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Phthalimides. III.[1,2] Ammonolysis, Aminolysis, Hydrazinolysis, Pyrolysis, and Action of Grignard Reagents on Phthalimide Derivatives

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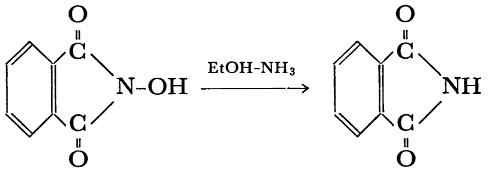
N-Hydroxyphthalimide undergoes ammonolysis to give phthalimide. *N*-(Aroyloxy)phthalimides undergo alcoholysis followed by ammonolysis to give mixtures of phthalimide and ester. *N*-(Arylsulfonyloxy)phthalimides undergo ammonolysis, followed by Lossen rearrangement to give mixtures of 2,4-quinazolinedione and ammonium salts of arenesulfonic acids. *N*-Hydroxyphthalimide undergoes aminolysis to give the corresponding *N*-arylphthalimides. *N*-Hydroxyphthalimide reacts with hydrazine hydrate and/or phenylhydrazine in acetic acid or ethanol to give the corresponding 1,4-phthalazinedione, or by fusion to give phthalimide and *N*-phenylphthalimide, respectively. Pyrolysis of *N*-hydroxyphthalimide gives phthalimide, and *N*-(aroyloxy)phthalimides give mixtures of phthalimide and carboxylic acids. *N*-(Arylsulfonyloxy)phthalimides give mixture of phthalimide and arenesulfonic acids. However, pyrolysis of *N*-(arylcarbamoyloxy)phthalimides gave *N*-arylphthalimides. *N*-Hydroxyphthalimide reacts with phenylmagnesium bromide to give 1,1-diphenyl-3-(phenylimino)-1,3-dihydroisobenzofuran *via* ring opening followed Beckmann rearrangement, while *N*-(arylsulfonyloxy)phthalimides react with arylmagnesium bromide to give mixtures of [*O*-(arylamino)phenyl]diarylmethanols, and arenesulfonic acids *via* ring opening followed by Lossen rearrangement.

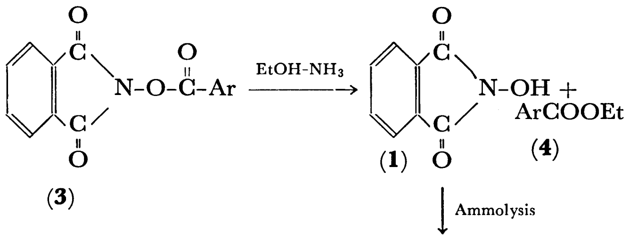
In a previous publication[1] *N*-(arylsulfonyloxy)phthalimides were reported to undergo base-catalyzed Lossen rearrangement with amines and acid-catalyzed Beckmann rearrangement with anhydrous aluminium chloride in the presence of aromatic substrates. We have reinvestigated the problem imide rearrangement and ring opening with different types of imides under different reaction conditions.

I. Ammonolysis. The hitherto unknown reaction of *N*-hydroxyphthalimide, and its *O*-arylsulfonyl and *O*-aroyl derivatives with ammonia was investigated. *N*-Hydroxyphthalimide (**1**) reacts with ethanolie ammonia to give phthalimide (**2**).



(**1**) (**2**)

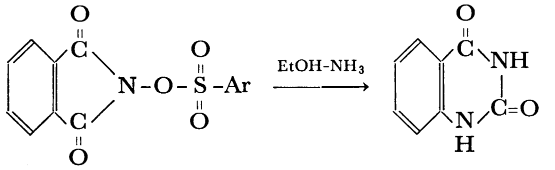
N-(Aroyloxy)phthalimides (**3**) undergo ammonolysis to give mixtures of phthalimide (**2**), esters (**4a**—**d**) *via* the intermediate *N*-hydroxyphthalimide (**1**).



(**3**) (**1**) (**4**) (**2**)

a: Ar=C_6H_5; **b**: Ar=$C_6H_4CH_3$(*p*-);
c: Ar=$C_6H_4OCH_3$(*p*-); **d**: Ar=C_6H_4Cl(*p*-).

The reaction is actually alcoholysis, followed by ammonolysis. It was found that *N*-(arylsulfonyloxy)-phthalimides (**5a** and **b**) undergo ammonolysis *via* Lossen-rearrangement to give mixture of 2,4-quinazolinedione (**6**) and ammonium salts of arenesulfonic acids (**7a** and **b**).

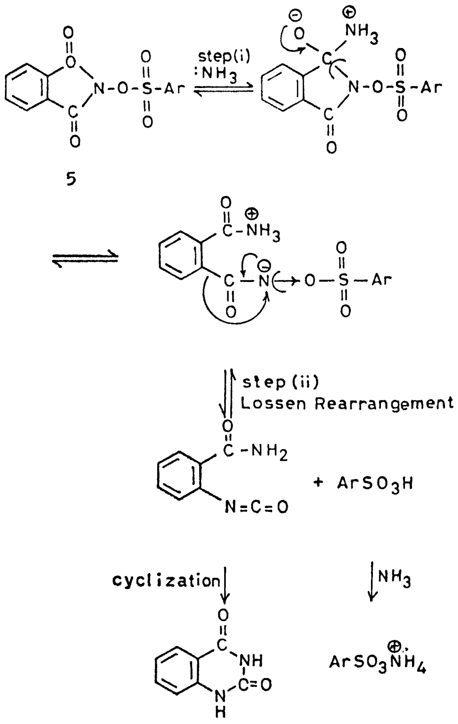


(**5**) (**6**)

+ $\mathrm{ArSO_3\overset{+}{N}H_4}$ (**7**)

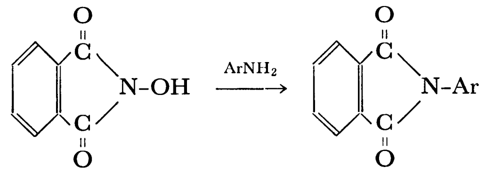
a: Ar=C_6H_5; **b**: Ar=$C_6H_4CH_3$(*p*-)

The reaction probably takes place according to Scheme 1.



Scheme 1.

II. Aminolysis. When **1** is allowed to react with aromatic amines, and/or amino acids, it undergoes aminolysis to give *N*-arylphthalimides (**8a**—**m**).

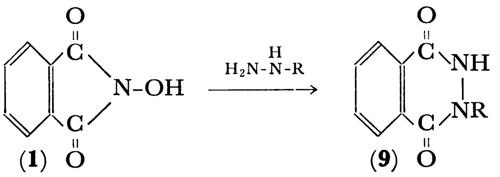


(**1**) (**8**)

a: Ar$=C_6H_5$, **b**: Ar$=C_6H_4CH_3(o)$, **c**: Ar$=C_6H_4CH_3(p)$,
d: Ar$=C_6H_4OCH_3(o)$, **e**: Ar$=C_6H_4OCH_3(p)$,
f: Ar$=C_6H_4Cl(o)$, **g**: Ar$=C_6H_4Cl(m)$, **h**: Ar$=C_6H_4Cl(p)$,
i: Ar$=C_6H_4Br(p)$, **j**: Ar$=C_6H_5NO_2(p)$,
k: $C_6H_4COOH(o)$, **l**: Ar$=C_6H_4COOH(m)$,
m: Ar$=C_6H_4COOH(p)$

III. Hydrazinolysis. A novel reaction of **1** with hydrazines was found to occur under different conditions.

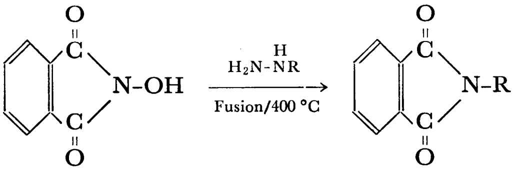
N-Hydroxyphthalimide (**1**) reacts with hydrzaines in acetic acid or ethanol to give the corresponding 1,4-phthalazinedione (**9a** and **b**)



(**1**) (**9**)

a: R=H **b**: R$=C_6H_5$

It was also found that **1** reacts with hydrazine hydrate, and/or phenylhydrazine by fusion at 400 °C to give phthalimide (**2**), and *N*-phenylphthalimide (**8a**), respectively



(**1**) **2**: R=H
8a: R$=C_6H_5$

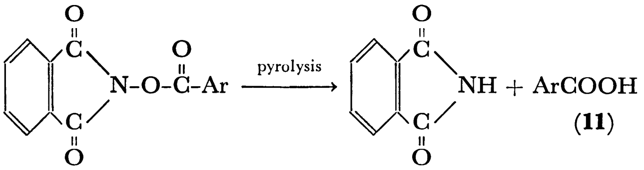
The reaction takes place according to Scheme 2.

This was confirmed by the fact that heating of *N*-anilinophthalimide (**10b**) at 200 °C for 2 h gives 2-phenyl-1,4-phthalazinedione (**9b**) in 67% yield, and the latter on pyrolysis at 400 °C giving *N*-phenylphthalimide (**8a**) in 65% yield.

The results shows that **9b** and **10b** are intermediates in Scheme 2.

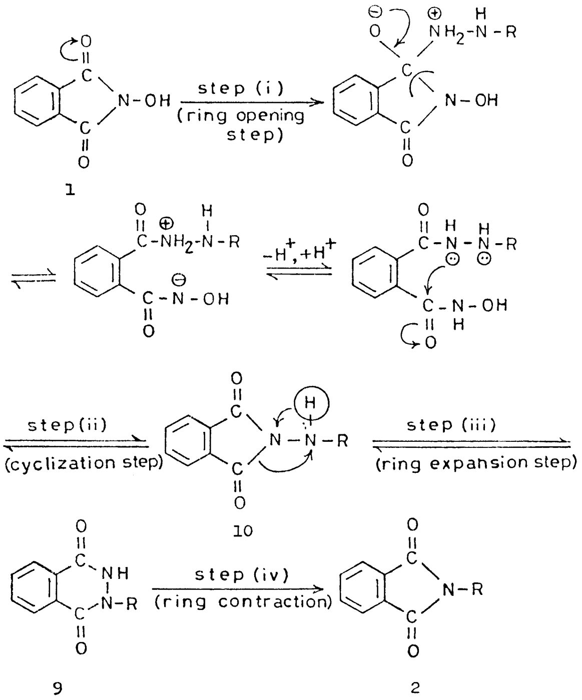
IV. Pyrolysis. It was found that **1** gives **2** on pyrolysis quantitatively. We studied the thermal decomposition of *N*-hydroxyphthalimide derivatives to see the effect of substituents on the mode of pyrolysis.

Pyrolysis of (**3a**—**d**) give mixtures of **2** and the corresponding acids (**11a**—**d**)



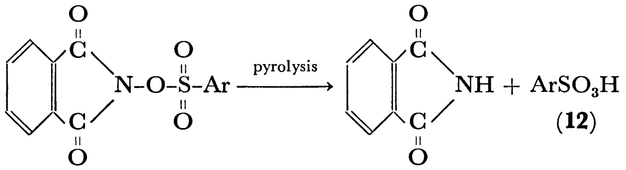
(**3**) (**2**)

a: Ar$=C_6H_5$, **b**: Ar$=C_6H_4CH_3(p)$,
c: Ar$=C_6H_4OCH_3(p)$, **d**: Ar$=C_6H_4Cl(p)$



Scheme 2.

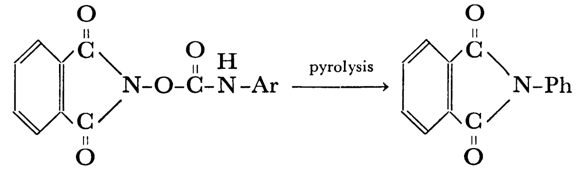
Similarly **5a** and **b** undergo pyrolysis to give mixtures of **2** and the corresponding arenesulfonic acids (**12**).



(**5**) (**2**)

a: Ar$=C_6H_5$, **b**: Ar$=C_6H_4CH_3(p)$

However, *N*-(arylcarbamoyloxy)phthalimides (**13a**—**d**) give *N*-arylphthalimides (**8a**, **e**, **h**, **j**) by pyrolysis.

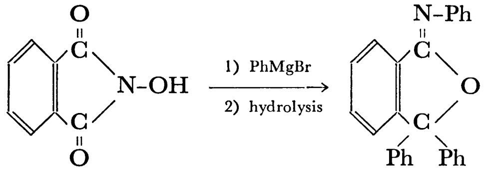


(**13**) (**8**)

a: Ar$=C_6H_5$, **e**: Ar$=C_6H_4OCH_3(p)$,
h: Ar$=C_6H_4Cl(p)$, **j**: Ar$=C_6H_4NO_2(p)$

V. Addition of Grignard Reagents. A novel reaction of **1** and **5** with Grignard reagents was studied.

N-Hydroxyphthalimides reacts with phenylmagnesium bromide to give 1,1-diphenyl-3-(phenylimino)-1,3-dihydroisobenzofuran (**14**).



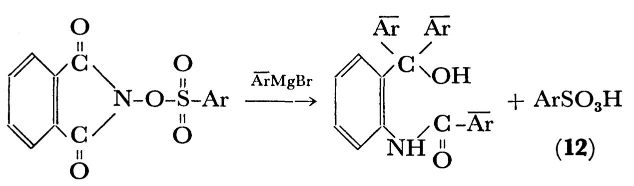
(**1**) (**14**)

The reaction might be the ring opening followed by

Beckmann rearrangement, and cyclization.

N-(Arylsulfonyloxy)phthalimides (**5**) were used instead of *N*-hydroxyphthalimide (**1**) in order to see the effect of the introduction of arylsulfonyl group on the imide reaction with Grignard reagent.

N-(Arylsulfonyloxy)phthalimide (**5a** and **b**) react with arylmagnesium bromide to give mixtures of [*O*-(arylamino)phenyl]diphenylmethanols (**15a**—**d**), and (**12a** and **b**).

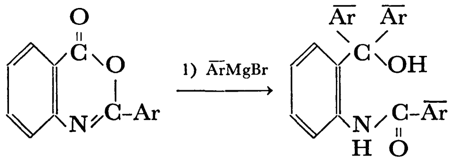


(**5**) (**15**)

a: $\overline{\mathrm{Ar}}=C_6H_5$, **b**: $\overline{\mathrm{Ar}}=C_6H_4CH_3(p)$,

c: $\overline{\mathrm{Ar}}=C_6H_4OCH_3(o)$, **d**: $\overline{\mathrm{Ar}}=C_6H_4OCH_3(p)$

Structures of products (**15a**—**d**) were confirmed from their identity with products obtained by the reaction of arylmagnesium bromides with the corresponding 2-aryl-3,1-benzoxazin-4-ones (**16**).



(**16**) (**15**)

The reaction is actually the ring opening of the phthalimide ring with Grignard reagents followed by Lossen rearrangement.

Experimental

All the melting points are not corrected. IR spectra were measured on a Unicam Sp 1200 spectrophotometer using KBr wafer technique. Mass spectrum was measured with A.E.I.M.S. 12 single focusing mass spectrophotometer at a beam energy of 70 eV. and accelerating voltage of 8 kV. The sample was introduced to the sources *via* a direct inlet system the operating temperature being 270 °C.

I. Ammonolysis of N*-Hydroxyphthalimide and Its Derivatives.*

A. Action of Ethanolic Ammonia on N*-Hydroxyphthalimide (**1**); Formation of **2***: A mixture of *N*-hydroxyphthalimide (**1**) (prepared *via* phthalic anhydride and hydroxylamine)[3] (0.005 mol) and concd ethanolic ammonia (40 ml) was heated under reflux for about 3 h, then concentrated, and cooled. The solid obtained was filtered off, and recrystallised from methanol to give **2** as white crystals (mp 231—232 °C, yield 82%). It was confirmed to be phthalimide **2** by comparison of mp and mixture mp with those of an authentic sample[4] and its IR spectrum.[5,6]

B. Action of Ethanolic Ammonia on N*-(Aroyloxy)phthalimides (**3a—d**); Formation of **2***: A mixture of *N*-(aroyloxy)phthalimides (**3**) (prepared from *N*-hydroxyphthalimide and aroyl halides)[7] (0.005 mol), and concd ethanolic ammonia (50 ml) was heated under reflux for 3 h, then cooled to afford white crystals. It was filtered off, and recrystallized from ethanol to give white crystals (mp 230—231 °C, yield 71%). It was confirmed to be phthalimide by comparison of mp and mixture mp with authentic sample.[4]

The filtrate was heated under reflux with KOH for 30 min, cooled and acidified with hydrochloric acid to yield the corresponding acids (**11a**—**d**) which were proved by mp and mixture mp.[8]

C. Action of Ethanolic Ammonia on N*-(Arylsulfonyloxy)phthalimides (**5a, b**); Formation of **6** and **7***: A mixture of *N*-(arylsulfonyloxyl)phthalimides (**5a** and **b**) (0.01 mol) and ethanolic ammonia (60 ml) was heated under reflux for 2 h, then cooled. The solid obtained was filtered off, and recrystallised from acetic acid to give **6** as white needles (mp >350°, yield 74%).

It was found to be 2,4-quinazolinedione (**6**) by mp and mixture mp with authentic sample[9,10], and IR spectrum which showed ν_{NH} in the region 3280—3080 cm^{-1}, and coupling carbonyl bands in the regions 1740—1700 and 1680—1660 cm^{-1}.

The mother liquor was concentrated to low bulk to give the corresponding ammonium salts of arenesulfonic acids (**7**) which was confirmed by means of mp and mixture mp.

II. Aminolysis of N*-Hydroxyphthalimide. Action of Primary Amines and Amino Acids on* N*-Hydroxyphthalimide (**1**); Formation of* N*-Arylphthalimides (**8a—m**)*: A mixture of 1 (0.01 mol), and aromatic amines and/or aminoacids (0.04 mol) in ethanol (20 ml) was heated under reflux for 3 h, then concentrated, and cooled. The solid products were filtered off and recrystallized from suitable solvent to give (**8a**—**m**), *cf.* Table 1. It was found to be *N*-arylphthalimides by means of mp and mixed mp[11—17] and IR spectra.[5,6]

III. Hydrazinolysis of N*-Hydroxyphthalimide.*

A. Action of Hydrazines on N*-Hydroxyphthalimide in Acetic Acid or Ethanol: Formation of **9***: A mixture of **1** (0.01 mol) and hydrazine (0.03 mol), in acetic acid or ethanol (10 ml) was heated under reflux for about 12 h, then cooled. The solid obtained was filtered off, and recrystallized from acetic acid to give **9** (*cf.* Table 1).

It was found to be 1,4-phthalazinediones (**9a** and **b**) by means mp and mixture mp[18,19] and IR spectra which showed $\nu_{C=O}$ (1640—1630 cm^{-1}) and ν_{NH} (3180—3170 cm^{-1}).

B. Reaction of Hydrazine Hydrate with N*-Hydroxyphthalimide by Fusion (**1**); Formation of **2***: A mixture of **1** (0.01 mol), and hydrazine hydrate (0.05 mol) was heated at (400 °C) on a sand bath for 1.5 h. The solid product was extracted with hot ethanol, and recrystallized from ethanol to give **2** as white crystals (mp 230—231 °C, yield 65%).

It was proved to be phthalimide (**2**) by means of mp, mixture mp[4], and IR spectrum.[5,6]

C. Action of Phenylhydrazine on N*-Hydroxyphthalimide (**1**) and/or Phthalic Anhydride; Formation of **8a***: A mixture of **1** (0.01 mol) and/or phthalic anhydride (0.01 mol) and phenylhydrazine (0.03 mol) was heated at (400 °C) on a sand bath for 2 h, then cooled. The product was extracted with hot ethanol and recrystalized from the same solvent to yield a white crystals mp 204—205°; yield 65%. It was found to be *N*-phenylphthalimide (**8a**) by means of mp and mixture mp,[11] and IR spectrum.[5,6]

IV. Pyrolysis of N*-Hydroxyphthalimide and Its Derivatives.*

A. Pyrolysis of N*-Hydroxyphthalimide (**1**); Formation of Phthalimide (**2**)*: *N*-Hydroxyphthalimide (**1**) was heated above its mp on a sand bath for 1 h. The solid product was obtained in sublimed needles; collected in an air condenser, mp 231—232 °C, yield 60%. It was found to be phthalimide (**2**) by means of mp and mixture mp,[4] and IR spectrum.[5,6]

B. Pyrolysis of N*-(Aroyloxy)phthalimides (**3a—d**); Formation of Phthalimide (**2**) and Benzoic Acids (**11a—d**)*: *N*-(Aroyloxy)-phthalimides (**3a**—**d**) were heated at 300 °C in a sand bath for 3 h. After cooling the solid product obtained was recrystallized from ethanol and charcoalized to give solid (**2**) (mp 230—231 °C, yield 70%). It was found to be phthalimide (**2**) by means of mp and mixture mp,[4] and IR spectra.[5,6]

Table 1. Formation of *N*-arylphthalimides (**8a**—**m**), 1,4-phthalazinediones (**9**), and phthalimides (**2**)

Base added	Product No.	Mp °C	Mixed mp °C	Yield %	Ref.
Aniline	**8a**	204—205[a]	204	79	11
o-Toluidine	**b**	180[a]	179—180	76	12
p-Toluidine	**c**	201—202[a]	201	58	13
o-Anisidine	**d**	155—156[a]	155	79	14
p-Anisidine	**e**	155[a]	153—155	78	15
o-Chloroaniline	**f**	140[a]	140	76	16
m-Chloroaniline	**g**	183—184[a]	183	82	16
p-Chloroaniline	**h**	194—195[a]	195	76	16
p-Bromoaniline	**i**	203—204[a]	203	68	17
p-Nitroaniline	**j**	271[a]	270—271	77	11
Anthranilic acid	**k**[c]	217[b]	216	65	17
m-Aminobenzoic acid	**l**	281—282[b]	281	69	17
p-Aminobenzoic acid	**m**	289—290[b]	290	72	2
Hydrazine hydrate	**9a**	340[b]	339	80	18
Phenylhydrazine	**b**	210[b]	210	79	19

a) Recrystallized from ethanol. b) Recrystallized from acetic acid. c) Reflux in the presence of a few drops of pyridine.

Table 2. Formation of benzoic acids (**11**)

Product	Mp °C	Mixed mp °C	Yield %	Ref.
11a	118—119	118—120	62	8
b	176	175—176	68	8
c	176—177	175—177	66	8
d	225	224—225	52	8

Table 3. Formation of *N*-arylphthalimides (**8**)

Compound No.	Mp °C	Mixed mp °C	Yield %	Ref.
8a	204—205	204	65	11
e	155	154	69	15
h	194—195	195	60	16
j	271—272	271	72	11

Table 4. Formation of [*O*-(aroylamino)phenyl]diarylmethanols (**15a**—**d**)

Product	Mp °C	Yield %	Formula	Annlysis (%)			IR		
					Found	Calcd	ν_{OH} cm^{-1}	ν_{NH} cm^{-1}	$\nu_{C=O}$ cm^{1}
15a	232	61	$C_{26}H_{21}NO_2$	C	81.32	82.34	3400	3290	1640
				H	5.54	5.54			
				N	3.60	3.69			
b	200—203	63	$C_{29}H_{27}NO_2$	C	81.75	82.66	3360	3320	1680
				H	6.45	6.40			
c	155	60	$C_{29}H_{27}NO_5$	C	74.21	74.20	3500	3300	1660
				H	5.94	5.75			
d	163	66	$C_{29}H_{27}NO_5$	C	75.17	74.20	3400	3360	1680
				H	6.22	5.75			

The mother liquors were concentrated by evaporation to give the corresponding benzoic acids,[11] identified by means of mp and mixture mp[8] (*cf.* Table 2).

C. Pyrolysis of N-*(Arylsufonyloxy)phthalimides (**5a** and **b**); Formation of **2** and Arenesulfonic Acids (**12a**, **b**)*: *N*-(Arylsulphonyloxy)phthalimides (**5**) were heated at (400 °C) on a sand bath for *ca.* 2 h, The solid products were recrystallized from ethanol with charcoalization to give white crystals mp 230—231 °C, yield 71%. It was found to be phthalimide (**2**) by means of mp and mixture mp[4] and IR spectrum.

The mother liquors were evaporated to dryness to give the corresponding arenesulfonic acids[20] (**12**).

D. Pyrolysis of N-*(Arylcarbamoyloxy)phthalimides (**13**); Formation of* N-*Arylphthalimides (**8a**, **e**, **h**, **j**)*: *N*-(Arylcarbamoyloxy)phthalimides (**13a**—**d**) were heated on a sand bath for 3 h. The products were extracted with hot ethanol and recrystalized from the same solvent. They were proved to be the corresponding *N*-arylphthalimides (**8**) by means of mp and mixture mp with authentic samples and IR spectra (*cf.* Table 3).

V. Action of Grignard Reagent on N-*Hydroxyphthalimide and Its Derivatives.*

A. Action of Phenylmagnesium Bromide on N-*Hydroxyphthalimide (**1**); Formation of 1,1-Diphenyl-3-phenylimino-1,3-dihydrobenzofuran (**14**)*: A solution of phenylmagnesium bromide (0.6 mol) in dry ether was added to a solution of *N*-hydroxyphthalimide (**1**) (0.1 mol) in dry ether. The reaction mixture was refluxed on a boiling water bath for 6 h and left to stand overnight. The reaction mixture was decomposed with ice-cold concentrated solution of ammonium chloride. The ethereal layer was separated, dried over anhydrous sodium sulfate, and the solvent was distilled off.

The solid product was filtered off and recrystallized from ethanol to give 1,1-diphenyl-3-(phenylimino)-1,3-dihydrobenzofuran (**14**) as colourless crystals (mp 188—190 °C, yield 68%). (Found: C, 86.4; H, 5.2%; Calcd for

$C_{26}H_{19}NO$: C, 86.4; H, 5.2%).

Structure **14** was confirmed by IR spectrum showing $\nu_{C=N}$ (1600 cm^{-1}), and MS showing [M^{+}; at (*m/e* 361); and M^{+} −16; at *m/e*=345].

B. Action of Grignard Reagents on N-*(Arylsulfonyloxy)phthalimides (**5a, b**); Formation of* [O-*(Arylamino)phenyl*] *Diarylmethanols (**15a—d**), and Arenesulfonic Acids (**13a, b**)*: The solution of arylmagnesium bromide (0.6 mol) in dry ether was added to a solution of *N*-(arylsulfonyloxy)phthalimides (**5**) (0.1 mol) in dry ether. The reaction mixture was heated under reflux on a boiling water bath for 6 h, and then allowed to stand overnight at room temperature. It was poured onto ice-cold concentrated solution of ammonium chloride. The ethereal layer was separated, dried over anhydrous sodium sulphate, and the solvent was distilled off. The solid product was filtered off and recrystalized from ethanol to give [*O*-(aroylamino)phenyl]diarylmethanols (**15a—d**) as white crystals (*cf.* Table 4). The mother liquor was concentrated by evaporation to give the corresponding arenesulfonic acids (**12**).[20]

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