The Reaction of Diphenylcyclopropenone with 1-Azirines. Synthetic and Mechanistic Implications[1]

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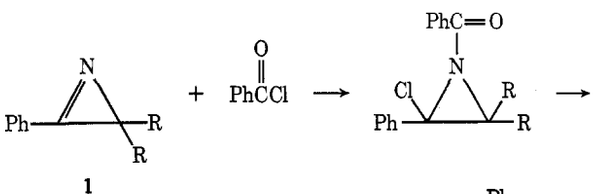
Received October 13, 1971

1-Azirines 1 react with diphenylcyclopropenone (2) to produce 1:1 adducts, which were proven to be 2,3-diphenyl-4-pyridones 6. That the 3 substituents in 6 originate from the 3 substituents on the azirine was shown by independent synthesis of 6a as well as by isolation of the 3*H*-4-pyridone 10 when 2-phenyl-3,3-dimethylazirine was used as a substrate. These results suggest a nucleophilic attack by the azirine nitrogen on C-2 of the cyclopropenone with subsequent rupture of the azirine 3–1 bond (C–N). The mechanistic pathway of the reaction is discussed.

Both 1-azirines (1) and cyclopropenones (2) represent versatile substrates which can act either as dipoles or dipolarophiles as well as by way of ionic intermediates. For instance, examples have recently become known in which additions to azirines occur across the C=N bond (eq 1),[2] the C–N bond (eq 2),[3] or the C–C bond in these heterocycles (eq 3).[4]



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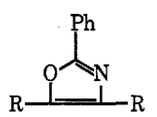

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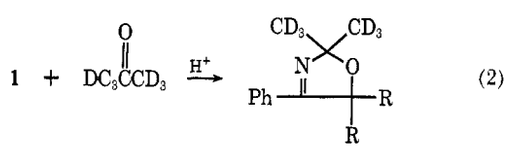

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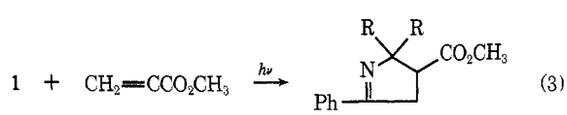


(3)

Similarly, ample evidence has accumulated for addition across the C=C bond (eq 4),[5] or the C=O bond of cyclopropenones (eq 5)[6] as well for regioselective ring opening of the C–C bond in these systems (eq 6,7).[7,8]

Our extensive studies of the chemical behavior[2,9] of azirines made it desirable to explore the interaction between this strained ring system and a polar cyclopropenone, with emphasis on reaction conditions, structure of products, and mechanistic implications.

(1) Chemistry of Small Ring Heterocycles. XIX. For the previous paper in this series, see ref 9e.

(2) F. W. Fowler and A. Hassner, *J. Amer. Chem. Soc.*, **90**, 2875 (1968).

(3) N. J. Leonard and B. Zwanenburg, *ibid.*, **89**, 4456 (1967).

(4) A. Padwa and J. Smolanoff, *ibid.*, **93**, 548 (1971).

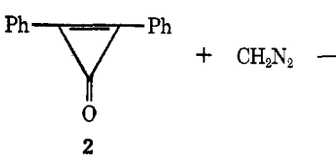
(5) P. T. Izzo and A. S. Kende, *Chem. Ind. (London)*, 839 (1964); R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Amer. Chem. Soc.*, **87**, 1320 (1965).

(6) L. Paquette, T. Barton, and N. Horton, *Tetrahedron Lett.*, **No. 50**, 5039 (1967).

(7) E. V. Dehmlow, *ibid.*, **51**, 5177 (1967).

(8) F. Toda, T. Mitote, and K. Akagi, *Chem. Commun.*, **5**, 228 (1969).

(9) (a) A. Hassner and F. W. Fowler, *J. Amer. Chem. Soc.*, **90**, 2869 (1968); (b) A. Hassner, R. J. Isbister, R. B. Greenwald, J. T. Klug, and E. C. Taylor, *Tetrahedron*, **25**, 1637 (1969); (c) A. Hassner and R. J. Isbister, *J. Amer. Chem. Soc.*, **91**, 6126 (1969); (d) A. Hassner, J. O. Currie, A. S. Steinfeld, and R. F. Atkinson, *Angew. Chem.*, **82**, 772 (1970); (e) D. J. Anderson and A. Hassner, *J. Amer. Chem. Soc.*, **93**, 4339 (1971).



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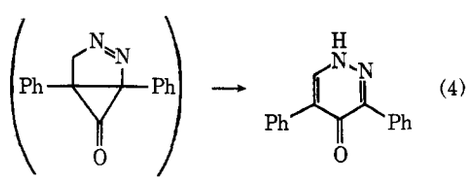

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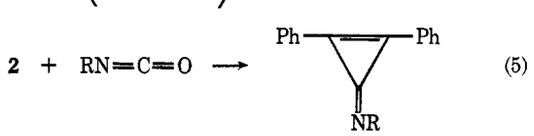

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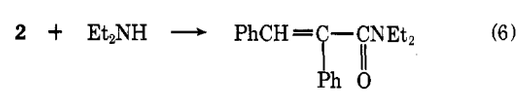

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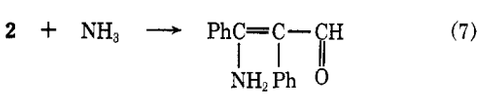


(7)

Results and Discussion

Diphenylcyclopropenone (2) underwent a slow reaction with mono- and disubstituted azirines (1) at temperatures above 100° (see Table I). Refluxing toluene

TABLE I

FORMATION OF PYRIDONE 6 BY HEATING OF AZIRINE 1 WITH CYCLOPROPENONE 2 IN TOLUENE

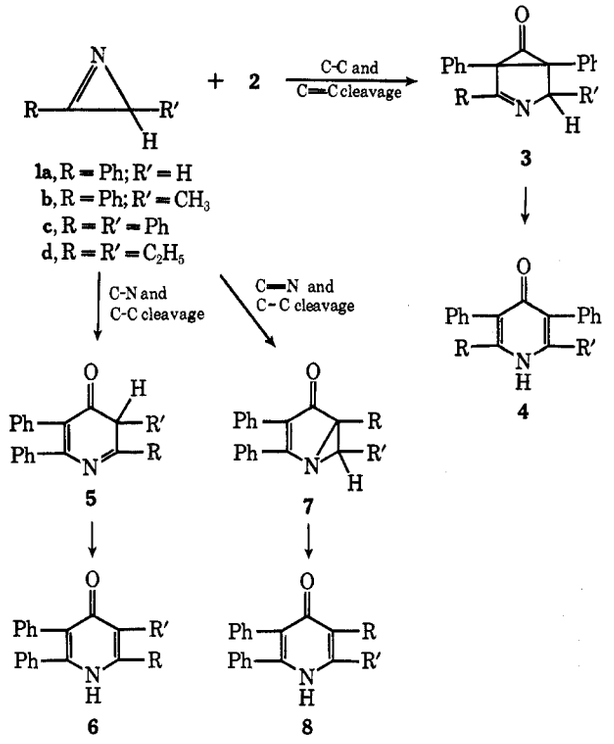
Azirine	Pyridone	Reaction time, days	Yield, %[a]
1a	2,3,6-Triphenyl-4(1*H*)-pyridone (6a)	2	27
1b	2,3,6-Triphenyl-5-methyl-4(1*H*)-pyridone (6b)	2 (4)	33 (50)
1c	2,3,5,6-Tetraphenyl-4(1*H*)-pyridone (6c)	2	27
1d	2,3-Diphenyl-5,6-diethyl-4(1*H*)-pyridone (6d)	3	33
9	3,3-Dimethyl-2,5,6-triphenyl-4(3*H*)-pyridone (10)	2	67[b]

[a] Yield actually represents per cent conversion, since examination of the alkyl region in the nmr spectra of the ether-soluble fractions showed only azirine for 1a–d, and azirine plus adduct for 9. The yields could be improved by refluxing for longer times, as shown with 1b. [b] By nmr; the isolated yield of pyridone 10 was 35% since it is appreciably soluble in ether.

was a convenient medium in which the rate of product formation was able to compete with polymerization of **2** and destruction of azirine **1**. Under these reaction conditions the crude product contained an appreciable amount of unreacted **1**. The product was isolated upon evaporation of the solvent and trituration with ether. The ether-insoluble material was a 1:1 adduct as indicated by elemental analysis, mass spectra, and nmr integration.

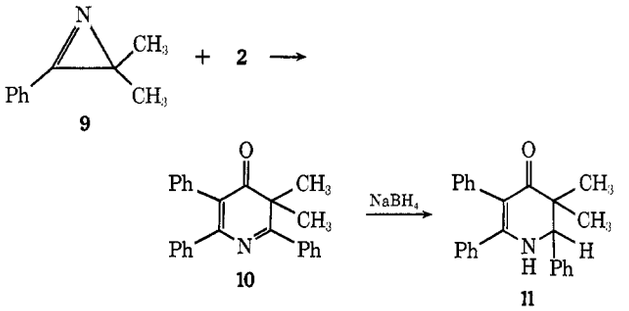
On the basis of the chemical behavior of **1** and **2** discussed above, a number of 2- and 4-pyridones, 3-hydroxypyridines, and azabicyclocyclohexanones come into consideration for the adduct. The ir spectra of adducts **6a** and **6b** (**6c** and **6d** were insoluble in $CHCl_3$) in dilute chloroform showed a sharp absorption ($W_{1/2}$ = 15 Hz) at 3400 cm^{-1}, a position and half-width reportedly[10a] characteristic of amidic NH. The only intense absorption in the carbonyl region of 1600–1800 cm^{-1} occurred at 1625 cm^{-1}. Such low carbonyl absorption is observed for 4-pyridones,[10b] suggesting **4**, **6**, and **8** as possible structures for the adducts. The pathways to these products involve C–C, C–N, or C=N cleavage of the azirine coupled with C=C or C–C cleavage of the cyclopropenone (see Scheme I).

SCHEME I



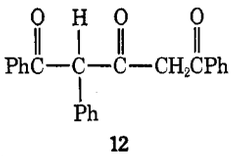
Structure **4** was eliminated, since the adduct of azirine **1d** with **2** showed two nonequivalent ethyl groups in the nmr spectrum.[11] Of the two remaining possibilities structure **8** is derived from a fused aziridine **7** prior to aromatization (Scheme I). If a 3,3-disubstituted azirine were used as a substrate, one might expect to isolate a bicyclic intermediate of type **7** because aromatization would require an energetically more unfavorable alkyl migration.

In fact, the adduct of 2-phenyl-3,3-dimethylazirine (**9**) showed two equivalent methyl groups in the nmr (not expected for a bicyclic aziridine of type **7** containing a geminal dimethyl grouping). Reduction of this adduct with $NaBH_4$ gave a material which showed two *non*equivalent methyl groups in the nmr spectrum. The ir spectrum showed a sharp NH peak at 3400 cm^{-1} and C=O absorption at 1625 cm^{-1}. In addition, the



uv spectrum, λ_{max} 230 nm (ϵ 15,000) and 345 (10,000), as well as the chemical shift of the C-2 methine proton at τ 5.3, are indicative of the 2,3-dihydro-4-pyridone structure **11** for the reduction product. These data are in excellent agreement with those reported[12] for 2,3-dihydro-2,6-diphenyl-4-pyridone. Hence, the structure of the adduct is **10**, suggesting that **6** is the adduct resulting from interaction of **2** with azirines **1a–d**.

Unequivocal proof was provided by an independent synthesis of **6a**. The experimental approach involved the cyclization of 1,2,5-triphenyl-1,3,5-pentanetrione (**12**) with ethanolic ammonia according to the procedure described by Light and Hauser[10b] for 1,5-disubstituted-1,3,5-pentanetriones.



1,2,5-Triphenyl-1,3,5-pentanetrione, for which structure **12** was reported,[13] was obtained by us in two forms (see Experimental Section). The initial form obtained was assigned a dienol structure (**13**) based on the observation of two enolic protons in the nmr spectrum.[14] A second form was obtained upon recrystallization of **13** from 95% ethanol.

Based on the observation of a strong 1680-cm^{-1} band in the infrared and the presence of two singlets in the olefinic region of the nmr spectrum, **14** is considered to be the most reasonable structure for this second form. Either **13** or **14** was converted with ammonia to pyridone **6a**, albeit in low yield (10%). The major product in both cases was identified through its nmr and mass spectra as the retro Claisen product 1,4-diphenyl-1,3-butanedione, in either of two enolic forms (**15** or **16**).

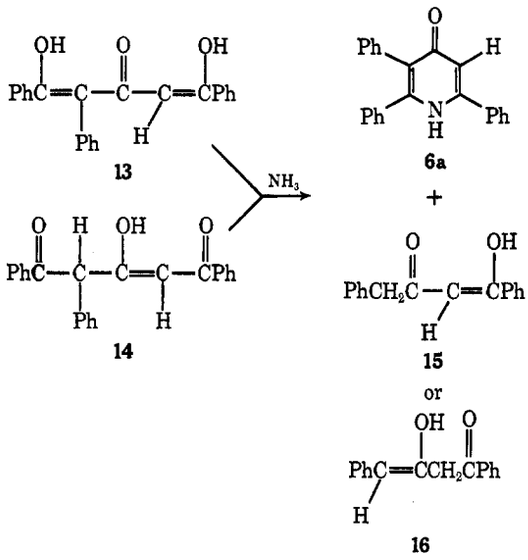
(10) (a) S. F. Mason, *J. Chem. Soc.*, 4874 (1957); L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Wiley, New York, N. Y., 1958, p 207. (b) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 538 (1960).

(11) The pathway involving C–C cleavage of the azirine and cycloaddition to give **3** is also unlikely on mechanistic grounds, because thermal excitation should result in preferential cleavage of the C–N bond, whereas C–C cleavage is usually the result of an electronically excited state.

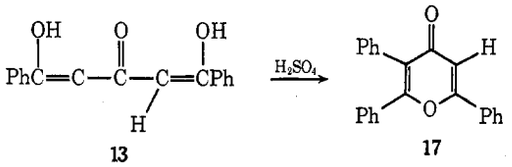
(12) N. Sugiyama, M. Yamamoto, and C. Kashima, *Bull. Chem. Soc. Jap.*, **43**, 902 (1970).

(13) M. Stavaux and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 2082 (1967).

(14) This dienol structure is similar to that proposed by Light and Hauser for several related triketones; see ref 10b.



2,3,6-Triphenyl-4*H*-pyran-4-one (**17**) was obtained in high yield upon treatment of **13** with cold concentrated sulfuric acid in a manner described for other triketones.[10b] The nmr spectrum of **17** was found to be

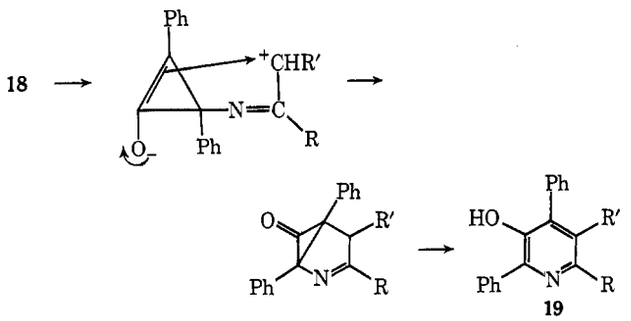


almost identical with that of pyridone **6a**, offering further confirmation of structure.

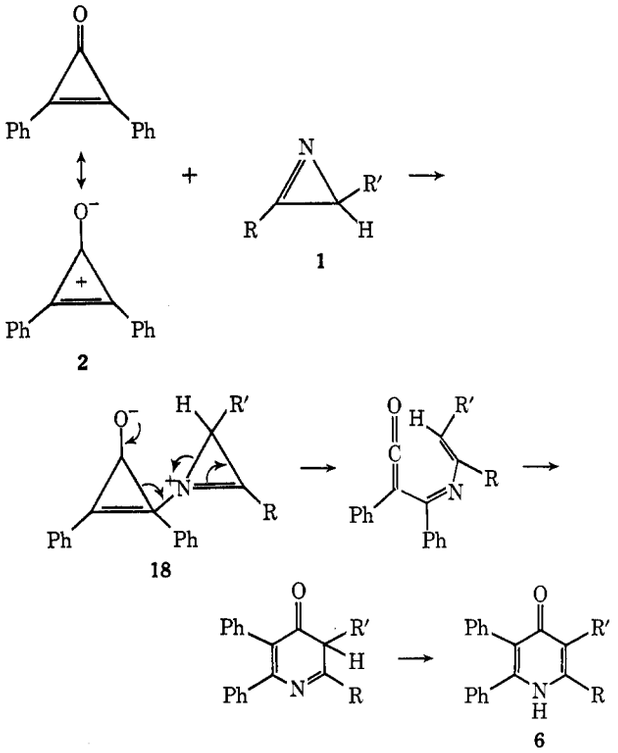
The results of the azirine cycloadditions are summarized in Table I.

The 4(1*H*)-pyridones **6** can be pictured as arising from the reaction of diphenylcyclopropenone (**2**) with substituted azirines (**1**) by way of nucleophilic attack of the weakly basic azirine nitrogen on the electrophilic cyclopropenone ring followed by an intramolecular Cope cyclization, as illustrated in Scheme II.[15a]

A possible competing reaction of intermediate **18**, analogous to a reaction described for the rearrangement of a norbornyl aziridine,[15b] should lead to a 3-hydroxy pyridine **19** and is therefore not occurring in this case.



SCHEME II



Experimental Section[16]

Reaction of 2-Phenylazirine (1a) with Diphenylcyclopropenone (2).—A solution of 2-phenyl-1-azirine (0.333 g, 0.0028 mol) and diphenylcyclopropenone (0.587 g, 0.0028 mol) in 23 ml of dry toluene was heated at reflux for 2 days. After this time, the solvent was evaporated and 25 ml of anhydrous ether was added to the residue. An insoluble white solid, **6a**, remained (0.250 g, 27% based on a 1:1 adduct):[17] mp 226–227° (unaffected by recrystallization from benzene–hexane); mass spectrum *m/e* (rel intensity) 323 (20.98, M^+), 322 [36.94, $(M-1)^+$], 178 (9.68, $PhC{\equiv}CPh^+$); ir ($CHCl_3$) 3500, 3400, 1625, 1580, 1555 cm^{-1}; nmr ($CDCl_3$) τ 3.05 (1 H singlet), 2.82, 2.77 (two 5 H singlets), 2.5 (5 H multiplet).

Anal. Calcd for $C_{23}H_{17}NO$: C, 85.42; H, 5.30; N, 4.33. Found: C, 85.47; H, 5.26; N, 4.15.

Reaction of 2-phenyl-3-methylazirine (1b) with 2 (0.0054 mol each) under reflux for 4 days led to 0.90 g (50% yield)[17] of pure **6b**: mp 251.5–252°; mass spectrum *m/e* (rel intensity) 337 (56.00, M^+), 336 [100, $(M-1)^+$], 178 (49.33, $PhC{\equiv}CPh^+$); ir ($CHCl_3$) 3400, 1625, 1580, 1550 cm^{-1}; nmr ($CDCl_3$) 7.93 (3 H singlet), 2.8, 2.73, 2.5 (three 5 H singlets, total aromatic region integrates for 16 H); uv (95% ethanol) λ_{max} 246 nm (ϵ 39,000); uv (0.13 *N* HCl–95% ethanol) λ_{max} 237 nm (ϵ 40,000).

Anal. Calcd for $C_{24}H_{19}NO$: C, 85.43; H, 5.68; N, 4.15. Found: C, 85.60; H, 5.83; N, 4.07.

Reaction of 2,3-diphenylazirine (1c) with 2 (0.0028 mol each) under reflux for 2 days gave 0.30 g (27% yield)[17] of pure **6c**: mp 330–331°; mass spectrum *m/e* (rel intensity) 399 (63.34, M^+), 398 [100, $(M-1)^+$], 178 (3.80, $PhC{\equiv}CPh^+$); ir (KBr) 3400, 3220, 1620, 1590, 1510 cm^{-1}; nmr (CH_3OD) τ 2.77 and 2.65 (singlets in 1:1 ratio).

Anal. Calcd for $C_{29}H_{21}NO$: C, 87.19; H, 5.30; N, 3.51. Found: C, 87.16; H, 5.34; N, 3.68.

Reaction of 2,3-diethylazirine (1d) with 2 (0.002 mol each) led after 3 days of refluxing to 0.2 g (33% yield)[17] of pure **6d**: mp 262–263°; mass spectrum *m/e* (rel intensity) 303 (66.64,

(15) (a) A pathway involving the trapping of a vinyl nitrene (a tautomer of the azirine **1**) by a dipolar ring-opened form of diphenylcyclopropenone (**2**) would also satisfy the results. At the present this path seems unlikely because heating of α-azidostyrene in benzene in the presence of **2** produced only azirine **1a** and no pyridone **6a**. (b) A. C. Oehlschlager and L. H. Zalkow, *J. Org. Chem.*, **30**, 4205 (1965).

(16) All melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer 457 spectrophotometer. Nmr spectra were recorded with a Varian A-60A spectrometer using tetramethylsilane as an internal standard. The elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

(17) Examination of the alkyl region in the nmr spectrum of the ether-soluble material demonstrated the presence of starting azirine only.

M^+), 302 [100, $(M - 1)^+$], 178 (70.00, PhC≡CPh$^+$); ir (KBr) 3400, 3220, 1625, 1615, 1580, 1525 cm^{-1}; nmr (50% CD_3OD–$CDCl_3$) τ 8.83, 8.70 (two overlapping 3 H triplets), 7.35, 7.22 (two overlapping 2 H quartets), 2.86, 2.77 (two 5 H singlets).

Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.05; H, 6.89; N, 4.58.

Reaction of 2-phenyl-3,3-dimethylazirine (9) with 2 (0.0028 mol each) under reflux for 2 days gave 0.35 g (35% yield)[18] of adduct **10**: mp 154.5–155.5° (unaffected by recrystallization from cyclohexane); mass spectrum *m/e* (rel intensity) 351 (100, M^+), 178 (99.12, PhC≡CPh$^+$); ir ($CHCl_3$) 1670, 1650, 1575, 1550 cm^{-1}; nmr ($CDCl_3$) τ 8.36 (6 H singlet), 2.82–2.15 (15 H multiplet).

Sodium Borohydride Reduction of 3,3-Dimethyl-2,5,6-triphenyl-4(3*H*)-pyridone (10).—Sodium borohydride (40 mg, 1.0 mmol) was added to a suspension of **10** (100 mg, 0.29 mmol) in 10 ml of absolute ethanol. Solution occurred immediately. After 18 hr at room temperature, the solvent was evaporated and the resulting white solid was treated with 10% aqueous ammonium chloride (10 ml). An ether extract (50 ml) was dried over $MgSO_4$, filtered, and evaporated to give 100 mg (100%) of a pale yellow solid: mp 216–217° (unaffected by recrystallization from benzene–hexane); mass spectrum *m/e* (rel intensity) 353 (100, M^+), 352 [25.40, $(M - 1)^+$], 178 (18.99, PhC≡CPh$^+$); ir ($CHCl_3$) 3400, 1625, 1580, 1550 cm^{-1}; nmr ($CDCl_3$) τ 8.9 (two 3 H singlets separated by 2 Hz), 5.3 (1 H doublet, J = 1.5 Hz, collapses to a singlet upon D_2O exchange), 4.85 (1 H, broad, disappears upon D_2O exchange), 2.95, 2.8, 2.6 (three 5 H singlets); uv (95% ethanol) λ_{max} 230 nm (ϵ 15,000), 345 (10,000); uv (0.7 NHCl–95% ethanol) λ_{max} 232 nm (ϵ 14,000) 347 (9000).

Anal. Calcd for $C_{25}H_{23}NO$: C, 84.95; H, 6.56; N, 3.93. Found: C, 84.72; H, 6.69; N, 3.94.

1,2,5-Triphenyl-1,2,5-pentanetrione (12).[13]—Under a dry nitrogen atmosphere, a solution of phenyl-2-propanone (13.4 g, 0.1 mol) and methyl benzoate (40.8 g, 0.3 mol) in 100 ml of dimethoxyethane (distilled from lithium aluminum hydride) was added to a stirred suspension of sodium hydride (50% oil dispersion, 24.0 g, 0.5 mol) in 300 ml of dimethoxyethane at reflux. The reaction mixture was refluxed for 5 hr, after which time the solvent was evaporated and 300 ml of diethyl ether was added to the pasty residue at 0°. Dropwise addition of cold water (200 ml) resulted in the formation of a bright yellow solid (30 g) which was insoluble in either the aqueous layer or the ethereal layer. This material was suspended in a two-phase mixture of saturated aqueous ammonium chloride (200 ml) and benzene (500 ml). After 3 days, solution was observed to have occurred. Evaporation of the benzene gave 26 g (65%) of bright yellow, hexane-soluble needles of **13** which did not exhibit a sharp melting point: mp 96–115°; ir ($CHCl_3$) 1510–1615 cm^{-1} (strong, broad); nmr ($CHCl_3$) τ 4.2 (1 H singlet), 2.9–2.35 (15 H multiplet), −3.1 (1 H singlet), −5.3 (1 H singlet).

(18) Examination of the alkyl region in the nmr spectrum of the ether-soluble material (0.65 g) demonstrated the presence of starting azirine and adduct in a 1:1 ratio. Based on this observation the actual conversion is 67%.

Recrystallization of **13** from 95% ethanol gave **14**, another tautomer of the triketone:[19] mp 110–112° (lit.[13] mp 105–108°); ir ($CHCl_3$) 1680, 1520–1620 cm^{-1}; nmr ($CDCl_3$) τ 4.23 (1 H singlet), 3.73 (1 H singlet), 2.85–2.45 (11 H multiplet), 2.25, 2.0 (two 2 H multiplets).

Cyclization of 1,2,5-Triphenyl-1,3,5-pentanetrione with Ammonia to Form 2,3,6-Triphenyl-4(1*H*)-pyridone (6a).[20]—To 1.0 g of 1,2,5-triphenyl-1,3,5-pentanetrione (either **13** or **14**) dissolved in 50 ml of absolute ethanol was slowly added commercial, anhydrous liquid ammonia until the flask was cold. The solution was evaporated to dryness, and the process was then repeated with the residue. Repeated recrystallization from benzene–hexane afforded **6a** as a white solid (0.1 g, 10%), mp 225–226°. The ir and nmr spectra of this material were identical with those of the adduct **6a** obtained from **2** and 2-phenylazirine. Nmr spectral analysis of the benzene–hexane-soluble fraction demonstrated the absence of starting triketone.

The hexane-soluble portion (0.60 g) had the following spectra: mass spectrum *m/e* 238 (M^+); ir ($CHCl_3$) 1500–1670 cm^{-1} (strong, broad); nmr ($CDCl_3$) τ 6.3 (2 H), 3.9 (1 H), 2.72 (5 H), 2.4 (5 H), −4.0 (1 H, broad). These spectral data indicate that the major product is an enol chelate form (either **15** or **16**) of 1,4-diphenyl-1,3-butanedione, resulting from a retro Claisen reaction. The material gave a crystalline copper chelate, mp 209–211° (lit.[21] mp 203–205°).

The Cyclization of Dienol 13 to 2,3,6-Triphenyl-4*H*-pyran-4-one (17).[18]—A 0.5-g sample of 1,2,5-triphenyl-1,3,5-pentanetrione (**13**) was dissolved in 10 ml of concentrated sulfuric acid at 0°. After 10 min at this temperature, the solution was poured into ice water. The resulting precipitate was collected on a funnel, washed with water, and recrystallized from benzene–hexane to give a white solid (0.35 g, 70%): mp 174.5–175°; mass spectrum *m/e* (rel intensity) 324 (58.48, M^+), 323 [100, $(M - 1)^+$], 178 (32.28, (PhC≡CPh$^+$); ir ($CHCl_3$) 1645, 1635, 1610, 1595 cm^{-1}; nmr ($CDCl_3$) τ 2.9 (1 H singlet), 2.75, 2.7 (two 5 H singlets), 2.35 (5 H multiplet).

Anal. Calcd for $C_{23}H_{16}O_2$: C, 85.16; H, 4.97. Found: C, 85.09; H, 4.86.

Registry No.—**2**, 886-38-4; **6a**, 33707-15-2; **6b**, 33666-41-0; **6c**, 33707-16-3; **6d**, 33666-42-1; **10**, 33707-17-4; **11**, 33815-38-2; **13**, 33707-18-5; **17**, 33707-19-6.

Acknowledgment.—Support of this work by Public Health Service Grant CA-04474 from the National Cancer Institute is gratefully acknowledged.

(19) This is evidently the form reported by Stavaux and Lozac'h; see ref 13.

(20) Patterned after the general procedure described by Light and Hauser; see ref 10b.

(21) K. G. Hampton, T. M. Harris, and C. H. Hauser, *J. Org. Chem.*, **29**, 3511 (1964).