

A Facile Rout to the Synthesis of Imines via Thioderivatives of Phthalimides

Sami A. Ali¹, Salim H. Hussien¹, Badie A. Ahmed²

¹ Basic Sciences Branch, College of Agriculture and Forestry, University of Mosul, Mosul, Iraq

² College of Sciences, University of Mosul, Mosul, Iraq

Abstract:

A number of mono and dithio aromatic phthalimides (3 and 4) were synthesized by condensation of phthalimides (2) with diphosphorous pentasulphide (P₂S₅) in dry dioxane. Reaction of (3 and 4) with ethyl amine afforded imines (5 and 6) in good yield. The structure of all compounds were identified by physical, chemical and spectroscopic data.

Introduction:

Various approaches to the synthesis of N-substituted phthalimides were reported in the literature, some of which were products of hydrolysis of imines[1], condensation of phthalic anhydride with amines[2], oxidation of phthalimidines[3] as well as oxidation of imides[4]. Different studies showed that phthalimides have biological activity, and used as plant growth regulator and as herbicide[5-7].

To our knowledge, it seems that little has been published on the synthesis of mono and dithio N-substituted phthalimides utilizing diphosphorous pentasulphide (P₂S₅). According to Gremlyn[8], thio succinimide was prepared by the reaction of succinimide with P₂S₅. Also P₂S₅ was used in the preparation of pyridine mono thioxocarboximide[1].

Although imines can be prepared by different methods[9-13], we herin report a new method to the synthesis of mono and diimines via the thiophthalimides derivatives.

Experimental:

Uncorrected melting points were determined using Galkenkamp melting point apparatus. I.R. spectra were recorded by using PyUnicam SP 1100 spectrophotometer as KBr disc. U.V. visible spectra were performed on double beam Shimadzu UV-160 (U.V. visible) spectrophotometer. Reactions progress were monitored by the T.L.C. technique using silica gel coated plate type linear-K (20x20 mm)Whatman Company . Column chromatography was carried out on silica (BDH 60-120 mesh), and petroleum ether as eluant.

Synthesis of N-substituted phthalimides (2):

General procedure[2]:

An appropriate aromatic amine (0.1 mole) was added to a solution of phthalic anhydride (14 g, 0.1 mol) in (60 ml) acetic acid with stirring, the reaction mixture was heated under reflux for 1 hr. water (20 ml) was added to initiate crystallization from acetic acid-water to give the corresponding phthalimides. Physical and spectral data of which are shown in Table (I).

Table (I): Physical and spectroscopic data of phthalimides (2a-f)

Comp. 2	R	Molecular formula	m.p. °C	Yield %	I.R. (cm ⁻¹) KBr disc			U.V. (EtOH) λ_{max} (nm)
					Ar C-H	C=O	C=C	
a	C ₆ H ₅	C ₁₄ H ₉ NO ₂	202-204	87	3010	1708	1608	294,278,274
b	o-ClC ₆ H ₄	C ₁₄ H ₈ ClNO ₂	154-156	90	3000	1710	1600	293,274,247
c	m-ClC ₆ H ₄	C ₁₄ H ₈ ClNO ₂	144-146	89	3000	1700	1600	299,250,225
d	p-Cl-m-NO ₂ C ₆ H ₃	C ₁₄ H ₇ ClN ₂ O ₂	215-218	90	3020	1710	1605	290,261,225
e	o-CH ₃ C ₆ H ₄	C ₁₅ H ₁₁ NO ₂	162-164	85	3010	1690	1600	300,294,240
f	-C ₅ H ₄ N	C ₁₃ H ₈ N ₂ O ₂	191-193	81	3000	1725	1610	292,258,235

Reaction of phthalimides (2a-f) with phosphorous pentasulphide:

General procedure:

An appropriate N-substituted phthalimides (2) (0.1mole) in dry dioxane (50 ml) was stirred and diphosphorous pentasulphide (0.05 mole, 11.1g) was added at once. The reaction mixture was heated under reflux with stirring for 1 hr. The mixture was filtered while hot and allowed to cool to room temperature. Evaporation of the solvent to dryness, followed by column chromatography (silica gel) of the resulting mass using petroleum ether (40-60°C) as eluant gave N-substituted thioxophthalimides (3a-f). Physical and spectroscopic data of (3a-f) are listed in Table (II).

Table (II): Physical and spectroscopic data of thioxophthalimides (3)

Comp. 3	R	Molecular formula	m.p. °C	Yield %	I.R. (cm ⁻¹) KBr disc				U.V. (EtOH) λ_{max} (nm)
					Ar C-H	C=O	C=C	C=S	
a	C ₆ H ₅	C ₁₄ H ₉ NOS	151-154	70	3010	1725	1610	1195	316,294,245
b	o-ClC ₆ H ₄	C ₁₄ H ₈ ClNOS	129-131	68	3000	1710	1600	1175	288,272,231
c	m-ClC ₆ H ₄	C ₁₄ H ₈ ClNOS	165-168	71	3010	1690	1590	1170	300,290,269
d	p-Cl-m-NO ₂ C ₆ H ₃	C ₁₅ H ₇ ClN ₂ O ₂ S	153-155	53	3010	1705	1600	1209	346,247,222
e	o-CH ₃ C ₆ H ₄	C ₁₅ H ₁₁ NOS	114-116	62	3000	1710	1600	1170	294,269,245
f	-C ₅ H ₄ N	C ₁₃ H ₈ N ₂ OS	169-171	58	3010	1710	1600	1190	310,291,239

Synthesis of dithiophthalimides (4a-f):

a. Direct method:

An appropriate N-substituted phthalimides (2) (0.1 mole) in dry dioxane (50 ml) was stirred and diphosphorous pentasulphide (0.2 mole, 44g) was added at once. The reaction mixture was heated under reflux with stirring for 1 hr. Working up as usual gave the dithiophthalimides; for physical and spectroscopic data see Table (III).

Table (III): Physical and spectroscopic data of dithiophthalimides (4)

Comp. 4	R	Molecular formula	m.p. °C	Yield %	I.R. (cm ⁻¹) KBr disc			U.V. (EtOH) λ_{\max} (nm)
					Ar C-H	C=C	C=S	
a	C ₆ H ₅	C ₁₄ H ₉ S ₂	188-190	62	3010	1610	1165	332,293 247
b	o-ClC ₆ H ₄	C ₁₄ H ₈ ClNS ₂	75-76	66	3000	1600	1230	331,295 244
c	m-ClC ₆ H ₄	C ₁₄ H ₈ ClNS ₂	179-181	57	3000	1591	1209	406,293 249
d	p-Cl-m-NO ₂ C ₆ H ₃	C ₁₃ H ₇ ClN ₂ O ₂ S ₂	200-201	59	3040	1591	1160	366,297 234
e	o-CH ₃ C ₆ H ₄	C ₁₅ H ₁₁ NS ₂	130-132	55	3010	1585	1210	335,294 243
f	-C ₅ H ₄ N	C ₁₃ H ₈ N ₂ S ₂	127-129	63	3000	1600	1230	336,300 246

b. Indirect method:

An appropriate N-substituted thioxo phthalimides (2) (0.1 mole) in dry dioxane (50 ml) was stirred and diphosphorous pentasulphide (0.1mole, 22.2g) was added

at once. The reaction mixture was heated under reflux with stirring for 1 hr., then the working up as usual gave the dithiophthalimides (4a-f).

Synthesis of imines (5 and 6) from thiophthalimides (4a-f and 3a-f):**General procedure:**

An appropriate N-Substituted thiophthalimides (4a-f and 3a-f) (0.05 mole) were stirred in dry dioxane (30 ml) with ethylamine (0.005mole, 0.2g) for 1 hr. at room temperature. The solvent was evaporated to leave an oil which was loaded on silica column and eluted with ethyl acetate in petroleum ether (40-60°C) (50%). This gave a solid material which was crystallized from ethyl acetate. For physical and spectral data see Table (IV).

Table (IV): Physical and spectroscopic data of imines (5 and 6)

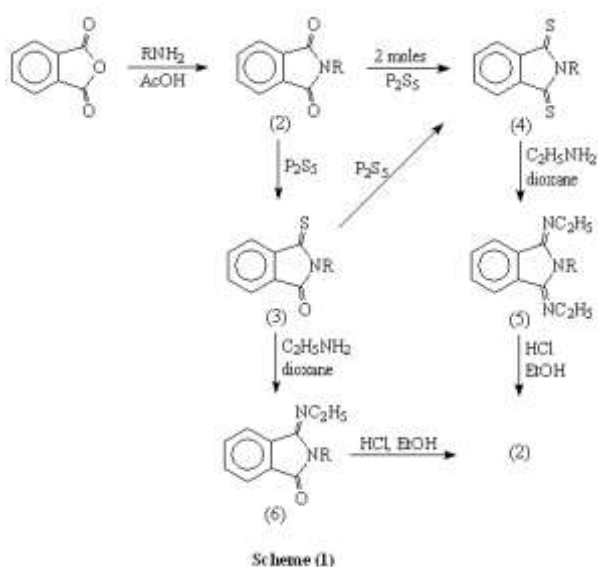
Comp. 5	R	Molecular formula	m.p. °C	Yield %	I.R. (cm ⁻¹) KBr disc				U.V. (EtOH) λ_{\max} (nm)
					Ar C-H	C=O	C=N	C=C	
a	C ₆ H ₅	C ₁₈ H ₁₉ N ₃	166-168	62	3000	-	1610	1580	515,287 253
b	o-ClC ₆ H ₄	C ₁₈ H ₁₈ ClN ₃	64-66	70	3000	-	1620	1585	570,348 229
c	m-ClC ₆ H ₄	C ₁₈ H ₁₈ ClN ₃	143-145	75	3000	-	1600	1590	510,403 295
d	p-Cl-m-NO ₂ C ₆ H ₃	C ₁₈ H ₁₇ ClN ₄ O ₂	168-171	60	3000	-	1610	1580	502,334 219
e	o-CH ₃ C ₆ H ₄	C ₁₉ H ₂₁ N ₃	108-112	70	3010	-	1600	1580	482,292 216
f	-C ₅ H ₄ N	C ₁₇ H ₁₈ N ₄	91-93	64	3100	-	1605	1590	510,284 247
a	C ₆ H ₅	C ₁₆ H ₁₄ N ₂ O	112-114	69	3010	1725	1610	1580	501,276 246
b	o-ClC ₆ H ₄	C ₁₆ H ₁₃ ClN ₂ O	83-85	70	3100	1730	1600	1590	490,261 298
c	m-ClC ₆ H ₄	C ₁₆ H ₁₃ ClN ₂ O	151-153	71	3010	1730	1610	1585	510,403 219
d	p-Cl-m-NO ₂ C ₆ H ₃	C ₁₆ H ₁₂ ClN ₃ O ₃	122-124	74	3000	1710	1601	1589	500,278 249
e	o-CH ₃ C ₆ H ₄	C ₁₇ H ₁₆ N ₂ O	108-112	63	3020	1720	1600	1582	504,402 295
f	-C ₅ H ₄ N	C ₁₅ H ₁₄ N ₃ O	131-133	68	3040	1715	1620	1588	510,414 248

Hydrolysis of imines (5a-f and 6a-f):

An appropriate imine (5 and 6) (0.01 mole) was dissolved in ethanol (10 ml) and concentrated hydrochloric acid (5 drops) was added. The reaction mixture was reflux for one hour, the solvent was evaporated, and the residue was chromatographed on silica gel column (5-30%) ethyl acetate in petroleum ether as eluant. Crystallization of the crude product from ethyl acetate petroleum ether gave product having identical (physical and spectroscopic) properties with (2) that obtained from reaction of phthalic anhydride and amine.

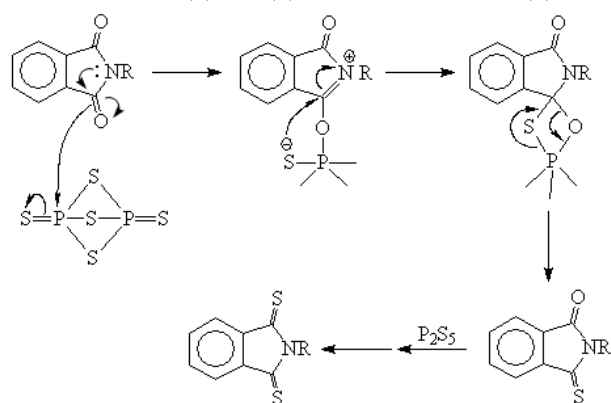
Results And Discussion:**a. Preparation of mono and dithiophthalimides (3a-f and 4a-f):**

Following the reaction sequence shown in Scheme (1), the mono and dithiophthalimides were prepared by the condensation of phthalimides (2) with diphosphorous pentasulphide (P₂S₅) in dry dioxane. The product (3) was isolated when one mole of P₂S₅ was used. Treatment of (3) with another mole of P₂S₅ afforded the dithioderivatives (4). Compound (4) can also be obtained directly when phthalimide (2) treated with two moles of P₂S₅.



The structures of (3a-f and 4a-f) were confirmed on basis of some spectral and chemical interconversion. The I.R. spectra (Table II) of (3a-f) showed the carbonyl absorption at ($1690-1725\text{ cm}^{-1}$) beside the thione group ($\text{C}=\text{S}$) which showed absorption bands at ($1170-1209\text{ cm}^{-1}$). The UV spectrum of (3d) as representative example (Table II) showed three bands at 346, 247 and 222 nm due to $n-\pi^*$ and $\pi-\pi^*$ related to $\text{C}=\text{O}$, $\text{C}=\text{S}$ and benzene ring. On the other hand, I.R. spectra of derivatives (4a-f), showed characteristic band at (1160 cm^{-1}) due to two thione groups combined with the absence of carbonyl absorption. U.V. spectra of (4d) showed λ_{max} at 336, 297 and 234 nm due to thione and benzene ring. Structure (4) was further confirmed by treating the mono thioxo (3) with excess P_2S_5 , to give the dithio derivatives (4). Beside that element test for sulphur in compounds (3) and (4) was positive[14].

Little is known about the mechanism of the thionated imide formation. A possible⁽¹⁾ pathway accounting for the formation of (3) and (4) is shown in Scheme (2).



b. Preparation of imines (5 and 6):

When thiophthalimides (4 and 3) were allowed to react with an excess of ethyl amine in dry dioxane at room temperature, imines (5 and 6) were obtained respectively as expected with evolution of H_2S .

The structure of imines were elucidated by spectroscopic data (Table IV) and by their conversion to the starting carbonyl compounds (2).

The I.R spectra of (5 and 6) exhibited characteristic band at 1610 cm^{-1} due to imine $\text{C}=\text{N}$, combined with the absence of the band at ($1115-1205\text{ cm}^{-1}$) due to $\text{C}=\text{S}$. This was further confirmed by element test for sulphur.

Finally it is interesting to know that the prepared imines (5 and 6) were hydrolysed by treating with ethanol in acidic medium to give product which was identical to the starting material (2).

References:

1. S.H. Hussien, "Condensation of amine with polycarbonyl compounds". Ph.D. Thesis, University of Cardiff, England, (1982).
2. S. Gabriel, Ber., 24, 3104, (1891).
3. I. Yamamoto, Y. Tabo and H. Gotha, Tetrahedron Lett., 2295, (1971).
4. J.L. Richard, US Patent, 3,525,747, (1970); Chem. Abstr., 73, 98985e, (1970).
5. L.M. Perscott, J.P. Hardly and D.A Klein., Microbiology. 2nd ed., Wmc. Brown Communication Inc., Australia, 412-414, (1996).
6. J.W. Lyga, R.M. Patera, G. Theodoides, R.P. Halling, R.W. Hotzmann and M.J. Phimmer, J. Am. Chem. Soc., 39(9), 1667-1678, (1991).
7. L.M. Prescott, J.P. Hardly. and D.A Klein., Microbiology. 3rd ed., Wmc Brown Communication Inc., Australia, 313-319, (1996).
8. R.J. Germlyn, J. Chem. Soc., 5547, (1961).
9. V. Grignard and R. Escourron, Compt. Rend., 180, 1883, (1925). Cited in Lana H.R., Ph.D. Thesis, Salahaddin Univ., (2005), p. 1.
10. I.M. Soffler and M. Katz, J. Am. Chem. Soc., 78, 1705, (1956).
11. R.T. Gilsdard and F.F. Mord, J. Am. Chem. Soc., 72, 4327, (1950).
12. J.J. Ritter, J. Am. Chem. Soc., 55, 3322, (1953).
13. Y. Bergman, P. Perlacutter and N. Thienthage, Green Chem., 6(11), 539, (2004).
14. N.D. Cheronis and J.B. Entrikin, "Identification of Organic Compounds". John Wiley and Sons Inc., (1978). ترجمة موفق ياسين شندالة، روعة غياث الدين ونزار الجبور، مديرية دار الكتب للطباعة والنشر، جامعة الموصل، (١٩٨٦).

طريقة سهلة لتحضير الايمينات من خلال المشتقات الكبريتية للفتاليميدات

سامي عبد علي^١ و سالم حامد حسين^١ و بديع علي احمد^٢

^١ شعبة العلوم الاساسية، كلية الزراعة والغابات، جامعة الموصل، الموصل، جمهورية العراق

^٢ قسم الكيمياء، كلية العلوم، جامعة الموصل، الموصل، جمهورية العراق

الملخص:

تغطي مشتقات الإيمين الجديدة. شخّصت المركبات المحضرة بالطرائق الكيميائية والفيزيائية والطيفية المتوافرة.

تم تحضير عدد من أحادي وثنائي ثايوفتاليميدات الأروماتية من مفاعلة الفتاليميدات الاروماتية مع ثنائي الفسفور خماسي الكبريت (P_2S_5) في الدايبوكسان الجاف. مفاعلة هذه المركبات الكبريتية الجديدة مع اثيل أمين