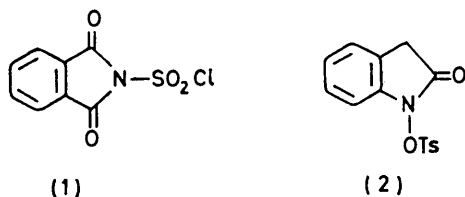


Radical Phthalimidation of Aromatic Compounds by Photolysis of *N*-Tosyloxypthalimide: a Route to Primary Aromatic Amines

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N-Tosyloxypthalimide (3) is a stable solid readily prepared from *N*-hydroxyphthalimide and toluene-*p*-sulphonyl chloride. It undergoes photolysis at room temperature, in Pyrex, in the presence of aromatic compounds (PhX) to give 12–100% yields of the corresponding *N*-arylphthalimides (4; X = H, MeO, Me, Bu^t, Ph, or Cl); hence, *via* hydrazinolysis, the corresponding primary arylamines can be obtained. Measurements of isomer ratios, rate ratios, and hence partial rate factors for the reaction show that phthalimido-radicals rather than nitrenium ions are involved. This is confirmed by comparison with corresponding data obtained from thermolysis of *N*-chlorosulphonylphthalimide in the same aromatic solvents.

ALTHOUGH hydrolysis¹ or hydrazinolysis² of *N*-alkylphthalimides has long been used as a method of preparing primary alkylamines, the method is not readily adaptable to the preparation of primary aromatic amines



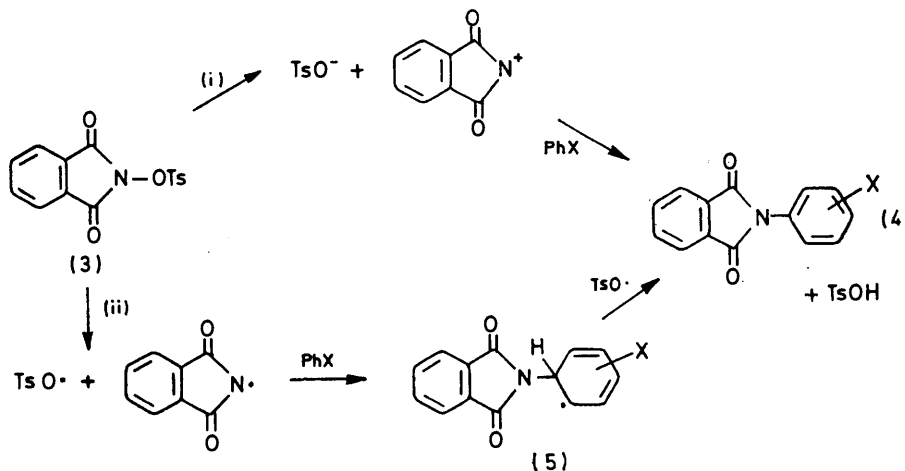
because the only convenient route to *N*-arylphthalimides is from phthalic anhydride and an arylamine.³ An alternative is the free radical phthalimidation of aromatic

formation of nitrenium ions from *N*-tosyloxypthalimide (2)⁵ (although Edwards has recently suggested that the reaction could involve radicals⁶) it was of interest to examine the possibility that *N*-tosyloxypthalimide (3) might give the corresponding nitrenium ion or the *N*-phthalimido-radical, either of which would be expected to be trapped by aromatic compounds (see Scheme).

In the event we have shown that *N*-tosyloxypthalimide readily undergoes photolysis at room temperature in aromatic solvents to give the required *N*-arylphthalimides (4) *via* a radical route.

RESULTS AND DISCUSSION

N-Tosyloxypthalimide (3), prepared from *N*-hydroxyphthalimide and toluene-*p*-sulphonyl chloride, appears to be identical with that material hitherto described as 'the



SCHEME

compounds by thermolysis of *N*-chlorosulphonylphthalimide (1) at 180–250° in the presence of copper(I) chloride,⁴ which proceeds in yields of 3–70% with the evolution of sulphur dioxide and hydrochloric acid.

In view of Gassman's demonstration of the ease of

p-toluenesulphonyl derivative of phthalic anhydride oxime.⁷ Although it is thermally stable at 155° its photolysis in aromatic solvents gives *N*-arylphthalimides (12–100%) and toluene-*p*-sulphonic acid, but no phthalimide. Hydrazinolysis² of the product gave the

¹ S. Gabriel, *Ber.*, 1887, **20**, 2224.

² H. R. Ing and R. H. F. Manske, *J. Chem. Soc.*, 1926, 2348.

³ M. L. Sherrill, F. L. Schaeffer, and E. P. Shoyer, *J. Amer. Chem. Soc.*, 1928, **50**, 474.

⁴ R. A. Lidgett, E. R. Lynch, and E. B. McCall, *J. Chem. Soc.*, 1965, 3754.

⁵ P. G. Gassman and G. A. Campbell, *Chem. Comm.*, 1971, 1437.

⁶ O. E. Edwards, G. Bernath, J. Dixon, J. M. Paton, and D. Vocelle, *Canad. J. Chem.*, 1974, **52**, 2123.

⁷ C. M. Buess and L. Bauer, *J. Org. Chem.*, 1955, **20**, 33.

corresponding arylamines, and the results are summarised in Table 1 together with the results of corresponding thermolyses of *N*-chlorosulphonylphthalimide in the presence of copper(I) chloride in a pressure vessel at 160° (2 days), which we have carried out for comparison. It can be seen that comparable or better yields of amines can be obtained by using the much simpler and more convenient photolysis of *N*-tosyloxypthalimide.

Table 1 also records the isomeric composition of mixtures of amines obtained from substituted aromatic compounds in the photolytic reaction, and the thermolysis of

The argument that phthalimido-radicals are involved would have been stronger if the corresponding isomer ratios obtained from the photolytic and thermolytic reactions of *N*-tosyloxy- and *N*-chlorosulphonyl-phthalimides had been closer than observed (Table 1). In view of (i) the large difference in temperature of the two reactions, (ii) the heterogeneous nature of that involving the *N*-chlorosulphonyl derivative, and (iii) the lack of information of the extent to which species such as (5) (see Scheme) may be oxidised to the *N*-arylpthalimide, or removed as dimers, say (this could be different in each

TABLE 1

X in PhX	Phthalimidation and phenylation of aromatic compounds*										
	Photolysis of R ₂ NO ₂ s (20°)			Thermolysis of R ₂ N·SO ₂ Cl (160°)			Phenylation † (80°)				
	XC ₆ H ₄ ·NH ₂ (%)	Isomeric composition (%)			XC ₆ H ₄ ·NH ₂ (%)	Isomeric composition (%)			Isomeric composition (%)		
2-		3-	4-	2-		3-	4-	2-	3-	4-	
H	18										
MeO	100	55	3	42	60	56	7	37	70	15	15
Me	23 ‡	39	14	47	30 ‡	54	23	23	67	19	14
Bu [†]	65	14	44	42	41	6	54	40	20	57	23
Ph	25	59	8	33	20	54	21	25	49	23	28
Cl	12 §	36	14	50	10	33	30	37	50	32	18
NO ₂					27	27	49	24	62	10	28

* R₂N = phthalimido. † Ref. 8. ‡ (PhCH₂)₂ (29%) was also formed. § Chlorobiphenyls (20%) were also formed.

N-chlorosulphonylphthalimide. The overall similarity in the pattern of substitution points to the participation of the same phthalimido-species in both reactions, and by comparison with the known isomer ratios obtained from radical phenylation⁸ (Table 1) this would appear to be the phthalimido-radical, as already postulated by Lidgett *et al.*⁴ in the case of thermolysis of *N*-chlorosulphonylphthalimide, on the basis of the isomer ratios obtained on reaction with biphenyl. That our reaction involved radicals also follows from the isolation of bibenzyl (29%) from the reaction carried out in toluene (Table 1).

We sought further confirmation of this from competition reactions involving pairs of aromatic solvents. The

reaction), it is our view that the comparison is valid. In partial support of this a comparative study of photolysis

TABLE 3

Partial rate factors for phthalimidation and *p*-methylbenzoyloxylation

X in PhX	Conditions*	$\frac{PhX}{Ph}K$	<i>o</i> -	<i>m</i> -	<i>p</i> -
MeO	PP	9.9	16.3	0.9	24.9
MeO	TP	5.4	9.1	1.1	12.0
MeO	B		26.6	0.3	26.3
Cl	PP	0.8	0.9	0.3	2.5
Cl	TP	1.0	1.0	0.9	2.4
Cl	B		0.9	0.4	1.2

* PP, photolysis of R₂N·OTs; TP, thermolysis of R₂N·SO₂Cl; B, *p*-MeC₆H₄·CO₂· attack.

TABLE 2

Phthalimidation of biphenyl at various temperatures

Temp. (°C)	Photolysis of R ₂ N·OTs			Temp. (°C)	Thermolysis of R ₂ N·SO ₂ Cl		
	Isomer ratio (%)				Isomer ratio (%)		
	2-	3-	4-		2-	3-	4-
160	46	14	40	160	54	21	25
20	59	8	43	260	46	25	29

results, summarised in Table 3, although not strictly comparable because it was impracticable to irradiate a mixture of low boiling solvents at 160°, confirm the radical nature of the reactions and further suggest that the phthalimido-radical is electrophilic. In this connection the similarity of the partial rate factors for attack by the closely related *p*-methylbenzoyloxyl radical (*p*-MeC₆H₄·CO·O·) on chlorobenzene and anisole is noteworthy (Table 3).⁹

and thermolysis showed that the isomer ratios became closer at the same temperature (Table 2).

We therefore conclude that (a) phthalimidation of aromatic compounds by photolysis of *N*-tosyloxypthalimide is easily achieved, particularly when the aromatic substrate is electron rich, *e.g.* anisole, and (b) the reaction proceeds *via* an electrophilic phthalimido-radical [Scheme, route (ii)] rather than *via* a nitrenium ion as is the case with the corresponding *N*-tosyloxindole.⁵

EXPERIMENTAL

G.l.c. was performed on a Pye 104 instrument fitted with a flame ionisation detector. Columns were glass (7 ft × 4 mm i.d.) packed with either Chromosorb W coated with Silicene OV225 (2.5% w/w) or Celite (80–100 mesh) pre-

⁸ D. H. Hey, *Adv. Free Radical Chem.*, 1967, **2**, 47.

⁹ M. E. Kurz and M. Pellegrini, *J. Org. Chem.*, 1970, **35**, 990; M. J. Perkins in 'Free Radicals,' vol. II, ed. J. Kochi, Wiley-Interscience, New York, 1973, p. 231.

treated with KOH (5% w/w) before coating with PEG 1500 (10% w/w).

Qualitative analysis was carried out by comparison of retention times with those for authentic materials and the results were confirmed by g.l.c.-mass spectrometry (Pye 104 chromatograph linked *via* a jet separator to a Micromass 12 spectrometer).

High speed liquid chromatography was carried out using an A.R.L. constant pressure pump. The detector was a variable wavelength Cecil CE212 u.v. monitor normally used at 254 nm. Columns were glass (50 cm \times 0.6 cm i.d.) packed with Spherisorb (5 μ). The mobile phase was 35% ethyl acetate in hexane, saturated with water.

G.l.c. was the routine method of analysis for the substituted anilines but liquid chromatography was used for analysis of the mixtures of nitroanilines, since these compounds are apparently thermally unstable. It was also found impossible to separate the 3- and 4-chloroanilines by g.l.c., whereas the liquid chromatograph accomplished this separation readily.

Quantitative analysis was carried out by the internal standard method, the response of the detector being determined by analysis of authentic mixtures.

Materials.—The substituted anilines were either commercially available or had been previously prepared by standard routes in our laboratory. They were redistilled or recrystallised before use as standards for the gas or liquid chromatographs. All solvents and substrates were redistilled before use and dried by standard methods. Biphenyl was purified by chromatography on alumina.

N-Chlorosulphonylphthalimide¹⁰ had m.p. 160–162° (lit.,¹⁰ 157–158°).

N-Tosyloxyphthalimide.—*N*-Hydroxyphthalimide¹¹ (32.6 g, 0.2 mol) was allowed to react with diethylamine (24 g) and toluene-*p*-sulphonyl chloride (38 g) in dry benzene (700 ml) until the solution became colourless (1 h). After filtration, the crude product was obtained from the filtrate. Recrystallisation from benzene gave *N*-tosyloxyphthalimide (40%), m.p. 162–163°, as colourless prisms (Found: C, 56.9; H, 3.5; N, 4.4. C₁₅H₁₁NO₅S requires C, 56.8; H, 3.5; N, 4.4%), δ (60 MHz; CDCl₃) 2.40 (3H, s), and 7.53 (A₂B₂, m) and 7.70 (s) (total 8H).

Photolysis of *N*-Tosyloxyphthalimide.—**General procedure.** *N*-Tosyloxyphthalimide (1 mmol) was dissolved in the aromatic substrate (200 ml) if liquid; in the case of biphenyl a solution of 5 g in cyclohexane (200 ml) was used. For reaction of biphenyl at high temperatures, the tosyloxy-compound (1 mol) was used in biphenyl (7.7 g) without a solvent.

Photolyses were carried out with a 90 W Hanovia medium-pressure lamp, Pyrex filtered, and the reaction was continued until all the starting material was consumed (t.l.c.) (usually *ca.* 20 h). All reactions were performed under nitrogen and moisture was excluded.

After completion of the reaction the solvent was removed under vacuum and the residue dissolved in ethanol (50 ml).

Hydrazine hydrate (1 g) was added and the mixture heated at reflux temperature for 4 h. After cooling, 12M-hydrochloric acid (5 ml) was added and the precipitate filtered off. The filtrate was evaporated to dryness and the residue dissolved in water (50 ml) and basified (KOH) before extraction with ether (3 \times 100 ml). The extract was dried (MgSO₄) and, after addition of an internal standard, evaporated to low bulk and analysed by gas or liquid chromatography as described above.

In cases where the intermediate *N*-arylphthalimides were isolated the procedure was modified as follows. After removal of solvent the reaction mixture was chromatographed on alumina (grade III) and, after elution with petroleum to remove traces of the aromatic substrate, the *N*-arylphthalimides were eluted with benzene.

In this manner we obtained, from the photolysis of *N*-tosyloxyphthalimide in benzene, *N*-phenylphthalimide (10%), identical (m.p., mixed m.p., and i.r. and n.m.r. spectra) with an authentic sample prepared from phthalic anhydride and aniline.³ Elution of the column with ether gave only tarry materials (0.13 g). The n.m.r. spectra of these tars showed broad lines in the aromatic region and they were not further investigated.

Similar work-up of the reaction mixture with anisole as substrate gave a white solid (60%), m.p. 127–149° (Found: C, 71.3; H, 4.3; N, 5.4%; *M*⁺, 253.073897. Calc. for C₁₅H₁₁NO₃: C, 71.1; H, 4.4; N, 5.5%; *M*, 253.073887). The n.m.r. spectrum showed a poorly resolved pair of lines at δ 3.7 and a complex multiplet in the range δ 7–8 (integral ratio 3 : 8). These data are all consistent with the material being a mixture of *N*-methoxyphenylphthalimides, and hydrazinolysis as above gave anisidines in the same isomer ratio as obtained after hydrazinolysis of the crude reaction mixture.

Further elution of the column gave no further products although the column material was discoloured.

N-Arylphthalimides decompose if left in contact with the alumina column for more than 1 h.

Thermolysis of *N*-Chlorosulphonylphthalimide.—*N*-Chlorosulphonylphthalimide (1 mol) was dissolved in the aromatic substrate (50 ml) and copper(I) chloride (5 mg) was added. For reactions in biphenyl, the phthalimide (1 mmol) was used with biphenyl (7.7 g) without added solvent. The mixtures were heated at *ca.* 160° until the starting material had all been consumed (t.l.c.) (normally 36–48 h). Where this temperature was above the b.p. of the solvent/substrate the reaction mixture was sealed in a stainless steel bomb with a glass liner and the bomb was heated in an oven at 180° for 3 days.

Work-up and analysis of these reaction mixtures were carried out as described for the photolyses.

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¹⁰ M. S. Kharasch and R. A. Mosher, *J. Org. Chem.*, 1952, **17**, 453.

¹¹ W. R. Orndorff and D. S. Pratt, *Amer. Chem. J.*, 1912, **47**, 89.