

## The Effect of Substituents on the Photochemistry of Phenazine *N*-oxides

By Angelo Albini, Antonietta Barinotti, Gian Franco Bettinetti, and Silvio Pietra,\* Istituto di Chimica Organica, dell'Università di Pavia, Viale Taramelli 10, 27100 Pavia, Italy

Disappearance quantum yields of a set of substituted phenazine *N*-oxides were determined; from these values and on the basis of the composition of 10% conversion mixtures, the formation quantum yields of the major reaction products [the lactams (4) and the oxepinoquinoxalines (5)] were estimated. By correlating quantum yields and spectroscopic properties of the *N*-oxides, it was confirmed that there are two different pathways for the formation of quinoxalines and lactams, the latter being formed only when the excited state has internal charge transfer character. This had already been suggested on the basis of solvent effects on the photoisomerization of phenazine *N*-oxide.

As part of a study on the photoisomerization of phenazine *N*-oxides, the preparative aspects of the photochemistry of 2-methoxy- and 2-chloro-phenazine *N*-oxides were examined.<sup>1c</sup> We report here the preparative results on other derivatives (2-methyl-, 2-cyano-, and 2-nitro-phenazine 10-oxide) and the quantum yields of the whole series, which allow estimation of the effect of substituents on the photoisomerization of phenazine *N*-oxides.

oxygenation takes place with the formation of the corresponding phenazine.† 2-Nitrophenazine 10-oxide (2e) did not photoisomerize in aprotic solvents and underwent only a very slow deoxygenation.

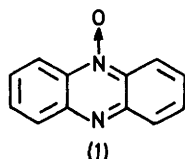
As shown in Scheme 1, two isomeric oxepinoquinoxalines (5) can be formed from each *N*-oxide, the oxygen migrating to either of the adjacent carbon atoms; in fact (5α) and (5δ) were formed from the *N*-oxides (2) and (5β) and (5γ) from the *N*-oxides (3).‡ Three isomeric

TABLE I  
Formation (%) of compounds (4α–δ) and (5α–δ) at ca. 10% conversion in CH<sub>3</sub>CN

Starting substrate	(4α)	(4γ)	(4δ)	(4β)	$\frac{(4\alpha) \text{ or } (4\beta)}{(4\gamma) + (4\delta)}$	(5α)	(5δ)	(5β)	(5γ)	$\frac{(5\alpha)}{(5\delta)}$ or $\frac{(5\beta)}{(5\gamma)}$
(2a)	15	15	14		0.52	14	25			0.56
(2b)	36	14	11.5		1.41	12	18			0.67
(2c)		34.5				23.5	30.5			0.77
(2d)	22.5	27.5	26.5		0.51					
(3a)		7.5	6.5	10	0.71			33	18	1.83
(3b)		2	1	2	0.67			85 <sup>a</sup>		∞

<sup>a</sup> (6β) and not (5β) was isolated in this case.

In every case, except 2-nitrophenazine 10-oxide (2e), the major products obtained in aprotic solvents from the substituted *N*-oxides (2) and (3) were the lactams (4) and the oxepinoquinoxalines (5) or the cyclobutafuroquinoxalines (6) which are secondary photoproducts deriving



from (5), *i.e.* the same kind of products obtained from phenazine *N*-oxide (1).<sup>1a,b</sup> Furthermore, some de-

† This reaction generally occurs to a greater extent in protic solvents and is quenched by oxygen.

‡ With the exception of (2d), which gave no products of type (5), and of (3b), which gave only one product of type (5).

lactams (4) were formed from each *N*-oxide (4α, γ, δ) from (2) and (4β–δ) from (3); this distribution of the regioisomers (4) requires a benzene ring to be perpendicular to the original molecular plane during the isomerization of (2) or (3) to (4).§

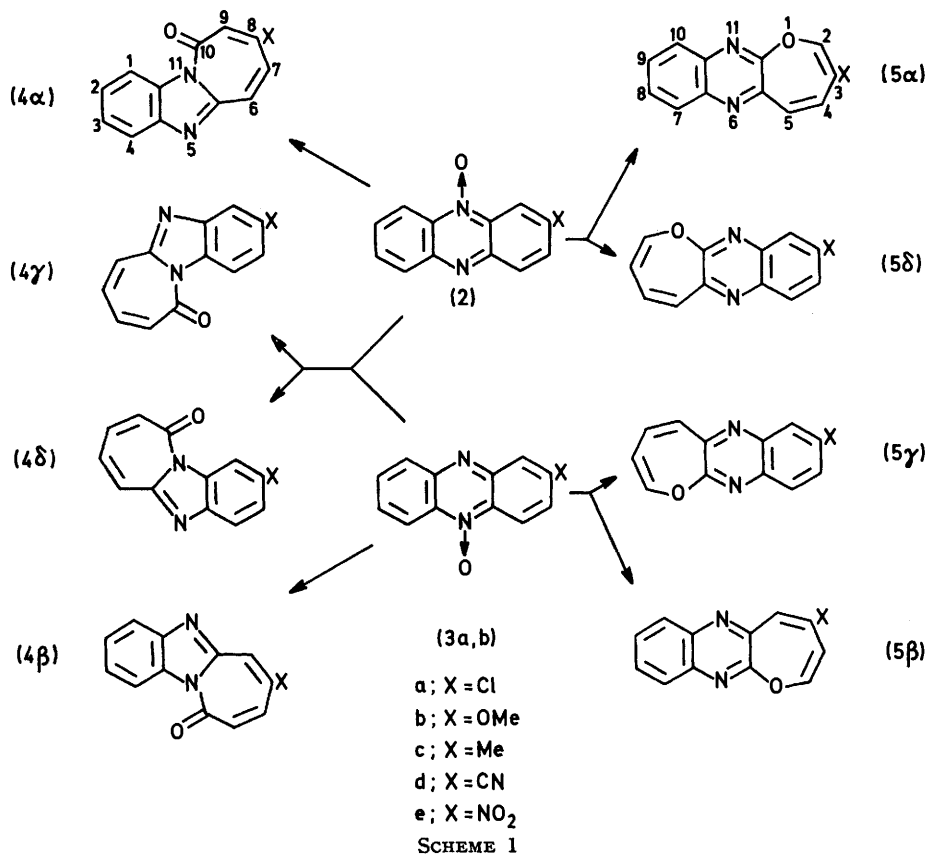
The quantum yields of disappearance of the *N*-oxides (2) and (3) are reported in Table 2. They are mainly of the same order of magnitude as  $\Phi_{-1}$  and are much lower only for the methoxy-derivative (3b) and the nitro-compound (2e). Low conversion preparative runs were carried out: the photoproducts were the same as in the

§ This situation was described by Kaneko<sup>2</sup> in the case of acridine *N*-oxides by means of a spiro-intermediate (9) derived from the 1,2-oxazepine (8).

<sup>1</sup> A. Albini, G. F. Bettinetti, and S. Pietra, (a) *Tetrahedron Letters*, 1972, 3657; (b) *J.C.S. Perkin II*, 1974, 342; (c) *Gazzetta*, 1975, 105, 15.

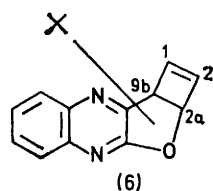
high conversion runs, as shown in Table 1.\* From these data  $\Phi_4$  and  $\Phi_5$  have been estimated, and are reported in Table 2 as  $\Sigma\Phi_4$  and  $\Sigma\Phi_5$ .

band in protic solvents.<sup>3b</sup> In some cases<sup>3</sup> the absorption spectra were interpreted on the basis of MO semi-empirical calculations; it was found that the first excited



Scheme 1 and Table 1 show that the pathways which lead to (4) and (5) (hereafter named reactions A and B respectively) are very different. In analogous cases,

singlet states derive from ( $n, \pi^*$ ) transitions or from ( $\pi, \pi^*$ ) transitions characterized by a strong internal charge transfer from the oxygen to the aromatic ring;



for instance acridine *N*-oxides,<sup>2</sup> the pathways to lactams and oxepins were supposed to differentiate after the formation of an oxaziridine which is common to the two ways (Scheme 2). On the basis of solvents and temperature effects in the photoisomerization of phenazine *N*-oxide (1) we propose that, in such cases, the photo-reactions are entirely different: namely reaction A arises from the internal charge transfer (I.C.T.) state and reaction B from the pure ( $\pi, \pi^*$ ) state.

A remarkable characteristic of the spectrum of most aromatic *N*-oxides is a blue shift of the first absorption

\* Obviously the (6 $\alpha$ – $\delta$ ) compounds were absent in the low conversion runs unless  $\Phi_6 \gg \Phi_5$  as in the case of (5 $\beta$ ; X = OCH<sub>3</sub>).

<sup>2</sup> S. Yamada, M. Ishikawa, and C. Kaneko, *Tetrahedron Letters*, 1972, 971.

TABLE 2

Quantum yields ( $\times 10^{-2}$ ) at ca. 10% conversion in CH<sub>3</sub>CN and intensity variation of the long wavelength absorption maximum passing from CH<sub>3</sub>CN to CH<sub>3</sub>CN–H<sub>2</sub>O (3 : 7)

Starting substrate	$\Phi_{-2(a)}$ <sup>a</sup>	$\Sigma\Phi_4$	$\Sigma\Phi_5$	$\Delta\epsilon/\epsilon$ <sup>b</sup>
(2c)	6.0	2.1	3.3	0.25
(2a)	3.9	1.7	1.3	0.27
(2b)	1.5	0.9	0.4	0.16
(3a)	3.1	0.8	1.7	0.15
(2d)	0.7	0.6		0.09
(3b)	0.4	0.05	0.35	0.02
(2e)	0.3			0.02

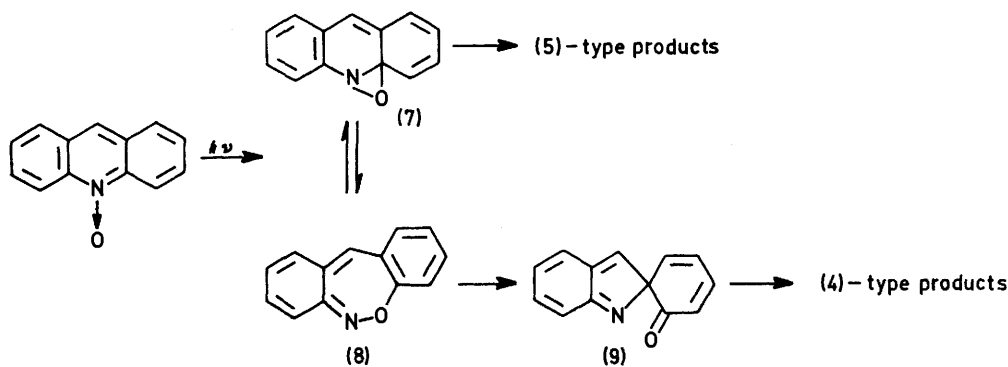
<sup>a</sup> For compound (1):  $\Phi_{-1}$  5.8;  $\Phi_4$  3.5;  $\Phi_5$  1.4.<sup>1b</sup> <sup>b</sup> The absorbance was measured at 422 for (2a), 433 for 2(b), 420 for (2c), 431 for (2d), 440 for (2e), 421 for (3a), and 432 nm for (3b)

this finding explains the effect of solvents which form hydrogen bonds. As for phenazine *N*-oxide, recent CNDO calculations showed that in this case the first

<sup>3</sup> (a) C. Leibovici and J. Streith, *Tetrahedron Letters*, 1971, 387; (b) E. Ochiai, 'Aromatic Amine Oxides,' Elsevier, Amsterdam, 1967, pp. 126–167.

transition corresponds to a ( $n, \pi^*$ ) excitation and is energetically near to the lowest ( $\pi, \pi^*$ ) transition.<sup>4</sup>

In the study of the photochemistry of (1) the variation ( $\Delta\epsilon$ ) in the intensity of the first electronic absorption band in passing from  $\text{CH}_3\text{CN}$  to  $\text{CH}_3\text{CN}-\text{H}_2\text{O}$  mixtures was assumed to be a simple parameter representative of the change in character of the first transition, and a connection was found between  $\Delta\epsilon$  and  $\Phi_4$  when the percentage of water in the solvent mixture was varied.<sup>1b</sup>



For the case under discussion, we estimated the solvatochromism of compounds (2) and (3) by the ratio of the decrease of absorption, passing from  $\text{CH}_3\text{CN}$  to  $\text{CH}_3\text{CN}-\text{H}_2\text{O}$  (3 : 7), to the absorption in pure  $\text{CH}_3\text{CN}$  ( $\Delta\epsilon/\epsilon$ ). Assuming that reaction A originates from an I.C.T. state, high values of  $\Sigma\Phi_4$  were expected, in aprotic solvents, for those substituted phenazine *N*-oxides having a high  $\Delta\epsilon/\epsilon$  value, and low values of  $\Sigma\Phi_4$  for those having a small  $\Delta\epsilon/\epsilon$  value because weak solvatochromism indicates, that, in aprotic solvents, the first excited state of such compounds has no I.C.T. character. The experimental data confirmed this prediction: as shown in Table 2 the sequence of the quantum yields of compounds (4) in  $\text{CH}_3\text{CN}$  are in accord with the decrease of the  $\Delta\epsilon/\epsilon$  values.

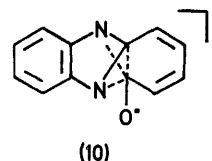
No relationship between  $\Sigma\Phi_5$  and  $\Delta\epsilon/\epsilon$  was expected nor was it found (Table 2). However substituents affect reaction B also: with the electron-attracting CN group  $\Sigma\Phi_5$  drops to zero.

The most noteworthy effect is the influence, in some cases dramatic, of the substituent on the choice between the two possible positions for oxygen attack. This regioselectivity has already been observed for other amine *N*-oxides and was considered to be evidence of a mechanism *via* oxaziridine as the observed orientation can be anticipated by MO calculations assuming this mechanism.<sup>5</sup>

Lastly the data on quantum yields of substituted phenazine *N*-oxides showed that  $\beta$ -substituents do not cause a substantial change in the spectrum and photochemical properties of phenazine *N*-oxide but gradually

alter the proportion of the I.C.T. state in comparison with the pure ( $\pi, \pi^*$ ) state. On the basis of the present and previous results, it can be concluded that reaction A involves an I.C.T. excited state; thus it is quenched by protic solvents or by substituents which are able to alter the characteristic of the excited state. As no intermediate seems to be involved, we suggest that, together with the shift of the oxygen, there is a skeletal twist so that a carbocyclic ring becomes perpendicular

to the original molecular plane, as represented, for instance, by formula (10) which summarizes the resonance



structures. This isomerization would be, in the broadest sense, of the type benzene  $\rightarrow$  benzvalene, analogous to that postulated in the photochemistry of pyridinium ion.<sup>6</sup> Compounds in which the heterocyclic ring is contracted or broken [lactams (4), benzoxazolylpentadienenitrile<sup>1a</sup>] are so formed. Reaction B involves a pure ( $\pi, \pi^*$ ) state without charge transfer; thus it also takes place in protic solvents. It leads to oxygen migrations in which the skeleton is preserved. Remarkable regioselectivity is often observed in reaction B, unlike reaction A; this is probably due to the existence of an energy minimum corresponding to the oxaziridine configuration.<sup>7</sup>

#### EXPERIMENTAL

U.v. spectra were recorded on Perkin-Elmer 137 and Beckman DU-2 spectrophotometers, i.r. spectra on a Perkin-Elmer 257 spectrophotometer, and n.m.r. spectra on a Perkin-Elmer R-12 instrument, using  $\text{Me}_4\text{Si}$  as internal standard. Commercial spectroscopic grade solvents were used without further purification. The phenazine *N*-oxides (2a, b, and e) and (3a and b) were prepared and purified according to literature methods.<sup>1c, 8</sup>

<sup>7</sup> (a) A. Albini, A. Barinotti, G. F. Bettinetti, and S. Pietra, *Gazzetta*, in the press; (b) K. B. Tomer, N. Harrit, I. Rosenthal, O. Buchardt, P. L. Kumler, and D. Creed, *J. Amer. Chem. Soc.*, 1973, **95**, 7402.

<sup>8</sup> S. Maffei and G. F. Bettinetti, *Ann. Chim. (Italy)*, 1955, **45**, 1031.

<sup>4</sup> F. Mark, personal communication.

<sup>5</sup> (a) C. Kaneko, S. Yamada, and C. Yokoe, *Tetrahedron Letters*, 1970, 2333; (b) Y. Kobayashi, I. Kumadaki, and H. Sato, *ibid.*, p. 2337.

<sup>6</sup> L. Kaplan, J. W. Pavlik, and K. E. Wilzbach, *J. Amer. Chem. Soc.*, 1972, **94**, 3283.

TABLE 3

Spectroscopic characteristic of compounds (4)—(6)

Compound	$\nu_{\text{CO}}/\text{cm}^{-1}$	$\lambda_{\text{max.}}/\text{nm}$ (log $\epsilon$ )
8-Methyl (4 $\alpha$ )	1 680	237 (4.15), 243 (4.18), 265 (4.22), 274 (4.20), 389 (3.55) <sup>a</sup>
3-Methyl (4 $\gamma$ )	1 680	239 (4.13), 246 (4.20), 277 (4.25), 402 (3.73) <sup>a</sup>
8-Cyano (4 $\alpha$ )	1 670	223 (4.32), 239 (4.31), 278 (4.42), 406 (3.61) <sup>b</sup>
3-Cyano (4 $\gamma$ )	1 675	245 (4.47), 259 (4.36), 368 (3.73) <sup>b</sup>
2-Cyano (4 $\delta$ )	1 682	264 (4.49), 274 (4.48), 370 (3.82) <sup>b</sup>
3-Methyl (5 $\alpha$ )		214 (4.30), 361 (3.81) <sup>a</sup>
9-Methyl (5 $\delta$ )		225 (4.35), 363 (3.94) <sup>a</sup>
2-Methyl (6 $\alpha$ )		241 (4.26), 246 (4.33), 330 (3.98), 347 (4.00) <sup>a</sup>
6-Methyl (6 $\delta$ )		247 (4.27), 251 (4.33), 330 (4.07) <sup>a</sup>

<sup>a</sup> In cyclohexane. <sup>b</sup> In MeCN.

2-Methylphenazine 10-Oxide (2c).—Compound (2c) was prepared from 2-nitro-4'-methyl-diphenylamine with 10%

$\text{H}_2\text{SO}_4$  (3 ml), and the esters were converted into the corresponding amides by heating at 74° for 7 h with a 25% methanolic solution of  $\text{NH}_3$ . The crude mixture of the amides was dehydrated using the method of Lehnert<sup>11</sup> ( $\text{TiCl}_4\text{-Et}_3\text{N}$ ) to give a mixture of 2-cyanophenazine and its 10-oxide (ca. 4 g). These were separated by column chromatography on silica gel (ethyl acetate-cyclohexane 1:1 as eluant) to give compound (2d) as yellow crystals (2 g, 43%), m.p. 232–233° (from nitroethane) (Found: C, 70.6; H, 3.2; N, 19.3.  $\text{C}_{13}\text{H}_7\text{N}_3\text{O}$  requires C, 71.0; H, 3.2; N, 19.0%).

Preparative Runs.—Solutions of compounds (2c–e) in acetonitrile ( $2 \times 10^{-3}\text{M}$ ) were irradiated with a water cooled medium-pressure mercury lamp (Hanau TQ-150), equipped with a Pyrex filter, until 70–80% conversion. The residue obtained by evaporation of the solvent at reduced pressure at room temperature was chromatographed on a silica gel column (Merck HR) in the ratio 1:1 000. The elution was

TABLE 4

Analytical data for compounds (4)—(6)

Methyl derivatives	M.p. (°C)	Found (%)			Formula	Required (%)					
		C	H	N		C	H	N			
(6 $\delta$ )	166–166.5 <sup>a</sup>	74.3	4.6	13.5	$\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}$	74.3	4.8	13.3			
(4 $\alpha$ )	110–111 <sup>a</sup>	74.3	4.8	13.4							
(4 $\gamma$ )	113–116 <sup>a</sup>	74.4	4.7	13.5							
(5 $\alpha$ )	96–97 <sup>b</sup>	$M^+$ , 210.079 0 <sup>d</sup>							$M^+$ 210.079 3		
(5 $\delta$ )	78–79 <sup>b</sup>	$M^+$ , 210.079 1									
(6 $\alpha$ )	104–105 <sup>b</sup>	$M^+$ , 210.079 8									
Cyano derivatives					$\text{C}_{13}\text{H}_7\text{N}_3\text{O}$	70.6	3.2	19.0			
(4 $\alpha$ )	191–192 <sup>c</sup>	70.7	3.3	18.9							
(4 $\gamma$ )	221–223 <sup>a</sup>	70.7	3.2	18.7							
(4 $\delta$ )	238–239 <sup>a</sup>	70.3	3.2	18.7							

<sup>a</sup> Crystallized from EtOH. <sup>b</sup> Purified by further column chromatography; silica gel, toluene as eluant. <sup>c</sup> Crystallized from  $\text{EtNO}_2$ . <sup>d</sup> On a DuPont 492 B mass spectrometer.

TABLE 5

N.m.r. spectral data for compounds (4), (5), and (6)<sup>a, b</sup>

Compound (4)	Chemical shift ( $\delta$ )						
	H-1	H-4			H-7	H-9	
8-Methyl (4 $\alpha$ )	8.70 (q)	7.85 (q)					
3-Methyl (4 $\gamma$ )	8.58 (d, J 9)	7.65 (s)					
2-Methyl (4 $\delta$ ) <sup>c</sup>	8.58 (d, J 2)	7.75 (q, J 9, 2)					
8-Cyano (4 $\alpha$ )	8.65 (q)				7.92 (q, J 10, 2)	7.12 (d, J 2)	
3-Cyano (4 $\gamma$ )	8.86 (d, J 9)	8.25 (s)					
2-Cyano (4 $\delta$ )	9.15 (s)	7.98 (d, J 9)					
Compound (5)	H-2		H-3		H-4		H-5
2-Methyl (5 $\alpha$ )	6.40 (s)				6.30 (d, J 11.5)		6.85 (d, J 11.5)
9-Methyl (5 $\delta$ )	6.48 (d, J 6.5)		5.55 (t, J 6.5)		6.25 (q, J 6.5, 11.5)		6.80 (d, J 11.5)
Compound (6)	H-1	H-2	H-2a	H-5	H-7	H-8	H-9b
2-Methyl (6 $\alpha$ )	6.30 (d, J 3)		5.52 (d, J 3)				4.38 (d, J 3)
6-Methyl (6 $\delta$ ) <sup>d</sup>	6.60 (t, J 3)	6.30 (d, J 3)	5.60 (t, J 3)	7.60 (d, J 2)	7.35 (q, J 8.5, 2)	7.82 (d, J 8.5)	4.50 (d, J 3)

<sup>a</sup> In  $\text{CDCl}_3$ . <sup>b</sup> Coupling constants in Hz; s = singlet, d = doublet, t = triplet, q = quartet. <sup>c</sup> Measured on a sample (impure) of the 8-methyl isomer (4 $\alpha$ ). <sup>d</sup> Complete resolution of the n.m.r. spectrum of the 6-methyl derivative, unlike the spectra of the corresponding chloro-derivatives, allows unambiguous identification, which confirms the previous assignment.<sup>1c</sup>

oleum at 10°, according to the procedure applied by Cross to other diphenylamines,<sup>9</sup> yellow crystals, m.p. 155–156° (from methanol), yield 27% (Found: C, 73.6; H, 4.8; N, 13.0.  $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}$  requires C, 74.2; H, 4.8; N, 13.3%).

2-Cyanophenazine 10-Oxide (2d).—Crude 2-carboxyphenazine 10-oxide (5 g)<sup>10</sup> were esterified with MeOH (100 ml) under reflux for 5 h in the presence of concentrated

<sup>9</sup> B. Cross, P. J. Williams, and R. E. Woodall, *J. Chem. Soc. (C)*, 1971, 2085.

performed with benzene-ethyl acetate or cyclohexane-ethyl acetate mixtures.

The irradiation of (3c) yielded the following products (percentage calculated on the reacted N-oxide): (4 $\alpha$ ,  $\gamma$ ,  $\delta$ ) 56% in total; (6 $\alpha$  and  $\beta$ ) 20% in total; 2-methylphenazine 9%. No completely satisfactory method was found for

<sup>10</sup> S. Maffei, S. Pietra, and A. M. Rivolta, *Ann. Chim. (Italy)*, 1952, **42**, 519.

<sup>11</sup> W. Lehnert, *Tetrahedron Letters*, 1971, 1501.

determining the composition of the isomeric mixtures although pure samples of the individual compounds, except (4 $\delta$ ), could be obtained. Compound (2d) yielded (4 $\alpha$ ) 24%, (4 $\gamma$ ) 13%, (4 $\delta$ ) 21%, 2-cyanophenazine 9%; no traces of products (5) or (6) were detected. Compound (2e) proved to be very photostable; the major product was 2-nitrophenazine.

In all cases irradiation in benzene produced very similar results.

*Low Conversion Runs.*—Solutions of (2a—e) or (3a and b) were irradiated as above. The residue of the evaporation was extracted with isopropyl ether or cyclohexane and the extract analysed by g.l.c. and/or column chromatography.

*Structure of Products.*—The identification of new products was determined by comparison of their spectral properties with those of other compounds of these series, the structures of which had been ascertained previously by chemical evidence.<sup>1a,c</sup> The main physicochemical characteristics of the new compounds are reported in Tables 3—5.

*Quantum Yield Measurements.*—The quantum yields were determined at 366 nm with a super high pressure mercury lamp (Osram 200 W/4 lamp, Schott PIL interference filter). Potassium ferrioxalate was used as actinometer.<sup>12</sup> The disappearance of the *N*-oxides (2) and (3) was followed by u.v. spectroscopy at the appropriate wavelength. The reaction was quenched at *ca.* 10% conversion.

Under these conditions the internal filter effect due to the photoreaction products was negligible. Although compounds (4) react further to unidentified products, the estimations of the  $\Phi_4$  are not greatly affected, and were checked by measuring absorbance and quantum yield of decomposition of these compounds.

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<sup>12</sup> L. C. Hatchard and C. A. Parker, *Proc. Roy. Soc., Ser. A*, 1956, **253**,318.