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Synthatic pathway of Bis phthaldicarboximide thion and isoimide via the reaction of phthalic anhydride with diamines

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Abstract

Thio Bis-N, N substituted phthaldicarboximides were synthesized from the reaction of phthalic anhydride with diamines (aliphatic and aromatic) in hot acetic acid. The products were treated with phosphorous pentasulphide N-substituted Phthalimidines were prepared by the reduction of N,N substituted phthaldicarboximide with zinc dust and hydrochloric acid in ether.

While isoimides was synthesis through the reaction of phthalic anhydride with diamines in the presence of trifloroacetic acid.

الخلاصة :

تم تحضير مركبات كيميائية من معوضات ثنائي فثال الكاربوكسيمايد الكبريتيه وذلك من تفاعل حامض الفثاليك اللامائي مع ثنائي الأمين (اروماتي واليفاتي) في حامض الخليك الساخن ثم مفاعلة النواتج مع ثنائي فسفور خماسي الكبريت . كذلك تم تحضير مركبات كيميائية من أختزال ثنائي فثالال الكاربوكسيمايد بواسطة الخارصين والأيثر .

تم تحضير عدد من مركبات الأيزوأمايد من خلال تفاعل الفثاليك اللامائي مع ثنائي الأمين بوجود ثالث فلورو حامض الخليك.

Introduction

A survey of the literature has revealed that phthalimides deri-vative and analogues of their potential in a number of areas such as amino piptidase inhabitation [1], anticonvulsants activity [2] and promotion of tumor necrosis factor alpha (TAIF alpha) production [3] .Many amides can be used for the preparation of synthetic polymers, which can be used as insulating coating in electrical equipment [4] and plastic heat resistant glass fiber [5]. A number of imides also can be used as plant growth regulators and some of them are usefully as herbicides [5,7] .

In view of interesting range of the products from the reaction of phthalaldehyde with diamine[8], it was decided to prepare these compounds by an alternative rout in order to confirm the various structures. The following synthesis was carried out by using phthalic anhydride instead of phthalaldehyde [9].

Experimental

Apparatus:

Melting point was measured on electro thermal IA9300, Digital series apparatus and were uncorr-ected. Infrared spectrum (FT.IR) were recorded on pye-unicam SP1100 spectrophotometer using K Br disc .

Ultra-Visible spectrum were performed on double beam Shimadzu U.V (U.V-160) spectro-meter. Thin layer chromatography (T.L.C) technique was used to monitored the reaction progress.

Synthesis of N,N substituted phthaldicarboximide :

Phthalic anhydride (1.48gm , 0.01 mol) and appropriate diamine compound (0.01 mol) were refl-uxed in (50 ml) acetic acid for one hour, the precipitate was filtered off and the product was recrystallized from acetic acid-water afforded the pure product , yield, melting point and spectral data are shown in Table (I) .

Synthesis of 2(N-acetyl amino 1H isoindole 1,3 dione :

Phthalic anhydride (1.48gm , 0.01 mole) and ethyldiamine or benzidine diamine(0.05 mol) were refluxed in (50 ml) acetic acid for one hour. The reaction mixture was filtered off while hot and the filtrate was allowed to cool. The solvent was evaporated to dryness and the residue was recrystallized from ethyl acetate petroleum ether (40-60ºc) to give the acetyl derivatives. The physical proper-ties and spectral data shown in Table (I).

Synthesis of dithio N,N diamine di-phthalimide :

N,N-substituted diphthalcarb-oximide (0.01 mol) and diphos-phorous pentasulphide (6.6gm, 0.02 mol) were treated under reflux in dry dioxan (100 ml) for one hour. The reaction mixture was filtered, allowed to cool and evaporated to dryness.

Purification of crude product was achieved by passing it through silica gel column using petroleum ether (40-60 ºC) as eluant to afforde the dithio diaminediph-thalimide. The physical and spectral data are shown in Table (II).

Synthesisof,N,N-phthaldicarboximide phthalimidines :

Asolution of N,N phthalaldicarboximide (0.01 mol) in aqueous ethanol (50 ml) was warmed on hot plate and zinc dust (3gm) was added at once with stirring concen-trated hydrochloric acid was added drop wise . The reaction mixture was heated under reflux with stirring for two hrs, cooled, followed by the addition of sodium hydroxide solution (20%).

The resulting white precipitate was removed by filtration, then washed with water (20×3)ml and dried. Recrystallization of the product from ethyl acetate petroleum ether (40-60ºc). The physical properties and spectral data are shown in Table (111) .

Synthesis of 3-ethoxy N,N sub-stituted phthaldicarboximide :

A solution of N,N substituted phthaldicarboximide (0.02 mol) in aqueous ethanol (50 ml) was warmed on hot plate and zinc dust

(3gm) was added at once with stirring concentrated hydrochloric acid was added drop wise. The reaction mixture was heated under reflux with stirring for two hrs, cooled, followed by the addition of sodium hydroxide solution (20%). The resulting white precipitate was removed by filtration, then washed with water (20×3)ml then dried. Recrystallization of the product from ethyl acetate-petroleum ether (40-60 ºC).The physical properties and spectral data are shown in Table (III).

Synthesis of isoimides :

A-Synthesis of phthalamic acid :

Phthalic anhydride (1.48 gm 0.1 mol) and appropriately diamine (ethylene diamine or benzidine diamine) (0.01 mol) were dissolve each in separate portions of chloroform (100 ml) in 250 ml conical flask. The amine was added in several portion to the anhydride with mixing between addition. After exothermic reac-tion, the mixture was allowed to stand for 30-60 minutes. Crude product was filtered and dried. Recrystallization from ethanol gave the product. The physical properties and spectral data are shown in Table (IV).

B-Synthesis of isoimide :

The product from the reaction between phthalic anhydride and diamine (ethylene diamines ben-zidine) (0.01 mol) was suspended by magnetic stirring in dry 1,4-dioxam (20 ml) and treated with trifloro acetic acid(TFAA) (1.7 ml). After stirring for 30 minutes the mixture was poured into cold water , the solid product was collected washed with 10% $NaHCO_3$ solution followed with water. Recrystallized from acetone. The physical properties and spectral data are shown in Table (V).

Result and Discussion

O- phthalaldehyde was reported as a key intermediate in the formation of polymer through condensation with diamine [8]. In view of interesting range of products we reported an alternative route to prepare the new compounds.

Attempt to prepare(1) as shown in scheme(I) were unsuccessful. The failer was attributed to further reaction of phthalimide with acetic acid to give the acetyl derivative (2) depending upon the reaction condition.

Reaction of equivalent amount of diamine and phthalic anhydride in hot acetic acid produce N,N diphthaldicarboximide (3), but when excess of diamine was allowed to react in acetic acid gave 2(2-acetyl derivatives) (2). The product (3) was formed from the reaction of two molecules of phthalic anhydried for each mole of amine. The infrared of products exhibited characteristic peak at 1710 cm^{-1} due to C=O group and no absorption band due to NH_2 group.

The structural of product (2) was confirmed by spectral and chemical interconversion. The infrared spectra of product showed the NH and C=O groups at 3610 cm^{-1} to 3450 cm^{-1} and 1710 cm^{-1} respectively. The UV spectra showed λ_{max} at 210-230 cm^{-1}. The present of the secondary amid ($NH-COCH_3$) was confirmed by treatment the product with hydroxylamine (NH_2OH) and ethanol in acidic medium the resultant was treated with ferric chloride ($FeCl_3$) (5%) gave positive test (bluish-red).

It is worth noticing that Kashmola [9] prepare the -N,N- substituted phthaldicarboximide in cold solution and did not obtain the acetyl derivative.

It is seem that little has been published on the synthesis of N, substituted thiodicarboximide uti-lizing diphosphorous penta-sulphide (P_2S_5). Gremlyn has used (P_2S_5) in the properties of thio succimide ([10-11]).

Following the reaction sequ-ence shown in Scheme (I) the mono and diphthalidicarboximide were prepared by treating compound(3)with diphosphorous-pentasulphide(P_2S_5)in dry dioxane, when (1 mol) of (P_2S_5) was used a mixture of (4 and 5) was obtain as shown by T.L.C.

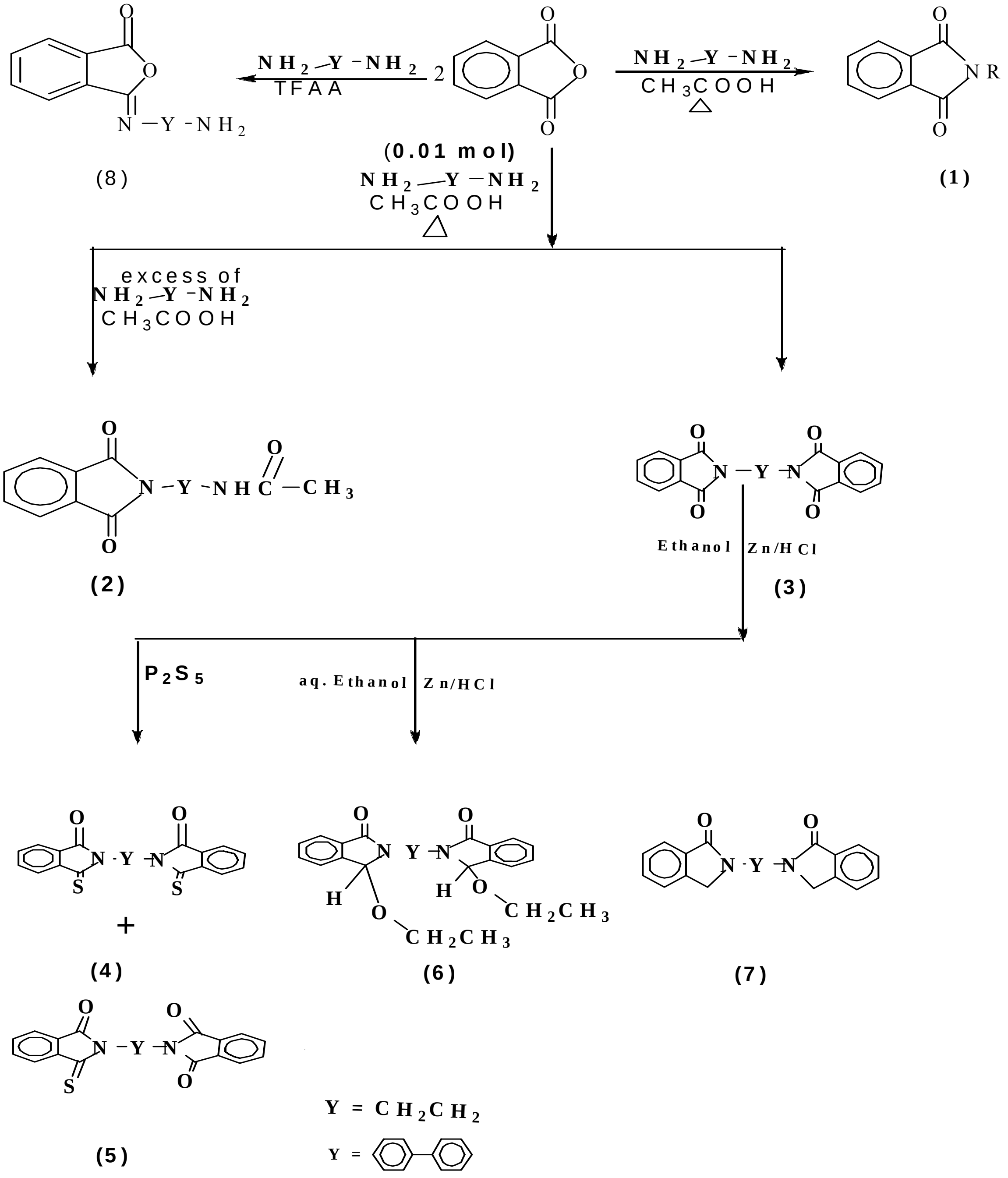
Silica gel column chromate-graphy separation of this mixture petroleum ether(40-60ºC) as eluant afforded compounds (4) and (5).

The structure of compounds (4) and (5) were confirmed on the basis of spectral and chemical inter conversion. The IR spectra Table (II) showed the carbonyl absor-ption at (1710-1725cm^{-1}) beside

the thion group (C=S) which showed band resonated at (1160-1220 cm^{-1}). The uv spectra showed λ_{max} (315-350), element test for sulpher give appositive test [12] indicate the conversion. When compound (3) was treated with (2mol) of (P_2S_5). The dithio derivation (4) were obtained. The IR spectra showed characteristic band around 1160 cm^{-1}, beside the element test for sulpher for compounds (4) and (5) was positive ,Little is known about the mechanism of the thionate diphthaldicarboximides.

The synthesis of phthalimidnes was carried out following the same procedure adopted for the preparation of the

N-alkyl phth-alimidines[13]. The reaction was carried out by treating -N,N-phthaldicarboximide (3) and Zinc dust in acidic media with either aqueous ethanol (20%) to get the phthalimidines (6) or with absolute ethanol to give 3-ethoxyphth-alimidines both in good yield Scheme (I).

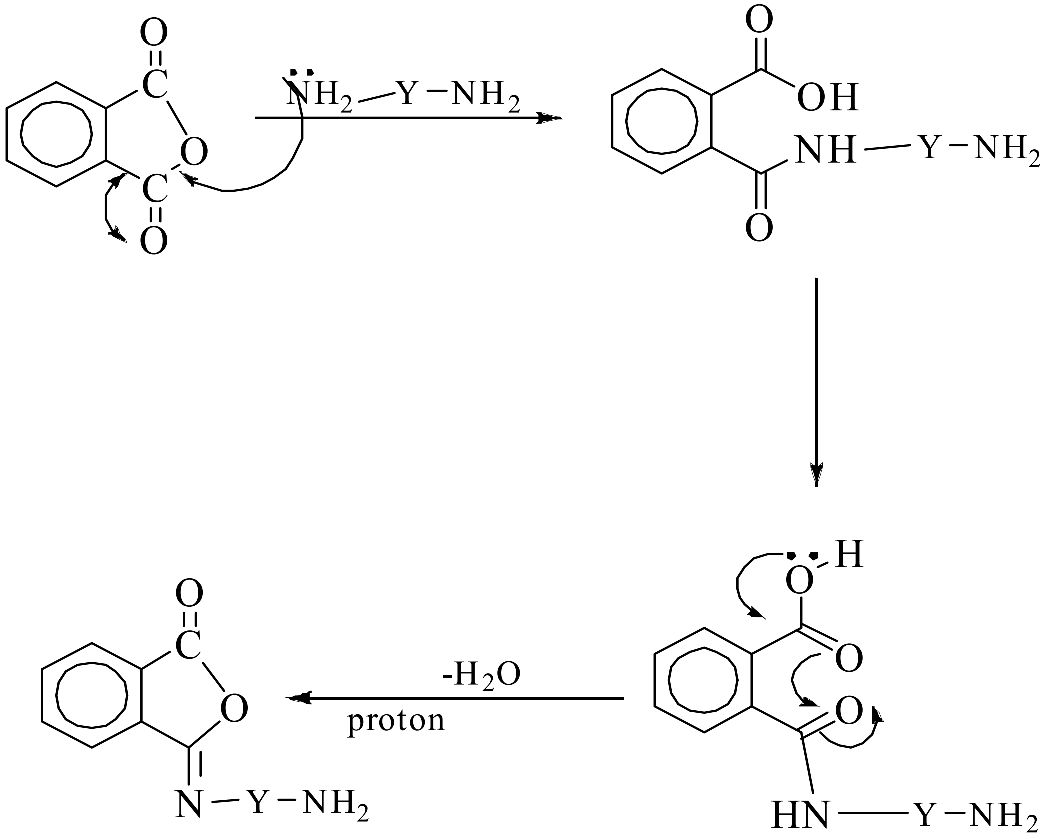


Scheme (I)

The structure of phth-alimidines were elucidated using spectral and chemical inter conversion. The IR spectral data for (6) Table (III) showed an ab-sorption band at (1690-1720 cm^{-1}) due to carbonyl groups and the Uv spectra λ_{max} (270-295cm^{-1}),while the IR spectra of 3-ethoxy phtha-limidines (7) Table (III) showed an absorption band at (1715 cm^{-1}) due to C=O groups and characteristic absorption band at around (1230 cm^{-1}) due to ether linkage.

A sample of isoimide were prepared by the reaction of phthalic anhydride with appropriate diamine by a modification of published method[14] Scheme (I). Physical properties and spectral data are shown in Table (IV) .

The suggested mechanism for the formation of isoimide shown in Scheme (II) .



Scheme (II)

The data obtained from the theoretical calculation [15,16] heat of formation and stretching energy strongly support the established structure of products and some in a good agreement with the spec-troscopic evidence Table(V).

Table (I) : Physical properties of compounds 2 and 3 .

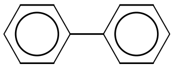
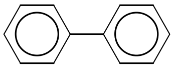
Comp. No.	Y	M.P °C	Yield %	IR (K Br) cm^{-1}			
				C–H	C=C	C=N	C=O
2	CH_2CH_2	178-180	49	3000	1610	1590	1710
		192-194	54	3010	1615	1590	1715
3	CH_2CH_2	226-228	51	3000	1600	1580	1690
		185-187	62	3100	1610	1590	1695

Table (II) : Physical properties of compounds 4 and 5 .

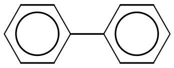
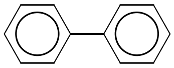
Comp. No.	Y	M.P °C	Yield %	IR (K Br) cm^{-1}				
				C–H	C=C	C=N	C=O	C=S
4	CH_2CH_2	160-161	40	3100	1610	1590	1710	1180
		153-155	30	3000	1600	1585	1695	1140
5	CH_2CH_2	170-171	35	3010	1600	1600	1700	1190
		160-163	30	3000	1600	1590	1715	1175

Table (III) : Physical properties of compounds 6 and 7 .

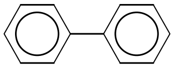
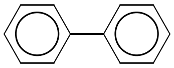
Comp. No.	Y	M.P °C	Yield %	IR (K Br) cm^{-1}		
				C–H	C=C	C–O
6	CH_2CH_2	188-190	55	3010	1605	----
		130-132	65	3000	1590	----
7	CH_2CH_2	127-124	40	3020	1610	1270
		200-203	45	3000	1600	1250

Table (IV) : Physical properties of compounds 8 .

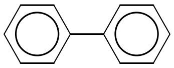
Comp. No.	**Y**	**M.P °C**	**Yield %**	**IR (K Br) cm^{-1}**			
				C–H	**C=C**	**C=N**	**C=O**
8	CH_2CH_2	144-146	60	3000	1600	1692	1795
		134-136	62	3100	1610	1690	1790

Table (V) :Physical properties of the compounds.

Comp. No.	**HF Cal/mol**	**G-free K/mol**	**Molecule formula**
1	64.8	524.88	$C_{18}H_{12}N_2O_4$
2	Zero	Zero	$C_{18}H_{12}N_2O_3S$
3	Zero	Zero	$C_{18}H_{12}N_2O_2S_2$
4	Zero	Zero	$C_{18}H_{12}N_2O\ S_2$
5	79.170	484.3	$C_{18}H_{14}N_2O_3$
6	-163.76	133.3	$C_{12}H_{11}N\ O_3$
7	79.96	423.1	$C_{12}H_{15}N\ O_3$

Hf=Heat of formation

G-free=Gibbs free energy

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