Photocyclization Reactions of Aryl Polyenes. IV.[1] The Syntheses of Isatogens and Isatogen-like Compounds

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Photochemical reactions of 1-*o*-nitrophenyl-4-phenyl-1,3-butadiene, 1,4-di-*o*-nitrophenyl-1,3-butadiene, 1-*o*-nitrophenyl-6-phenyl-1,3,5-hexatriene, and 1,6-di-*o*-nitrophenyl-1,3,5-hexatriene all gave the appropriate 2-substituted isatogen. The related *m*- and *p*-nitrophenyl polyenes were inert to the irradiation conditions. A six-membered ring isatogen-like compound, 2-phenyl-3-oxo-benzo[*d,e*]quinoline-*N*-oxide was prepared by irradiation of 1-[1′-(8′-nitronaphthyl)]-2-phenylacetylene. A seven-membered ring isatogen-like compound, 6-phenyl-7-oxo-dibenzo[*b,d*]azepine-*N*-oxide, was prepared by heating 1-[2-(2′-nitrobiphenyl)]-2-phenylacetylene.

Les réactions photochimiques de *o*-nitrophényle-1 phényle-4 butadiène-1,3, du di-*o*-nitrophényle-1,4 butadiène-1,3, de l'*o*-nitrophényle-1 phényle-6 hexatriène-1,3,5, et du di-*o*-nitrophényle-1,6 hexatriène-1,3,5 donnent toutes les isatogènes appropriées substituées en 2. Les *m*- et *p*-nitrophényle polyènes correspondants sont inertes, s'ils sont soumis à une irradiation. Un composé cyclique à six chaînons du type isatogène, l'oxyde-*N* de la phényle-2 oxo-3 benzo[*d,e*]quinoline a été préparé par irradiation du [(nitro-8′ naphtyle)-1′]-1 phényle-2 acétylène. Un composé cyclique à sept chaînons du type isatogène, l'oxyde-*N* de phényle-6 oxo-7 dibenzo[*b,d*]azépine a été préparé en chauffant le [(nitro-2′ biphényle)-2]-1 phényle-2 acétylène.

Introduction

The photocyclization and oxidation of substituted stilbenes have been shown to give substituted phenanthrenes (1), provided one of the substituents is not a nitro group (2). The photocyclization–oxidation reaction of 1,4-diaryl-1,3-butadienes, where the aryl groups are phenyl or substituted phenyl groups, gave mixtures of substituted 1-phenylnaphthalenes (3, 4). It was thought that the irradiation of 1-*m*- and 1-*p*-nitrophenyl-4-phenyl-1,3-butadienes (**1** and **2**) may give 1-*m*- and 1-*p*-nitrophenylnaphthalenes respectively, since photocyclization in this case can occur to a phenyl ring not substituted by a nitro group. In any case, irradiation of **1** and **2** gave no reaction. It has been shown that irradiation of 1,6-diphenyl-1,3,5-hexatriene gives chrysenes (3) but 1-*m*- and 1-*p*-nitrophenyl-6-phenyl-1,3,5-hexatrienes (**3** and **4**) are inert to photochemical reaction conditions (see Experimental).

The irradiation of 1-*o*-nitrostilbene gave 2-phenylisatogen (5), a reaction which can be more readily explained in the photochemistry of the nitro group (5, 6) than in the photocyclization–oxidation of the diaryl polyene.

Isatogens are an interesting group of compounds in that a number of them have shown marked anti-microbiological activity (7) and thus it was decided to examine the syntheses of isatogens in more detail. It was of interest to know whether the extended conjugated system of 1-*o*-nitrophenyl-4-phenyl-1,3-butadiene (**5*a***) and 1-*o*-nitrophenyl-6-phenyl-1,3,5-hexatriene (**5*b***) would influence the photochemical formation of 2-substituted isatogens (Scheme 1).

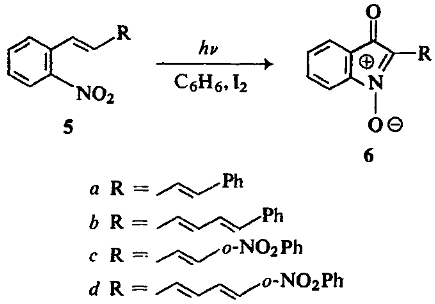
Results and Discussion

Thus, irradiation of 3.8×10^{-3} *M* solutions of **5*a*** and 7.9×10^{-3} *M* iodine in dry benzene under nitrogen gave, after 3 days, a 12% yield of red crystals of 2-styrylisatogen (**6*a***). The structure of **6*a*** was confirmed by comparison with a sample synthesized by another route (8).

Irradiation of 3.6×10^{-3} *M* solutions of **5*b*** and 8.0×10^{-3} *M* iodine in dry benzene under nitrogen gave, after 3 days, a dark red product, 2-(4-phenylbuta-1,3-dien-1-yl)isatogen (**6*b***) in a 25% conversion from **5*b***. In addition, 60% of the starting material was recovered.

The photochemical reaction of *o,o*′-dinitrostilbene gave 2-(*o*-nitrophenyl)isatogen (5). The analogous photo-reactions of 1,4-di-*o*-nitrophenyl-1,3-butadiene (**5*c***) and 1,6-di-*o*-nitrophenyl-1,3,5-hexatriene (**5*d***) were attempted to determine the affect of the additional nitro group

[1]For Part III, see ref. 23.



SCHEME 1

on the photochemical formation of isatogens and to explore the possibility of formation of bis isatogens (Scheme 1).

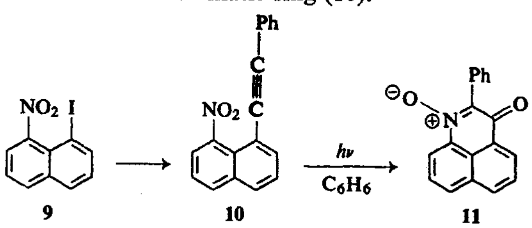
Thus, the photo reaction of a 3.4×10^{-3} *M* solution of **5c** and 8.0×10^{-3} *M* iodine in dry benzene under nitrogen for 3 days gave a 30% yield of 2-(*o*-nitrostyryl)isatogen (**6c**). Similarly irradiation of **5d** gave a 9.1% conversion to 2-(4-*o*-nitrophenylbuta-1,3-dien-1-yl)isatogen (**6d**) and a 30% recovery of starting material. On the other hand, 1,6-di-*m*- and 1,6-di-*p*-nitrophenyl-6-phenyl-1,3,5-hexatrienes (**7** and **8**) respectively were inert to the irradiation conditions.

Isatogens **6c** and **d** were purified by preparative t.l.c. and irradiated. No further reactions occurred and no bis isatogens were formed.

The structures of isatogens **6a–d** were determined primarily from spectroscopic data. The i.r. spectra were especially informative and showed —C═O— stretching vibrations at 1710 cm^{-1} and $—\overset{+}{N}—O^{\ominus}—$absorption peaks at 1170 cm^{-1} typical of the isatogen structure. The mass spectra of isatogens **6a–d** showed parent ions and were consistent with the fragmentation pattern of the published mass spectra of known isatogens (9). All isatogens were dark red compounds and had correct elemental analyses. The n.m.r. spectra of **6a** and **b** were uninformative and simply showed multiple absorption peaks between 6.5 and 7.5 p.p.m.

Isatogen-like compounds containing six- and seven-membered rings have not been prepared and it was thought that the photochemical reactions of suitable nitrostilbene derivatives could lead to the appropriate isatogen analog. Recently, however, Bond and Hooper (10) have shown that isatogens can be synthesized through tolan intermediates and it was decided to attempt the syntheses of isatogen-like compounds by this method.

The reaction of 1-iodo-8-nitronaphthalene (**9**) with cuprous phenylacetylide in pyridine for 72 h gave a mixture of 1-[1′-(8′-nitronaphthyl)]-2-phenylacetylene (**10**) and starting iodo **9**. The presence of **10** was shown by a sharp band in the i.r. spectrum of **10** at 2242 cm^{-1}, characteristic of the —C≡C— stretching frequency. The crude acetylene **10** was irradiated for 72 h in dry benzene under nitrogen to give, after purification by preparative t.l.c., a 15% yield of the dark red, 2-phenyl-3-oxo-benzo[*d,e*]quinoline-*N*-oxide (**11**), a six-membered ring isatogen analog (Scheme 2). The i.r. spectrum of **11** was characteristic of an isatogen-like compound and showed absorption peaks at 1710 and 1723 cm^{-1} (—C═O) and a weak absorption at 1173 cm^{-1} due to the $\overset{+}{N}—O^{\ominus}$ group. The n.m.r. spectrum of **11** showed an absorption peak at 8.96 p.p.m. due to the two ortho protons of the 2-phenyl substituent. The two ortho protons of the phenyl substituent of 2-phenylisatogens are known to be shifted downfield relative to the other protons attached to an aromatic ring (10).



SCHEME 2

The reaction of 2-iodo-2′-nitrobiphenyl (**12**) with cuprous phenylacetylide in pyridine under reflux for 72 h gave a mixture of *o*-(2′-nitrophenyl)tolan (**13**) and starting iodo **12**. The mixture was heated further for 72 h with excess cuprous acetylide to give a 2.6% yield of a dark-brown product, 6-phenyl-7-oxo-dibenzo[*b,d*]azepine-*N*-oxide (**14**), a seven-membered ring isatogen-like compound (Scheme 3). The i.r. spectrum of **14** showed typical carbonyl absorption at 1712, 1721, and 1728 cm^{-1} and a weak ($—\overset{+}{N}—O^{\ominus}$) absorption peak at 1187 cm^{-1}. The n.m.r. spectrum of **14** showed peaks at 8.38 p.p.m. due to the ortho protons of the 6-phenyl substituent.

The spectral data of all the compounds are consistent with the assigned structures.

The mechanism of formation of isatogens from the photoreaction of *o*-nitrostilbenes has been discussed by other workers (5, 6) but firm

TABLE 1. Spectral characteristics of substituted-nitrophenyl polyenes

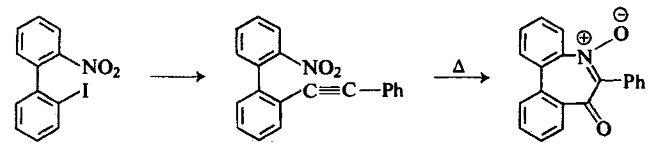
Compound	Substituent	The u.v. spectra (benzene) λ_{max} (nm) (ε)	The i.r. spectra (KBr) ν(cm^{-1})	Mass spectra m/e M^+(% of base peak)
1	*m*-Nitro	336.5 (65 400), 328 (62 200)	1540, 1353, 995	251 (18.1)
2	*p*-Nitro	370 (22 900), 284 (17 600)*	1608, 1535, 1351, 998	251 (35)
3	*m*-Nitro	352 (75 700), 349 (71 600)	1539, 1355, 1004	277 (12.5)
4	*p*-Nitro	402 (32 700), 324 (18 700), 313 (19 000)	1521, 1351, 1003	277 (100)
5*a*	*o*-Nitro	311 (33 900)*	1622, 1610, 1521, 1350, 991	251 (20)
5*b*	*o*-Nitro	333.5 (32 700)	1602, 1522, 1349, 989	277 (59)
5*c*	Di-*o*-nitro	340 (11 600), 278 (18 800)*	1604, 1511, 1345, 974	296 (100)
5*d*	Di-*o*-nitro	390.5 (17 400), 370 (19 400), 326 (20 600)	1603, 1512, 1340, 997	322 (49)
7	Di-*m*-nitro	355 (17 000), 347 (16 900)	1533, 1355, 997	322 (100)
8	Di-*p*-nitro	3950 (24 200)	1541, 1346, 996	322 (73)

*Solvent 95% ethanol.

Table 2. Physical properties of isatogens and isatogen-like compounds

Compound	Yield (%)	Melting point (°C)	Formula	Analysis Calculated C	H	N	Found C	H	N
6a	12	186–188*	$C_{16}H_{11}NO_2$	73.00	4.18	10.63	73.37	4.39	10.31
6b	25	175–176	$C_{18}H_{11}NO_2$	78.52	4.73	5.09	78.24	4.67	4.97
6c	30	229–230	$C_{16}H_{10}N_2O_4$	65.31	3.42	9.52	65.20	3.40	9.30
6d	9.1	204–206	$C_{18}H_{12}N_2O_4$	67.48	3.75	8.75	67.21	3.64	8.51
11	15	183–185	$C_{18}H_{11}NO_2$	79.14	4.03	5.12	79.34	4.23	5.43
14	2.6	239–240	$C_{20}H_{13}NO_2$	80.26	4.35	4.68	80.59	4.66	4.47

*Literature 180–183° (8).



12 **13** **14**

Scheme 3

evidence regarding postulated intermediates is lacking. The formation of **11** and **14** by photochemical and thermal means respectively is significant in the fact that the steric requirements necessary for the formation of isatogens (five-membered ring) is *not* stringent and the formation of six and seven-membered ring isatogen-like compounds is readily achieved.

Experimental

All melting points were determined on a Kofler hot stage and are uncorrected. The i.r. spectra were recorded on a Perkin–Elmer 257 i.r. spectrometer using KBr discs. The u.v. spectra were measured using a Cary 14 u.v. spectrometer and benzene as a solvent. The n.m.r. spectra were measured on a Varian A60 spectrometer using tetramethylsilane as an internal standard ($\delta = 0$ p.p.m.) and deuterochloroform as solvent. Mass spectra were recorded on a Hitachi–Perkin–Elmer RMU-6 mass spectrometer. Silica gel was used for thin- and thick-layer chromatography. All photochemical reactions were carried out in a Rayonet photochemical reactor using RPR 3500 Å lamps. Microanalyses were performed by A. B. Gygli of Toronto.

Synthesis of 1-Nitrophenyl-4-phenyl-1,3-butadienes

A typical example is given for the preparation of 1-*o*-nitrophenyl-4-phenyl-1,3-butadiene (*5a*). To a mixture of 3.43 g (0.026 mol) of cinnamaldehyde and 12.0 g (0.025 mol) of *o*-nitrobenzyltriphenylphosphonium chloride in 100 ml methanol, was added 130 ml of 0.2 *M* lithium methoxide. The mixture was allowed to crystallize overnight after which crystals of *5a* were obtained in 30% yield; m.p. 96–97° (lit. 98–99° (11)).

1-m-Nitrophenyl-4-phenyl-1,3-butadiene (1)

The m.p. 145–146° (lit. 145–146° (12)); yield 46%.

1-p-Nitrophenyl-4-phenyl-1,3-butadiene (2)

The m.p. 180–181° (lit. 181.5–182° (13)); yield 36%.

Synthesis of 1,4-Di-o-nitrophenyl-1,3-butadiene (5c)

1,4-Di-*o*-nitrophenyl-1,3-butadiene (*5c*) was prepared by reacting *o*-nitrobenzyltriphenylphosphonium chloride and *o*-nitrocinnamaldehyde by the Wittig procedure identical to that given above. Product *5c* was obtained in 49% yield; m.p. 219–220° (lit. 210–220° (14)).

Preparation of 1-Nitrophenyl-6-phenyl-1,3,5-hexatrienes

A typical example is given for the preparation of 1-*o*-nitrophenyl-6-phenyl-1,3,5-hexatriene (*5b*). To a mixture of 2.0 g (0.0126 mol) of 5-phenylpenta-2,4-dien-1-al (15) and 6.0 g (0.0126 mol) of *o*-nitrobenzyltriphenylphosphonium chloride in 30 ml methanol was added 50 ml of 0.4 *M* lithium methoxide. The mixture was allowed to crystallize overnight after which crystals of *5b*, m.p. 104–105°, were obtained in 17% yield.

Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.98; H, 5.42; N, 5.04. Found: C, 78.19; H, 5.21; N, 5.14.

1-m-Nitrophenyl-6-phenyl-1,3,5-hexatriene (3)

The m.p. 184–185° (lit. 184–185° (13)); yield 54%.

1-p-Nitrophenyl-6-phenyl-1,3,5-hexatriene (4)

The m.p. 194–195° (lit. 194–196° (16)); yield 63%.

Preparation of 1,6-Di-nitrophenyl-1,3,5-hexatrienes

A typical example is given for the preparation of 1,6-di-*o*-nitrophenyl-1,3,5-hexatriene (*5d*). To a mixture of 2.25 g (0.015 mol) of *o*-nitrobenzaldehyde and 3.25 g (0.007 mol) of 2-butene-1,4-bis(tri-*n*-butylphosphonium chloride) (17) in 50 ml methanol was added 60 ml of 0.2 *M* lithium methoxide. The mixture was allowed to crystallize overnight after which crystals of *5d*, m.p. 232–233°, were obtained in 64% yield.

Anal. Calcd. for $C_{18}H_{14}N_2O_4$: C, 67.08; H, 4.38; N, 8.69. Found: C, 67.01; H, 4.75; N, 8.37.

1,6-Di-m-nitrophenyl-1,3,5-hexatriene (7)

The m.p. 165–166°; yield 83%.

Anal. Calcd. for $C_{18}H_{14}N_2O_4$: C, 67.08; H, 4.35; N, 8.69. Found: C, 67.24; H, 4.22; N, 8.54.

1,6-Di-p-nitrophenyl-1,3,5-hexatriene (8)

The m.p. 218–219° (lit. 218–219° (17)); yield 62%.

Spectral Properties of the Substituted-nitrophenylpolyenes

The spectral data of these compounds are given in Table 1.

Synthesis of Mono-nitrobenzyltriphenylphosphonium Halides

The mono-nitrobenzyltriphenylphosphonium halides were prepared by a procedure identical to that given previously (4).

o-Nitrobenzyltriphenylphosphonium Chloride

The m.p. 233–234° (lit. 230° (18)).

m-Nitrobenzyltriphenylphosphonium Bromide

The m.p. 260–262° (lit. 261° (19)).

p-Nitrobenzyltriphenylphosphonium Bromide

The m.p. 279–279.5° (lit. 275–275.5° (13)).

Irradiation of Nitrophenyl Polyenes

The general techniques of irradiation on a preparative scale have been described previously (4). The photocyclization reaction products were isolated by preparative thick layer chromatography (t.l.c.) using hexane:benzene (1:2) as eluant. All the photocyclization products moved slower than the starting *o*-nitrophenyl polyenes on t.l.c. Since, in general, the results have already been mentioned, only details of identification are given (see Tables 2 and 3).

Preparation of 1-Phenyl-2-[1′(8′-nitronaphthyl)]-acetylene (10)

A mixture of 0.5 g (0.0167 mol) of 1-iodo-8-nitronaphthalene (20) and 0.275 g (0.0167 mol) of cuprous phenylacetylide (21) in 50 ml of dry pyridine was heated under reflux for 72 h in a nitrogen atmosphere. The pyridine was removed under reduced pressure and the residue was extracted with a benzene:water (1:1) mixture. The benzene layer was purified by preparative t.l.c. to give an inseparable mixture of what appeared to consist of the starting material 1-iodo-8-nitronaphthalene and the tolan (**10**). The i.r. spectrum of the mixture showed an absorption peak at 2242 cm^{-1}.

The Irradiation Product of 1-Phenyl-2-[1′(8′-nitronaphthyl)]-acetylene

The isatogen-like analog 2-phenyl-3-oxo-benzo[*d,e*]-quinoline-*N*-oxide was identified by its physical and spectral properties given in Tables 2 and 3 and by its n.m.r. spectrum which showed signals at 8.96 for H-2 (doublet) and 8.12–8.64 p.p.m. for H-9 (multiplet).

Preparation of 6-Phenyl-7-oxo-dibenzo[b,d]azepine-N-oxide (14)

A mixture of 1.0 g (0.0036 mol) of 2-iodo-2′-nitrobiphenyl (22) and 0.5 g (0.00306 mol) of cuprous phenylacetylide (20′) in 50 ml of dry pyridine was heated under reflux for 72 h in an atmosphere of nitrogen. Then the pyridine was removed under reduced pressure and the residue was extracted with benzene:water (1:1) mixture. The benzene layer was purified by preparative t.l.c. to give two products. The first consisted of a mixture of what appeared to be 2-iodo-2′-nitrobiphenyl (**12**) and *o*-(2′-nitrophenyl)tolan (**13**) (the i.r. spectrum of the mixture showed an absorption peak at 2226 cm^{-1}). The other product, a dark brown compound, was found to be 6-phenyl-7-oxo-dibenzo[*b,d*]azepine-*N*-oxide (**14**) identified by its physical and spectral properties (Tables 2 and 3) and by its n.m.r. spectrum which showed signals at 8.38 for H-2 (doublet) and 7.58–7.18 p.p.m. for H-11 (multiplet).

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