

A NEW 1,3-DIPOLAR CYCLOADDITION REACTION
THE FORMATION OF AZOMETHINE YLIDS FROM SPIRO-ISOXAZOLIDINES*

Otohiko Tsuge and Ichiro Shinkai

Research Institute of Industrial Science, Kyushu University,
Hakozaki, Fukuoka 812, Japan

(Received in Japan 5 August 1970; received in UK for publication 24 August 1970)

The 1,3-dipolar cycloaddition of nitrones to olefins to form isoxazolidines is well established,¹ and it is also known that nitrones react with α,β -unsaturated ketones to give isoxazolidines.² Recently, we have reported that *p*-substituted benzylideneacenaphthenones (I) which are cyclic α,β -unsaturated ketones possessing a cisoid arrangement of the conjugated double bond with carbonyl group, showed a different behavior from ordinary α,β -unsaturated ketones such as chalcones.³

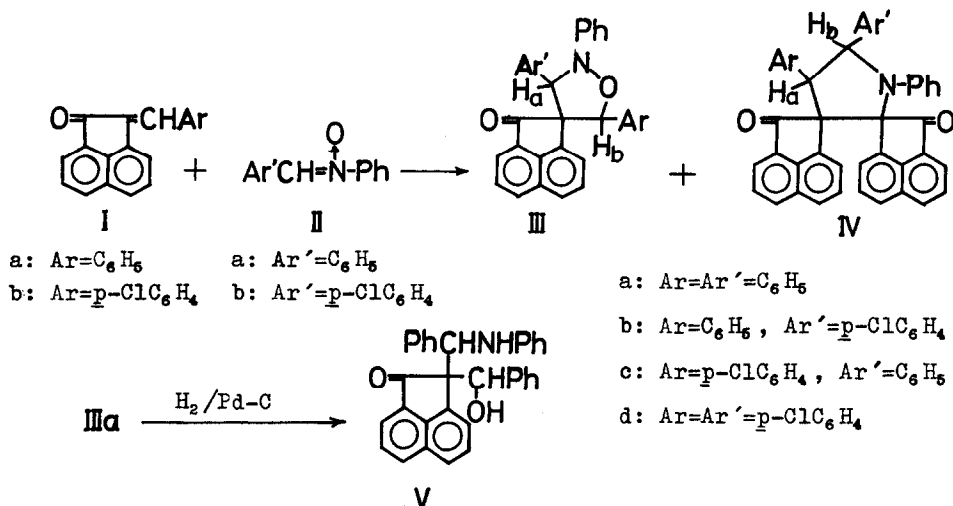
However, little attention has been paid to the 1,3-dipolar cycloaddition of nitrones to I. In the course of a study of the 1,3-dipolar cycloaddition of C,N-diarylnitrones (II) to I, we found that spiro-isoxazolidines formed in the cycloaddition decomposed on heating or photolysis, affording azomethine ylids.

When a solution of equivalent amounts of Ia and the nitrone IIa in xylene was refluxed, colorless needles IIIa and pale yellow prisms IVa were obtained, accompanied by a trace amount of diacenaphthylidenedione (biacenedione).

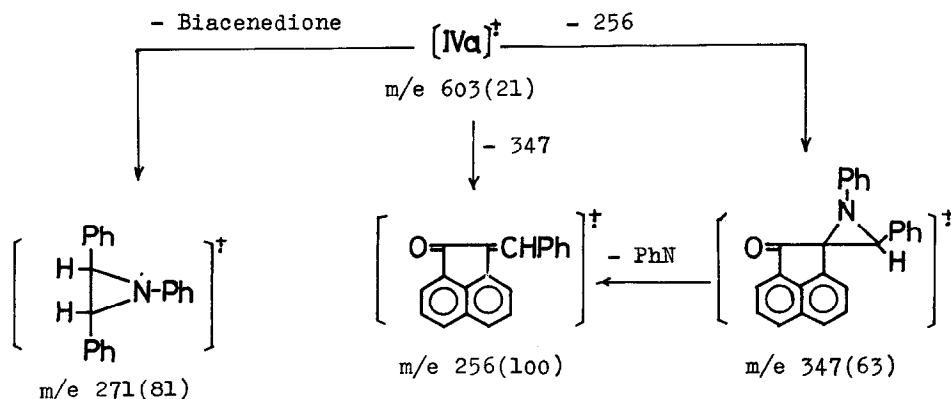
The compound IIIa was confirmed to be the expected spiro-isoxazolidine by the following evidence. The results of elemental analysis and mass spectrum are consistent with the molecular formula $C_{32}H_{25}O_2N$ (M^+ m/e 453). The structure of IIIa is supported by the ir and nmr spectra⁴ shown in Table I. Furthermore, the catalytic hydrogenolysis of IIIa in the presence of Pd-C(10%) in dioxane at room temperature gave the aminoalcohol V, mp 159-160°C dec, in 87% yield.

V: molecular formula $C_{32}H_{25}O_2N$; ir (KBr) 3430 (OH), 3340 cm^{-1} (NH); nmr

(CDCl_3) τ 4.93 (m, 2H, OH and NH , exchanged with D_2O), 4.48 (s, 1H, $\text{Ph}-\text{CH}-\text{NH}-$), 4.17 (s, 1H, $\text{Ph}-\text{CH}-\text{OH}$), 1.8-3.3 (m, 21H, aromatic protons); mass spectrum m/e 455 (M^+), 349 ($\text{M}^+ - \text{PhCHO}$), 256 ($349^+ - \text{PhNH}$).



On the other hand, the molecular formula of IVa agreed with $\text{C}_{44}\text{H}_{29}\text{O}_2\text{N}$ which was equivalent to that derived from a 2:1 adduct of Ia and IIa under the elimination of benzaldehyde. On the basis of the ir, nmr (Table I) and mass spectra, it is deduced that IVa is the bis-spiropyrrrolidine. The fragmentation of IVa on electron impact is as follows (rel intensity).



Similar reactions of Ia or Ib with IIa or IIb gave the corresponding spiro-

isoxazolidines IIIb-IIIc and bis-spiropyrrolidines IVb-IVc respectively. The results and physical properties of III and IV are summarized in Table I. Although the reaction of Ib with IIa gave two isomeric spiroisoxazolidines, IIIc and IIIc', their configurations are not clear yet.

TABLE I

Reaction time, hr	Compound	Yield %	M.p. °C	Ir, cm ⁻¹ C=O	Nmr (CDCl ₃)			Mol.wt. m/e
					Ha, τ	Hb, τ	Jab, Hz	
18	IIIa	48	187-188	1714	4.21 (s)	4.06 (s)		453
	IVa	24	281-282	1739, 1720	5.30 (d)	3.56 (d)	10.2	603
10	IIIb	37	167-168	1706	4.31 (s)	4.13 (s)		487
	IVb	8	269-270	1733, 1717	5.36 (d)	3.94 (d)	10.2	637
5	IIIc	32	172-173	1710	4.25 (s)	4.11 (s)		487
	IIIc'	19	149-150	1720	4.87 (s)	3.89 (s)		487
	IVc	7	260-261	1732, 1718	5.36 (d)	3.63 (d)	10.2	637
10	IIIc	33	185-186	1718	4.29 (s)	4.12 (s)		521
	IVc	27	266-267	1732, 1720	5.44 (d)	3.62 (d)	10.2	671

III: colorless needles, IVb-IVc: pale yellow needles, IVd: pale yellow prisms.

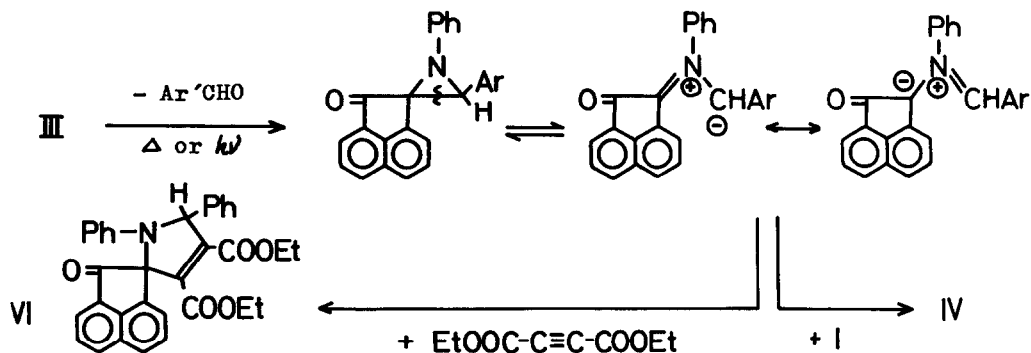
In order to elucidate whether the formation of IV is derived from III, the thermal decomposition of III in the presence of I was carried out in a refluxed xylene. The compound IV was formed together with a trace amount of biacenedione: the results are as follows (yield %).



Furthermore, when a solution of equivalent amounts of IIIa and Ia in benzene was irradiated by 100W high-pressure mercury lamp with a Pyrex filter at room temperature for 12 hr, IVa was obtained in 43.5% yield, accompanied by a trace amount of biacenedione.

On the basis of the above observations, the pathway for the formation of IV can be illustrated by the following scheme. That is, the spiroaziridine intermediate is derived from III under the elimination of benzaldehyde (Ar'-

CHO) converts into the 1,3-dipole, azomethine ylid,⁵ which reacts with I to give IV.



The above pathway was supported by the following experiment. When a solution of IIIa and diethyl acetylenedicarboxylate in xylene was refluxed for 10 hr, IVa and the spirodihydropyrrole VI, mp 169-170°C, were obtained in 35 and 29% yields respectively, together with a trace amount of biacenedione.

Structural elucidation of VI was accomplished by its nmr and mass spectra as well as by the elemental analysis. Molecular formula: $C_{23}H_{27}O_5N$ (M^+ m/e 517), nmr ($CDCl_3$): τ 9.48 (t, 3H, CH_3), 8.98 (t, 3H, CH_3), 6.41 (d-q, 2H, CH_2), 5.98 (q, 2H, CH_2), 5.36 (s, 1H, $\rightarrow CH$), 1.9-3.5 (m, 16H, aromatic protons).

Studies of the related reactions are in progress in our laboratory.

REFERENCES

- * Studies of Acenaphthene Derivatives. XXII. Part XXI: O. Tsuge, I. Shinkai and M. Koga, *J. Org. Chem.* in submitted.
- 1) J. Hamer and A. Macaluso, *Chem. Revs.*, **64**, 473 (1964); G. R. Delpierre and M. Lamchen, *Quart. Revs. (London)*, **19**, 329 (1965).
 - 2) R. Huisgen, H. Hauck, R. Grashey and H. Seidl, *Chem. Ber.*, **101**, 2043, 2568 (1968).
 - 3) O. Tsuge, I. Shinkai and M. Tashiro, *Tetrahedron Letters*, **1968**, 3631; *Bull. Chem. Soc. Japan*, **42**, 181, 185 (1969); *Kogyo Kagaku Zasshi*, **72**, 1680 (1969).
 - 4) The Ha and Hb signal were assigned on the basis of the fact that the spiroisoxazolidine prepared from benzylidene- α -d-acenaphthenone and I Ia did not show the signal at τ 4.06 in the nmr spectrum.
 - 5) The conversion of aziridines to azomethine ylids was first observed by R. Huisgen et al: *J. Amer. Chem. Soc.*, **89**, 1753 (1967).