylaziridine** (**1**).—To a mixture of 5.55 g (0.025 mol) of *trans*-2-phenyl-3-benzoylaziridine (**2**)[27] and 2.52 g (0.025 mol) of triethylamine in 100 ml of anhydrous benzene was added with stirring a solution of 3.50 g (0.025 mol) of benzoyl chloride in 75 ml of anhydrous ether. The mixture was stirred at room temperature for 2 hr and filtered; the precipitate that formed was washed well with water to dissolve the triethylamine hydrochloride. Careful low-temperature recrystallization from heptane–benzene gave 6.0 g of **1** as white needles, mp 127.5–129°.

The infrared spectrum (potassium bromide pellet) was characterized by bands at 5.95, 6.88, 7.06, 7.46, 8.10, 9.70, and 13.91 $\mu$. The nmr spectrum in deuteriochloroform shows a multiplet centered at $\tau$ 2.40 (10 H), a doublet at 5.63 (1 H, $J$ = 2.5 Hz), and a doublet at 5.92 (1 H, $J$ = 2.5 Hz). The ultraviolet spectrum (95% ethanol) has maxima at 254 m$\mu$ ($\epsilon$ 23,500) and 316 (278).

*Anal.* Calcd for $C_{22}H_{17}O_2N$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.72; H, 5.22; N, 4.30.

**Acid-Catalyzed Addition of Methanol to *trans*-1,3-Dibenzoyl-2-phenylaziridine.**—A solution of 2.0 g of *trans*-1,3-dibenzoyl-2-phenylaziridine (**1**) in 50 ml of methanol containing 1 drop of concentrated hydrochloric acid was allowed to reflux for 1 hr. The mixture was concentrated *in vacuo*, and the crude residue

(19) H. W. Heine and R. E. Peavy, *Tetrahedron Lett.*, 3123 (1965).
(20) H. W. Heine, R. Peavy, and A. J. Durbetaki, *J. Org. Chem.*, **31**, 3924 (1966).
(21) A. Padwa and L. Hamilton, *Tetrahedron Lett.*, 4363 (1965).
(22) A. Padwa and L. Hamilton, *J. Heterocycl. Chem.*, **4**, 118 (1967).
(23) R. Huisgen, W. Scheer, and H. Huber, *J. Amer. Chem. Soc.*, **89**, 1753 (1967).
(24) J. W. Lown, R. K. Smalley, and G. Dallas, *Chem. Commun.*, 1543 (1968).
(25) P. B. Woller and N. H. Cromwell, *J. Heterocycl. Chem.*, **5**, 579 (1968).
(26) All melting points are corrected and boiling points are uncorrected. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark, and Alfred Bernhardt Laboratories, Hohenweg, Germany. The infrared absorption spectra were determined on a Perkin-Elmer Infracord spectrophotometer, Model 137. The ultraviolet absorption spectra were measured with a Cary recording spectrophotometer, using 1-cm matched cells. The nuclear magnetic resonance spectra were determined at 60 Mc with the Varian Associates high-resolution spectrophotometer. Tetramethylsilane was used as an internal standard.
(27) N. H. Cromwell, R. D. Babson, and C. A. Harris, *J. Amer. Chem. Soc.*, **65**, 312 (1943).

was cooled to give 2.1 g (95%) of a white solid. Recrystallization from methanol gave colorless needles, mp 158–159°. The structure of this material is assigned as 2-benzamido-1,3-diphenyl-3-methoxypropanone (3) on the basis of the following observations.

*Anal.* Calcd for $C_{23}H_{21}O_3N$: C, 76.86; H, 5.89; N, 3.90. Found: C, 76.51; H, 8.58; N, 3.89.

The infrared spectrum (potassium bromide pellet) shows strong absorptions at 3.05, 5.91, 6.09, 6.58, 6.91, 7.62, 8.21, 8.97, 12.53, 13.28, and 14.25 $\mu$. The nmr spectrum ($CDCl_3$) is characterized by a multiplet centered at $\tau$ 2.49 (16 H), a doublet of doublets centered at $\tau$ 3.88 (1 H, $J$ = 6 Hz, J = 6 Hz), a doublet at $\tau$ 5.28 (1 H, $J$ = 6 Hz) and a singlet at $\tau$ 6.82 (3 H, $OCH_3$). The mass spectrum (70 eV) lacked a parent ion but exhibited prominent peaks at $m/e$ (relative intensity) 327 (16, P − MeOH), 206 (12), 121 (25), 106 (33), 105 (100), 77 (43), 32 (19), and has metastable peaks at 56 and 130. The ultraviolet spectrum in 95% ethanol exhibited a maximum at 247 m$\mu$ ($\epsilon$ 18,650).

**Acid-Catalyzed Addition of Ethanol to *trans*-1,3-Dibenzoyl-2-phenylaziridine.**—A mixture of 2.0 g of *trans*-1,3-dibenzoyl-2-phenylaziridine (1) and 1 drop of concentrated hydrochloric acid in 50 ml of absolute ethanol was allowed to reflux for 1 hr. The mixture was concentrated *in vacuo* and the crude residue was cooled to give 1.1 g (92%) of white solid. Recrystallization from absolute ethanol gave colorless needles, mp 136–137°. The structure of this material is assigned as 2-benzamido-1,3-diphenyl-3-ethoxypropanone (4) on the basis of the following observations.

*Anal.* Calcd for $C_{24}H_{23}O_3N$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.16; H, 6.20; N, 3.79.

The infrared spectrum (potassium bromide pellet) exhibits bands at 3.01, 6.59, 6.75, 6.95, 7.33, 8.01, 9.10, 10.28, 12.88, 13.22, and 14.05 $\mu$. The nmr spectrum ($CDCl_3$) shows a multiplet at $\tau$ 2.40 (16 H), a doublet of doublets at 3.83 (1 H, $J$ = 7 Hz, $J$ = 7 Hz), a doublet at 5.15 (1 H, $J$ = 7 Hz), a complex multiplet centered at 6.68 (2 H) which contained a superimposed doublet of doublets ($J$ = 7 Hz, $J$ = 7 Hz) and a triplet at 9.04 (3 H, $J$ = 7 Hz). The mass spectrum (70 eV) lacked a parent ion but has prominent peaks at $m/e$ (relative intensity) 327 (14, P − EtOH), 135 (19), 106 (9), 105 (100), 77 (45), 45 (19), and has metastable peaks at 56, 84 and 130. The ultraviolet spectrum in 95% ethanol showed a maximum at 247 m$\mu$ ($\epsilon$ 14,000).

**Treatment of 2-Benzamido-1,3-diphenyl-3-alkoxypropanones 3 and 4 with Base.**—A mixture of 0.5 g of either 2-benzamido-1,3-diphenyl-3-methoxypropanone (3) or 2-benzamido-1,3-diphenyl-3-ethoxypropanone (4) and 30 ml of a freshly prepared 0.4 $N$ sodium methoxide solution was stirred at 30° for 2 hr. The reaction mixture was diluted with water and extracted twice with benzene. The benzene extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent *in vacuo* left a white solid which was recrystallized from methanol to give 0.4 g (96%) of colorless prisms, mp 138–139°. The structure of this compound was assigned as ($\alpha$-benzamido)-*cis*-benzalacetophenone (5) on the basis of the following data.

*Anal.* Calcd for $C_{22}H_{17}O_2N$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.68; H, 5.28; N, 4.31.

The infrared spectrum (potassium bromide pellet) shows absorptions at 3.10, 6.09, 6.63, 6.78, 6.95, 7.58, 7.79, 7.97, 10.26, 10.77, 11.06, 12.21, 12.48, 12.68, 13.24 and 14.03 $\mu$. The nmr spectrum ($CDCl_3$) was characterized by a multiplet at $\tau$ 2.43 (16 H), and a singlet at 3.36 (1 H). The mass spectrum (70 eV) indicated a molecular ion at $m/e$ (relative intensity) 327 (9) and exhibited major peaks at 206 (8), 106 (9), 105 (100), 77 (45), 51 (8) and has metastable peaks at 56 and 130. The ultraviolet spectrum (in 95% ethanol) was characterized by maxima at 228 m$\mu$ ($\epsilon$ 22,320), 256 (18,460) and 294 (17,310).

**Oxidation of ($\alpha$-Benzamido)-*cis*-benzalacetophenone (5).**—A sample of 0.6 g of ($\alpha$-benzamido)-*cis*-benzalacetophenone (5) was dissolved in 8 ml of hot glacial acetic acid. To this solution was added 12 ml of a hot saturated solution of chromium trioxide in glacial acetic acid and the mixture was allowed to stir for 45 min. The dark green reaction mixture was poured onto ice-water and filtered. The residue was washed well with water and the solid was recrystallized from benzene–heptane to give white needles of N-phenylglyoxalbenzamide (6), mp 138–139°.

The infrared spectrum (potassium bromide pellet) showed strong bands at 5.80, 5.92, 6.10, 6.80, 7.44, 8.01, 8.22, 10.29, 10.99, 12.36, and 12.81 $\mu$.

Structure 6 was confirmed by an alternate synthesis involving the oxidation of 2,5-diphenyloxazole.[6] To a sample of 0.5 g of 2,5-diphenyloxazole, dissolved in 7 ml of hot glacial acetic acid, was added 12 ml of a hot saturated solution of chromium trioxide in glacial acetic acid. After 5 min the reaction mixture was poured onto ice water and filtered to give a quantitative yield of N-phenylglyoxalbenzamide. Recrystallization from heptane–benzene gave 6 as white needles, mp 138–139°. The infrared spectrum was identical in all respects with that of 6 obtained from the oxidation of 5.

**Acid Hydrolysis of *trans*-1,3-Dibenzoyl-2-phenylaziridine (1).**—A mixture of 0.5 g of 1, 15 ml of dioxane, and 25 ml of a 10% hydrochloric acid solution was allowed to reflux for 10 hr. The reaction mixture was diluted with water and extracted twice with benzene. The combined benzene extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent *in vacuo* left a crude white solid whose infrared spectrum indicated a mixture of benzoic acid and a new compound.

Fractional crystallization from benzene–heptane gave a white crystalline solid, mp 125–126°. The infrared spectrum of this material was identical in all respects with that of N-phenacylbenzamide (7). A mixture melting point of 7 with an authentic sample of N-phenacylbenzamide was undepressed.

**Treatment of *trans*-1,3-Dibenzoyl-2-phenylaziridine (1) with Sodium Methoxide.**—A solution of 0.1 g of 1 in 25 ml of freshly prepared 0.4 $N$ sodium methoxide-methanol solution was allowed to stir at room temperature for 8 hr. The reaction mixture was diluted with water and extracted with ether. The ethereal layer was washed with water and dried over anhydrous sodium sulfate, and the solvent removed *in vacuo* to give 0.09 g (94%) of a yellow-white solid. Recrystallization from methanol–water afforded colorless needles, mp 99.5–101°. The infrared spectrum of this material was identical in all respects with that of *trans*-2-phenyl-3-benzoylaziridine (2). A mixture melting point with authentic *trans*-2-phenyl-1-benzoylaziridine (2) was undepressed.

**Thermal Isomerization of *trans*-1,3-Dibenzoyl-2-phenylaziridine (1).**—A mixture of 1.0 g of 1 and 25 ml of benzene (or xylene) was allowed to reflux for 10 hr. Evaporation of the solvent *in vacuo* left a crude yellow solid which decomposed to a brown oil upon standing in air. Recrystallization of the crude yellow solid from heptane–benzene gave 0.85 g (85%) of light yellow prisms, mp 110–111°. Storage of this material in a moisture-free atmosphere prevented further decomposition. The structure of this material is assigned as 1,4-diphenyl-4-benzoyloxy-2-azabutadiene (14) on the basis of the following observations.

*Anal.* Calcd for $C_{22}H_{17}O_2N$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.47; H, 5.20; N, 4.16.

The infrared spectrum (potassium bromide pellet) is characterized by bands at 5.80, 6.10, 6.91, 8.11, 8.48, 9.22, 9.38, 9.74, 10.21, 12.96, and 13.27 $\mu$. The nmr spectrum ($CDCl_3$) exhibits a complex multiplet at $\tau$ 1.72 (3 H) and a complex multiplet at 2.60 (14 H). The mass spectrum (70 eV) shows a molecular ion at $m/e$ (relative intensity) 327 (35) and prominent peaks at 223 (10), 222 (55), 221 (10), 167 (18), 106 (19), 105 (100), 90 (14), 89 (13), 77 (72), and metastable peaks at 34, 50, 56, 126 and 151. The peak at $m/e$ 167 corresponds to phenyltropylium which is presumably derived by fragmentation and rearrangement of the 222 peak (*i.e.*, loss of C=O and HCN). This is supported by the metastable at 126. The ultraviolet spectrum in absolute ethanol showed maxima at 230 m$\mu$ ($\epsilon$ 24,710) and 338 (28,670).

Heating a mixture of 0.5 g of 1, 1.0 g of dimethylacetylene dicarboxylate, and 25 ml of benzene gave only 14 and recovered acetylene.

**Base-Catalyzed Ring Opening of *trans*-1,3-Dibenzoyl-2-phenylaziridine (1).**—To a 0.6-g sample of 1 in 15 ml of glyme (distilled from lithium aluminum hydride) was added, under a nitrogen atmosphere, 0.9 g of sodium hydride (60% in mineral oil.)[28] The mixture was allowed to stir for 4 hr at room temperature during which time the color changed from pale yellow to orange-red. The insoluble material formed was filtered and the mother liquor was diluted with water and extracted with benzene. The benzene extracts were dried over anhydrous magnesium sulfate and removal of the solvent *in vacuo* left a white solid. Recrystallization from benzene–heptane gave white needles,

(28) Similar results were obtained when anhydrous potassium *t*-butoxide was used as the base.

mp 162.5–163°. The structure of this material is assigned as (α-benzamido)-*trans*-benzalacetophenone (**8**) on the basis of the following observations.

*Anal.* Calcd for $C_{22}H_{17}O_2N$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.50; H, 5.34; N, 4.24.

The infrared spectrum (potassium bromide pellet) is characterized by bands at 3.01, 6.06, 6.62, 6.78, 7.32, 7.89, 8.22, 10.27, 11.02, 11.57, 11.80, 12.48, 13.20, 13.64, and 14.06 μ. The nmr spectrum ($CDCl_3$) is characterized by a complex multiplet at τ 2.53 which contained a sharp singlet at 2.97. The mass spectrum (70 eV) had a molecular ion at *m/e* (relative intensity) 327 (19) and other major peaks at 222 (8), 206 (10), 106 (10), 105 (100), 78 (10), 77 (44), 51 (8), 40 (9), and metastable peaks at 56 and 130. The ultraviolet spectrum in 95% ethanol exhibited maxima at 233 mμ (ε 17,900), 257 (20,020), and 280 (16,820).

**Oxidation of (α-Benzamido)-*trans*-benzalacetophenone (8).**—A sample of 0.5 g of (α-benzamido)-*trans*-benzalacetophenone (**8**) was dissolved in 7 ml of hot glacial acetic acid and 10 ml of a hot saturated solution of glacial acetic acid was added. The combined solution was allowed to stir for 30 min. The dark green reaction mixture was then poured onto ice water and filtered. The residue was washed well with water and recrystallized from heptane–benzene to give white needles, mp 138–139°. This material was identified as N-phenylglyoxalbenzamide (**6**) by comparison of its infrared spectrum with that of authentic **6**. A mixture melting point of this material with an authentic sample of N-phenylglyoxalbenzamide **6** was undepressed at 138–139°.

**Iodide Ion Catalyzed Isomerization of *trans*-1,3-Dibenzoyl-2-phenylaziridine (1).**—A mixture of 2 g of **1** and 3 g of anhydrous sodium iodide in 50 ml of acetone was allowed to reflux for 3 hr. The solvent was removed *in vacuo* and the residue taken up in benzene. The benzene layer was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo* afforded 1.95 g (97%) of a white solid which was recrystallized from methanol to give white needles, mp 82.5–84°. The structure of this material is assigned as *trans*-2,4-diphenyl-5-benzoyl-2-oxazoline (**15**) on the basis of the following observations.

*Anal.* Calcd for $C_{22}H_{17}O_2N$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.70; H, 5.31; N, 4.24.

The infrared spectrum of this material (potassium bromide pellet) is characterized by bands at 5.91, 6.06, 6.89, 7.44, 8.03, 9.37, 10.26, 11.98, 12.74, and 12.97 μ. The nmr spectrum ($CCl_4$) shows a complex multiplet at τ 2.41 (15 H) and an AB quartet at 6.38 (2 H, $J$ = 6.5 Hz). The ultraviolet spectrum (pentane) is characterized by a maximum at 240 mμ (ε 22,100).

**Irradiation of *trans*-2,4-Diphenyl-5-benzoyl-2-oxazoline (15) in Benzene.**—A solution of 1.0 g of *trans*-2,4-diphenyl-5-benzoyl-2-oxazoline (**15**) of 1 l. of pentane was irradiated with an internal water-cooled mercury arc lamp (Hanovia Type L, 450 W) with a Pyrex filter to eliminate wavelengths below 280 mμ. Purified nitrogen was passed through the solution for at least 45 min before irradiation commenced, and a positive pressure of nitrogen was maintained throughout. Aliquots were withdrawn and analyzed by tlc. After 4 hr, the spot on a thin layer plate due to **15** has almost disappeared and two new spots had appeared in its place. Concentration of the solution *in vacuo* left a mixture of two compounds which could be separated by preparative thick layer chromatography.[29] The two products were identified as (β-benzamido)-*trans*-benzalacetophenone (**13**) and 5-benzoyl-2,4-diphenyloxazole (**18**).

Recrystallization of **13** from benzene heptane afforded 0.9 g (90%) of pale yellow prisms, mp 117–118°. The structure of this material is assigned as (β-benzamido)-*trans*-benzalacetophenone (**13**) on the basis of the following observations.

*Anal.* Calcd for $C_{22}H_{17}O_2N$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.41; H, 5.28; N, 4.07.

The infrared spectrum of this material in a potassium bromide pellet shows bands at 5.91, 6.15, 6.30, 6.40, 6.70, 6.85, 7.59, 7.68, 7.75, 8.03, 8.16, 8.79, 9.56, 9.78, 10.93, and 13.89 μ. The nmr spectrum ($CDCl_3$) shows a broad singlet at τ − 3.01 (1 H), a complex multiplet at 2.31 (15 H), and a singlet at 3.63 (1 H). The mass spectrum (70 eV) indicated a molecular ion at 3.63 (1 H). The mass spectrum (70 eV) indicated a molecular ion at *m/e* (relative intensity) 327 (2) and prominent peaks at 223 (20), 222 (100), 105 (56), 77 (47), 51 (8) and a metastable peak at 56. The ultraviolet spectrum in 95% ethanol was characterized by maxima at 257 mμ (ε 18,600) and 341 (22,760).

Structure **13** was further confirmed by the following chemical degradation. A mixture of 0.5 g of **13**, 15 ml of dioxane, and 15 ml of a 10% hydrochloric acid solution was allowed to reflux for 8 hr. The reaction mixture was diluted with water and extracted with benzene. The benzene layer was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* afforded a crude solid. Recrystallization from heptane–benzene gave pale yellow prisms, mp 76–77°. The infrared spectrum of this material was identical in all respects with that of dibenzoylmethane. A mixture melting point of this material with authentic dibenzoylmethane was undepressed at 76–77°.

Recrystallization of **18** from benzene–heptane gave white needles, mp 139.5–140.5°. The structure of this material was assigned as 5-benzoyl-2,4-diphenyloxazole (**18**) on the basis of the following observations.

*Anal.* Calcd for $C_{22}H_{15}O_2N$: C, 81.21; H, 4.65; N, 4.31. Found: C, 81.12; H, 4.69; N, 4.21.

The infrared spectrum of this material in a potassium bromide pellet was characterized by bands at 6.06, 6.54, 7.37, 8.12, 8.61, 11.77, 12.76 and 13.96 μ. The nmr spectrum ($CDCl_3$) showed only a multiplet centered at τ 2.09. The mass spectrum (70 eV) exhibited a molecular ion at *m/e* (relative intensity) 325 (98) and prominent peaks at 39 (11), 51 (15), 63 (25), 77 (43), 89 (100), 105 (19), 117 (10), 165 (9), 192 (77), and 193 (14). The ultraviolet spectrum exhibited maxima at 265 mμ (ε 27,340) and 328 (13,620).

Structure **18** was further confirmed by an alternate synthesis from *trans*-2,4-diphenyl-5-benzoyl-2-oxazoline (**15**). A mixture of 0.20 g (0.0006 mol) of oxazoline **15** and 0.14 g (0.006 mol) of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in 15 ml of benzene was allowed to reflux for 3 hr. A brown solid precipitated out as the reaction proceeded. The reaction mixture was then filtered and the filtrate concentrated *in vacuo* to give a dark oil. Preparative thick layer chromatography of the mixture produced only a single component which was recrystallized from benzene–heptane to afford white needles, mp 139.5–140.5°. The infrared spectrum of this material was identical in all respects with that of a sample of **18** obtained from the photolysis. A mixture melting point of the two samples was undepressed at 140°.

**Acid Hydrolysis of *trans*-2,4-Diphenyl-5-benzoyl-2-oxazoline (15).**—A mixture of 0.5 g of *trans*-2,4-diphenyl-5-benzoyl-2-oxazoline (**15**), 10 ml of 95% ethanol, and 10 ml of water was allowed to reflux for 18 hr. The reaction mixture was diluted with water and extracted with benzene. The benzene layer was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a yellow oil which was crystallized from chloroform–heptane to give 0.5 g (90%) of white needles, mp 138.5–140°. The structure of this product is assigned as N-1-phenyl-2-hydroxy-2-benzoylethylbenzamide (**16**) on the basis of the following observations.

*Anal.* Calcd for $C_{22}H_{19}O_3N$: C, 76.50; H, 5.55; N, 4.06. Found: C, 76.29; H, 5.56; N, 4.04.

The infrared spectrum of this material (potassium bromide pellet) was characterized by bands at 3.01, 5.92, 6.07, 6.58, 6.72, 7.11, 7.60, 7.80, 7.95, 9.01, 10.15, 13.14, 13.76, and 14.32 μ. The ultraviolet spectrum in 95% ethanol showed a maximum at 236 mμ (ε 17,620). The nmr spectrum ($CDCl_3$) was characterized by a multiplet centered at τ 2.41 (15 H), a doublet at 3.0 (1 H, $J$ = 9 Hz, NH), a doublet of doublets at 4.28 (1 H, $J$ = 9 Hz, $J$ = 1.8 Hz, CHNH), a poorly resolved doublet of doublets at 4.52 (1 H, $J$ = 4, $J$ = 1.8 Hz, CHOH) and a poorly resolved doublet at 5.64 (1 H, $J$ = 4 Hz, OH). Addition of deuterium oxide to the nmr tube simplified the spectrum and gave a multiplet at 2.41 (15 H), a doublet at 2.94 (1 H, $J$ = 9 Hz, NH), a doublet of doublets at 4.28 (1 H, $J$ = 9 Hz, $J$ = 1.8 Hz, CHNH) and a sharp doublet at 4.52 (1 H, $J$ = 1.8 Hz, CHOD). In order to complete the deuterium exchange, a sample of 0.1 g of **16** was dissolved in 10 ml of methanol–OD containing 1 drop of deuterium chloride (20% in $D_2O$). The solution was heated to reflux for 1 hr. The solvent was then removed *in vacuo* leaving a white solid whose nmr spectrum contained a multiplet at τ 2.41 (15 H) and an AB quartet at 4.39 (2 H, $J$ = 1.8 Hz, DOCHCHND).

**Oxidation of N-1-Phenyl-2-hydroxy-2-benzoylethylbenzamide (16).**—A solution of 0.3 g of N-1-phenyl-2-hydroxy-2-benzoyl-

(29) Thick layer plates were prepared by spreading a slurry of 150 g of Merck $PF_{254+256}$ silica gel and 350 ml of distilled water onto 10 × 20 cm glass plates to an average thickness of 1.5 cm. The plates were allowed to dry at room temperature for 24 hr prior to use.

ethylbenzamide (16) in 5 ml of glacial acetic acid containing 10 ml of a hot saturated solution of chromium trioxide in glacial acetic acid was allowed to stir for 10 min. The dark green reaction mixture was poured onto ice water and filtered. The residue was washed with water and recrystallized from methanol to give a quantitative yield of dibenzamide as white needles, mp 144–145° (lit.[30] 144°). This material was identified as dibenzamide by a comparison of its infrared spectrum with that of an authentic sample prepared by the method of Lamberton and Standage.[30] A mixture melting point of these two materials was undepressed at 144–145°.

If the oxidation was allowed to proceed for only 2 min a partial oxidation product (17) as well as dibenzamide could be isolated by preparative thick layer chromatography. The structure of this material is assigned as N-1-phenyl-1-phenylglyoxylmethylbenzamide (17), mp 170–171°, on the basis of the following observations.

The infrared spectrum (in a potassium bromide pellet) was characterized by absorptions at 3.02, 5.84, 5.96, 6.06, 6.53, 6.89, 7.48, 7.71, 9.95, 11.82, 12.45, 13.20, 14.06, and 14.50 $\mu$. The mass spectrum (70 eV) exhibited a molecular ion at $m/e$ 343, prominent peaks at 222 (3.0), 221 (16.0), 165 (2.0), 106 (9.0), 105 (100), 52 (2.0), 51 (14.0), 50 (4.0), and had metastable peaks at 56 and 142.

**Catalytic Hydrogenation of 1,4-Diphenyl-4-benzoyloxy-2-aza-butadiene (14).**—A mixture of 0.08 g of 14 in 200 ml of dry methanol was hydrogenated in a Parr shaker over 0.1 g of 10% palladium on carbon at 50 psig for 3 hr. The catalyst was then removed by filtration and the filtrate concentrated *in vacuo* to leave a white solid, mp 206–208°. The structure of this compound was assigned as the benzylphenethylammonium salt of benzoic acid (19) on the basis of the following observations.

The infrared spectrum of 19 in a potassium bromide pellet showed broad adsorptions at 3.0 to 4.2, 6.3, 6.5, and 7.25 $\mu$ all of which are characteristic of benzoic acid salts. Additional bands appeared at 9.4, 9.8, 11.9, 13.3, 13.9, and 14.2 $\mu$.

The structure of 19 was confirmed by generation of benzylphenethylamine from 19. A 0.05-g sample of 19 was dissolved in a 10% sodium carbonate solution and extracted with ether. The ether extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent *in vacuo* gave an oil which was identical in all respects with an authentic sample of benzylphenethylamine.

Alternatively, treatment of 0.1 g of benzylphenethylamine with 0.1 g of benzoic acid in 3 ml of ether afforded a white precipitate. This material, mp 206–208°, was identical in all respects with the material isolated from the catalytic hydrogenation.

**Treatment of 1,4-Diphenyl-4-benzoyloxy-2-aza-butadiene (14) with Sodium Methoxide.**—A mixture of 0.3 g of 6 was dissolved in 20 ml of a freshly prepared 0.4 $N$ sodium methoxide–methanol solution and was allowed to stir at room temperature for 4 hr. The colored reaction mixture was diluted with water and extracted twice with ether. The ethereal layer was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* afforded a crude bright yellow solid. Recrystallization from benzene–pentane produced yellow needles, mp 235–237° dec. The structure of this material was assigned as 2,5-dibenzoyl-3,6-diphenyl-1,4-dihydropyrazine (20) on the basis of the following observations.

*Anal.* Calcd for $C_{30}H_{22}O_2N_2$: C, 81.43; H, 5.01; N, 6.33. Found: C, 81.79; H, 5.23; N, 6.08.

The infrared spectrum (potassium bromide pellet) was characterized by bands at 3.09, 6.26, 7.06, 7.69, 8.05, 10.93, 11.31, 12.90, 13.47, and 14.25 $\mu$. In order to demonstrate that the band at 3.09 was due to an N–H stretching mode, 0.01 g of 20 was allowed to reflux in methanol-OD for 1 hr. The solvent was removed *in vacuo* and the infrared spectrum revealed that the band at 3.09 $\mu$ (N–H) had disappeared and that a new band at 4.08 $\mu$ (N–D) had appeared. The nmr spectrum was characterized by a complex multiplet centered at $\tau$ 2.42. The mass spectrum (70 eV) had a molecular ion at $m/e$ (relative intensity) 442 (3) and prominent peaks at 41 (37), 43 (62), 44 (40), 55 (38), 56 (16), 57 (80), 69 (30), 71 (50), 77 (68), 85 (33), 105 (100), 323 (35), 338 (40), 349 (30), 426 (60), 427 (20), and 428 (12). The ultraviolet spectrum in cyclohexane exhibited maxima at 235 m$\mu$ ($\epsilon$ 9100), 259 (6000), and 366 (5450).

**Registry No.**—1, 24290-58-2; 3, 24807-13-4; 4, 24807-14-5; 5, 24806-70-0; 6, 24807-15-6; 8, 24806-71-7; 13, 23112-19-8; 14, 24294-71-1; 15, 24806-73-3; 16, 24807-17-8; 17, 24807-18-9; 18, 24807-19-0; 19 benzylphenethylammonium salt, 24807-20-3; 20, 24807-21-4.

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# Pyridazines. XXXV. Oxidation Products of Some Simple and Bicyclic Pyridazines

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N-Oxides of imidazo[1,2-*b*]pyridazine and *s*-triazolo[4,3-*b*]pyridazine have been obtained by direct oxidation with concentrated hydrogen peroxide in polyphosphoric acid. With several bicyclic compounds further oxidation afforded pyridazine derivatives. 6-Amino bicyclic compounds were resistant toward N-oxidation but afforded the corresponding 6-nitro compounds. Several displacement reactions on substituted pyridazine N-oxides have been performed, and it was also shown that nmr spectral characteristics can be used for distinguishing the site of N-oxidation.

We recently reported[1] the first representative of azoloazine N-oxides with bridgehead nitrogen, *i.e.*, *s*-triazolo[4,3-*b*]pyridazine 5-oxides, which were synthesized by cyclization of the appropriate pyridazine N-oxides since previous direct N-oxidation procedures have failed. We now report the successful direct N-oxidation of such bicyclic systems with concentrated hydrogen peroxide in polyphosphoric acid.

Imidazo[1,2-*b*]pyridazine and 85% hydrogen peroxide in polyphosphoric acid below 40° afforded the 5-oxide (2, X = CH; R = H) in moderate yield. However, with a large excess of the oxidizing agent 3-nitropyridazine 1-oxide was formed by degradative oxidation. A greater tendency toward degradation compared with N-oxidation could be observed with 6-chloro- or 6-methoxyimidazo[1,2-*b*]pyridazine which were transformed into 6-chloro-3-nitropyridazine 1-oxide and 6-methoxy-3-nitropyridazine, respectively. In the last case, the possible alternative structure of the product as a methoxynitrosopyridazine N-oxide could

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