Synthesis of some new imines via mono and dithiopyridine dicarboximides

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Abstract

A number of substituted mono and dithiopyridine dicarboximides were synthesized by condensation of pyridine dicarboximides with diphosphorous pentasulphide (P_2S_5) in dry dioxane. Reaction of mono and dithiopyridine dicarboximides with ethylamine afforded imines in good yields. The structure of all compounds were identified by physical, chemical and spectroscopic data.

الخلاصة

تم تحضير عدد من معوضات احادي وثنائي ثايو بريدين ثنائي الكاربوكسـيمايد مـن مفاعلـة 2،3-بريدين ثنائي الكاربوكسيمايد مع ثنائي الفسفور خماسي الكبريت (P_2S_5) في الدايوكسان الجاف. مفاعلة هـذه المركبات الكبريتية الجديدة مع اثيل امين اعطت مشتقات الايمين. شخصت هذه المركبات المحضرة بـالطرق الكيميائية والفيزيائية والطيفية المتوافرة.

Introduction

The chemistry of heteroaromatic pyridine dicarboxyimide, the so called aza-isoindole or aza-phthalimide has not been extensively studies and has received little attention[1].

The pyridine dicarboxyimides are useful intermediate in the production of agricultural chemicals, especially selective weed killers, plant growth regulators and some of them are useful as herbicide[2], and these compounds are showed to possess an anti-influenza properties with low toxic side effects[3].

To our knowledge, it seems that little what has been published on the synthesis of mono and dithio N-substituted pyridine dicarboximide utilizing diphosphorous penta sulphide (P_2S_5). According to Gremlyn[4] thiosuccinimide was prepared by the reaction of succinimide with (P_2S_5). Diphosphorous pentasulfide was also used in the preparation of monothiophthalimides[5].

Although imines can be prepared by different methods[6-8], we herin report a new method to synthesis mono and diimines via the thio pyridine dicarboximides derivatives.

Experimental

Uncorrected melting points were determined using Galken Kamp 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 U.V-160 (U.V visible) spectrophotometer.

Reactions progress were monitored by T.L.C technique using silica gel coated plates type linear K (20 × 20) mm Whatman company. Column chromatography was carried out on silica (BDH 60-120 mesh) using petroleum ether (40-60 ^oC) as eluant

and U.V light was used to visualize the spots.

Synthesis of pyridine 2,3-dicarboxylic anhydride (1)[9]

Pyridine 2,3-dicarboxylic acid (0.01 mole, 1.6 gm) in acetic anhydride (0.02 mole, 20.4 ml) was heated under reflux for (30 min). On cooling, a solid crystals were separated. The crystalline substance was filtered off and washed with acetic acid (2 × 10 ml) to give the anhydride as white crystals (12.2 gm, 80%), m.p. 137-139 °C [Lit.[9] 138 °C].

Synthesis of N-substituted pyridine-2,3-dicarboximides (2a-f)

General procedure[10]

Pyridine 2,3-dicarboxylic anhydride (0.08 mole, 0.124 gm) and an appropriate amine (0.08 mole) were refluxed in acetic acid (15 ml) for 1 hr. The reaction mixture was filtered while hot, allowed to cool and evaporated to dryness. The residue was crystallized from acetic acid-water to give the desired product. For physical and spectral data see Table (I).

Synthesis of thioxopyridine dicarboximides (3a-f) and (4a-f)

An appropriate pyridine dicarboximide (0.1 mole, 2 gm) and (0.1 mole, 22.2 gm,) diphosphorous pentasulfide were heated under reflux in dry dioxane (100 ml) for 1 hr. The mixture was filtered while hot, allowed to cool and evaporated to dryness. Chromatographics separation on silica gel (120 gm) using petroleum ether (40-60 °C) as eluant gave isomers (3) and (4). For physical and spectral data see Table (II).

Synthesis of dithiopyridine dicarboxyimide

General procedure

a. Direct synthesis[10]

An appropriate pyridine dicarboxyimides (0.1 mole) and diphosphorous pentasulphide (44.4 gm, 0.2 mole) were heated under reflux in dry dioxane (100 ml) for 1 h. The reaction mixture was filtered while hot, 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 °C) as eluant to afford the dithiopyridine dicarboxyimide. For physical and spectra data see Table (III).

b. Indirect synthesis[5]

An appropriate thioxopyridine dicarboxyimide (3) or (4) (0.1 mole) and diphosphorous pentasulphide (P_2S_5) (22.2 gm, 0.1 mole) were heated for 1 hr. The mixture was filtered while hot, allowed to cool and evaporated to dryness. Chromatographic purification on silica gel using petroleum ether (40-60 °C) as eluant, gave the dithiopyridine dicarboximide (7).

Synthesis of imines (5,6 and 8) from thioxo and dithiopyridine dicarboximide

An appropriate N-substituted thiopyridine dicarboxyimide (0.05 mole) were stirred in dry dioxane (30 ml) with ethyl amine (0.2 gm, 0.05 mole) 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 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).

Hydrolysis of imines (5,6 and 8)

An appropriate imine (0.01 mole, 0.75 gm) was dissolved in ethanol (10 ml), concentrated hydrochloric acid (5 drops) was then added. The reaction mixture was refluxed for 1 hr, the solvent was evaporated and the residue was chromatographed on silica gel column (5-30 %) ethyl acetate-petroleum ether (40-60 °C) was used as eluant. Crystallization of the crude product from ether-petroleum ether (40-

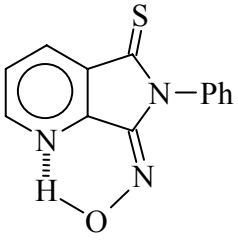
60 ^{o}C) gave product having identical physical and spectroscopic properties with (2) obtained from reaction of pyridine 2,3-dicarboxylic acid with amine.

Results and Discussion

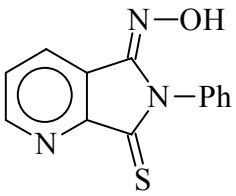
As a key intermediate in projected synthesis of various heterocyclic compounds a series of aromatic pyridindicarboximides were synthesized. When an equimolar of pyridine 2,3-dicarboxylic anhydride[9] (this was obtained from the corresponding dicarboxylic acid which could be obtained by the well established method from the readily available 8-hydroxy quinoline[11]) and an appropriate aromatic amines was refluxed in acetic acid, N-substituted pyridine dicarboximides were obtained in good yields[10].

The structure of compounds (2a-f) were confirmed on the basis of the following evidences. The infrared spectra of products (Table I) showed the carbonyl absorption at around 1725 cm^{-1}. The U.V. spectra showed λ_{max} at 215-320 nm.

Following the reaction sequence shown in Scheme (I) the mono and dithiopyridine dicarboximides were prepared by treating pyridine dicarboximide (2a-f) with diphosphorous pentasulphide (P_2S_5) in dry dioxane. When 1 mole of (P_2S_5) was used, a mixture of compounds (3 and 4) was obtained as shown by T.L.C. Silica gel column chromatography separation of this mixture using petroleum ether (40-60°C) as eluent afforded compound (3) and (4).



(A)



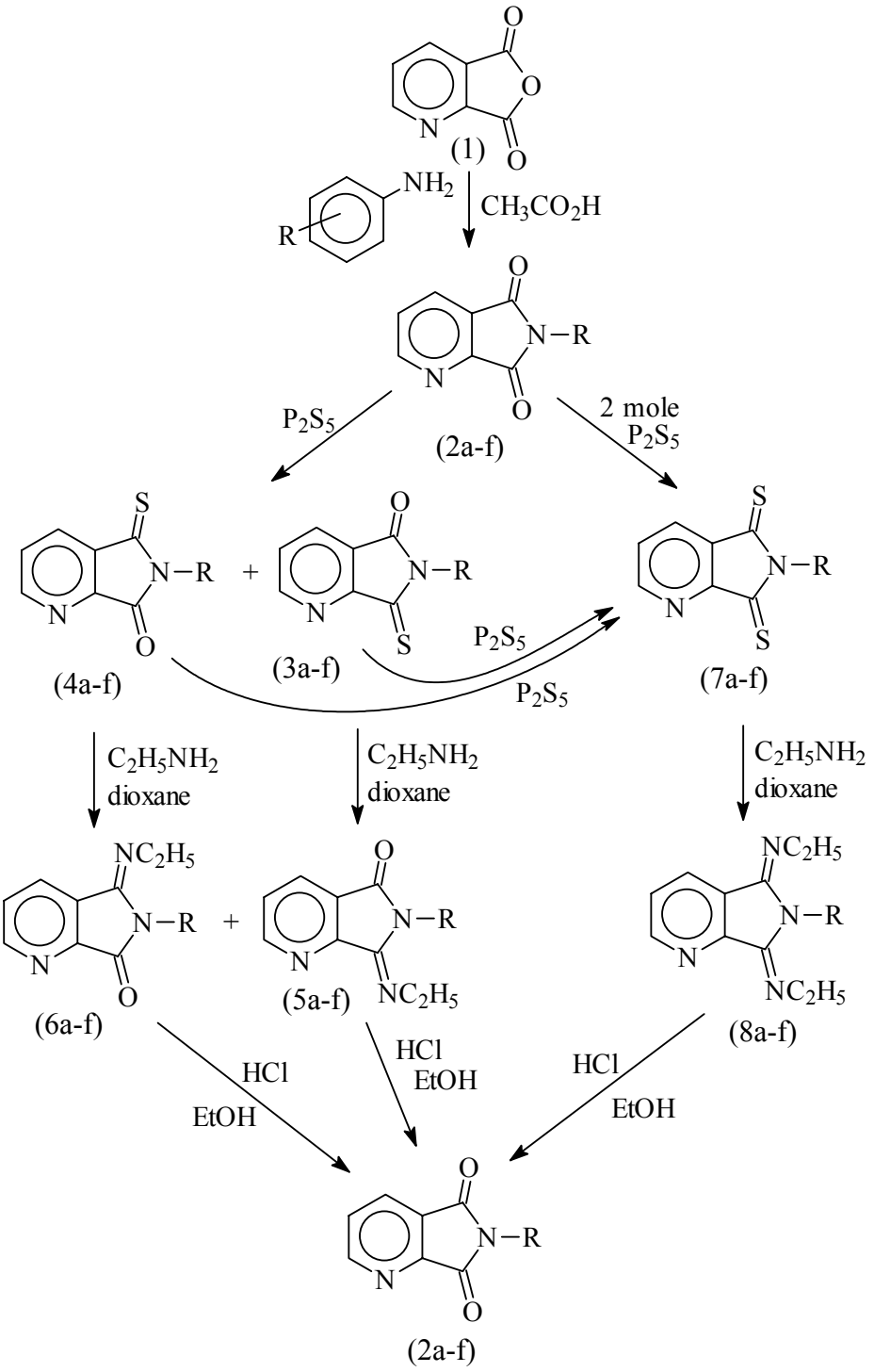
(B)

Identification of these two isomers was achieved by preparation of the oxime derivatives (A) and (B) of (3a) and (4a) as a representative compounds, and subsequent i.r. measurements.

Isomer (A) has melting point (192-194 ^{o}C) and showed a broad absorption in the i.r. spectrum at (3180 cm^{-1}) characteristic for bonded hydroxyl group confirming the proposed structure (A). While the isomer (B) has melting point (168-170 °C) and showed a sharp absorption at (3350 cm^{-1}) due to the free hydroxyl group which confirm the structure of (B) isomer[12].

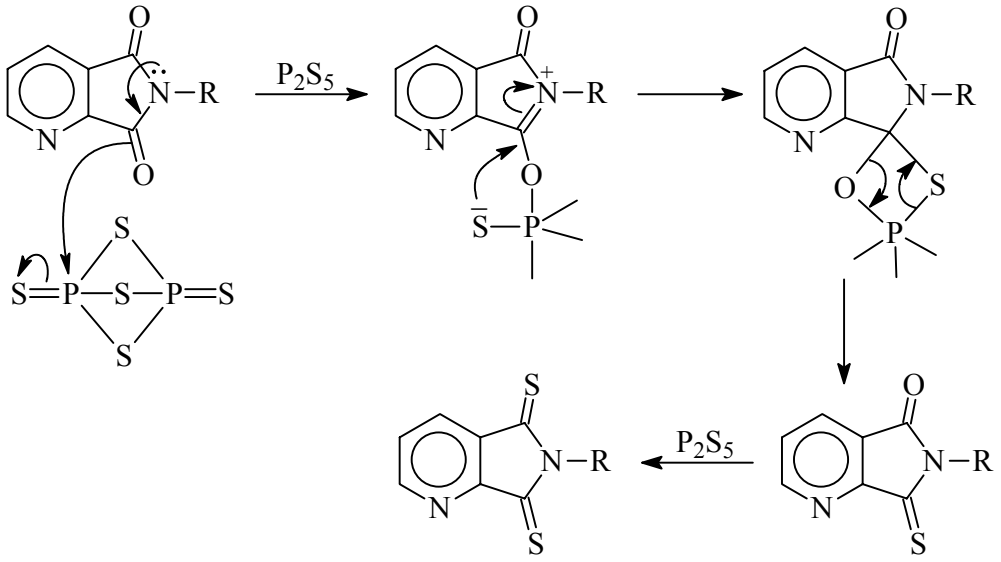
The structures of (3a-f) and (4a-f) were confirmed on the basis of spectral and chemical interconversion. The i.r. spectra (Table II) showed the carbonyl absorption at (1710-1730) cm^{-1} beside the thione group (C=S) which showed band resonated at (1160-1210) cm^{-1}. The U.V spectra showed λ_{max} (315-345) nm.

When compounds (2a-f) were treated with two moles of (P_2S_5), the dithio derivative (7a-f) were obtained. The structure of these products were confirmed by spectral data. The i.r. spectra (Table III) showed a characteristic band around (1150-1210) cm^{-1} due to two thio groups, and the absence of carbonyl absorption. U.V. spectra of (7a-f) showed λ_{max} (335-390) nm. Structure (7) was further confirmed by treating the thioxo derivatives (3 and 4) with excess (P_2S_5) to give the dithio derivative (7). Beside that, element test for sulphur in compounds (3,4 and 7) was positive[13].


(1)
CH_3CO_2H
(2a-f)
P_2S_5
2 mole P_2S_5
(4a-f)
(3a-f)
(7a-f)
P_2S_5
P_2S_5
$C_2H_5NH_2$ dioxane
$C_2H_5NH_2$ dioxane
$C_2H_5NH_2$ dioxane
(6a-f)
(5a-f)
(8a-f)
HCl EtOH
HCl EtOH
HCl EtOH
(2a-f)

Scheme (I)

Little is known about the mechanism of the thionated pyridine dicarboximide formation. A possible pathway[5] accounting for the formation of (3,4 and 7) is shown in (Scheme II).



Scheme (II)

When thioxo- and dithiopyridine dicarboximides (3,4 and 7) were allowed to react with an excess of ethyl amine in dry dioxane at room temperature, imines (5,6,8) were obtained respectively as expected with exclusion of H_2S gas.

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

The i.r. spectra of (5,6 and 8) exhibited characteristic band around (1610 cm^{-1}) due to (C=N) and the absence of the (C=S) band at (1115-1205) cm^{-1}. This also confirmed by element test for sulphur.

Acidic hydrolysis of imines (5,6 and 8) in ethanol gave products which are identical to the starting materials (2).

It is worth noticing that the ease of hydrolysis can be facilitated by some sterric hindrance-induced skew of the two imino groups from the isoindole plane[14].

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

Comp. 2	R	Molecular formula	m.p. °C	Yield %	IR (cm^{-1}) KBr disc			U.V (EtOH)
					ArC-H	C=O	C=C	λ_{max} (nm)
a	C_6H_5	$C_{13}H_9O_2N_2$	55-57	40	3000	1730	1610	305,300,215
b	o-ClC_6H_4	$C_{13}H_7ClNO_2$	154-157	35	3010	1725	1600	310,285,228
c	m-ClC_6H_4	$C_{13}H_7ClNO_2$	165-168	51	3000	1721	1610	295,256,225
d	p-Cl,m-$NO_2C_6H_3$	$C_{13}H_6ClN_3O_4$	191-193	58	3010	1715	1600	305,278,215
e	o-$CH_3C_6H_4$	$C_{14}H_{10}N_2O_2$	178-180	45	3010	1728	1605	320,290,230
f	C_5H_4N	$C_{13}H_7N_3O_2$	132-133	43	3020	1710	1610	303,281,222

Table (II): Physical and spectroscopic data of thioxopyridine (3a-f) and (4a-f)

Comp. 3	R	Molecular formula	m.p. °C	Yield %	IR (cm^{-1}) KBr disc				U.V (EtOH)
					ArC-H	C=O	C=C	C=S	λ_{max} (nm)
a	C_6H_5	$C_{14}H_8N_2OS$	78-79	25	3000	1730	1600	1140	340,295,225
b	o-ClC_6H_4	$C_{14}H_7ClN_2OS$	121-123	30	3010	1710	1610	1135	315,300,242
c	m-ClC_6H_4	$C_{14}H_7ClN_2OS$	110-113	23	3050	1725	1605	1110	344,312,222
d	p-Cl,m-$NO_2C_6H_3$	$C_{14}H_6ClN_2OS$	160-162	16	3010	1720	1600	1120	335,290,225
e	o-$CH_3C_6H_4$	$C_{15}H_{10}N_2OS$	155-157	19	3000	1720	1600	1135	330,285,240
f	C_5H_4N	$C_{13}H_7N_3OS$	93-95	20	3020	1715	1610	1138	345,270,250
Comp. 4									
a	C_6H_5	$C_{14}H_8N_2OS$	65-67	19	3000	1720	1600	1135	344,285,225
b	o-ClC_6H_4	$C_{14}H_7ON_2ClS$	105-107	16	3000	1730	1605	1140	340,300,250
c	m-ClC_6H_4	$C_{14}H_7ON_2ClS$	97-99	22	3010	1725	1600	1140	335,310,222
d	p-Cl,m-$NO_2C_6H_3$	$C_{14}H_6ClN_2OS$	154-156	17	3010	1710	1610	1130	345,285,240
e	o-$CH_3C_6H_4$	$C_{15}H_{10}N_2OS$	142-144	18	3000	1730	1610	1120	330,290,230
f	C_5H_4N	$C_{13}H_7N_3OS$	79-81	20	3000	1710	1600	1130	335,270,222

Table (III): Physical and spectroscopic data of dithiopyridine dicarboxyimide (7a-f)

Comp. 7	R	Molecular formula	m.p. °C	Yield %	IR (cm^{-1}) KBr disc			U.V (EtOH)
					ArC-H	C=C	C=S	λ_{max} (nm)
a	C_6H_5	$C_{14}H_8N_2S_2$	91-93	22	3010	1600	1205	340,295,225
b	o-ClC_6H_4	$C_{14}H_7ClN_2S_2$	108-110	25	3000	1605	1190	363,310,250
c	m-ClC_6H_4	$C_{14}H_7ClN_2S_2$	78-80	35	3020	1595	1210	390,270,242
d	p-Cl,m-$NO_2C_6H_3$	$C_{14}H_6ClN_3O_2S_2$	140-141	30	3050	1600	1150	335,300,247
e	o-$CH_3C_6H_4$	$C_{15}H_{10}N_2S_2$	215-217	38	3000	1608	1190	366,294,210
f	C_5H_4N	$C_{13}H_{10}N_2S_2$	80-82	31	3010	1610	1210	380,300,232

Table (IV): Physical and spectroscopic data of imines (5,6 and 8)

Comp. 5	R	Molecular formula	m.p. °C	Yield %	IR (cm^{-1}) KBr disc				U.V (EtOH)
					ArC-H	C=O	C=N	C=C	λ_{max} (nm)
a	C_6H_5	$C_{17}H_{18}N_4$	60-62	37	3040	-	1605	1585	270,231,215
b	o-ClC_6H_4	$C_{17}H_{17}ClN_4$	108-110	70	3000	-	1620	1580	273,255,210
c	m-ClC_6H_4	$C_{17}H_{17}Cl\ N_4$	80-83	65	3010	-	1610	1582	288,242,215
d	p-Cl,m-$NO_2C_6H_3$	$C_{17}H_{16}ClN_5O_2$	99-99.5	24	3010	-	1600	1590	295,260,230
e	o-$CH_3C_6H_4$	$C_{18}H_{20}N_4$	174-176	45	3020	-	1610	1580	290,255,215
f	C_5H_4N	$C_{16}H_{17}N_5$	202-204	58	3000	-	1600	1575	285,244,232
Comp. 6									
a	C_6H_5	$C_{15}H_{13}N_3O$	117-119	45	3010	1730	1610	1580	482,290,215
b	o-ClC_6H_4	$C_{15}H_{12}ClN_3O$	165-167	51	3000	1735	1620	1590	510,280,240
c	m-ClC_6H_4	$C_{15}H_{12}ClN_3O$	234-236	40	3025	1715	1600	1580	515,403,297
d	p-Cl,m-$NO_2C_6H_3$	$C_{15}H_{11}ClN_4O_3$	210-212	41	3000	1720	1610	1580	502,334,210
e	o-$CH_3C_6H_4$	$C_{16}H_{16}N_3O$	194-196	40	3000	1730	1601	1585	490,284,295
f	C_5H_4N	$C_{15}H_{12}N_4O$	210-212	35	3000	1710	1600	1590	510,287,235
Comp. 8									
a	C_6H_5	$C_{15}H_{13}N_3O$	110-112	30	3000	1730	1580	1580	510,276,240
b	o-ClC_6H_4	$C_{15}H_{12}ClN_3O$	158-160	32	3020	1730	1590	1590	504,260,290
c	m-ClC_6H_4	$C_{15}H_{12}ClN_3O$	225-227	38	3100	1715	1582	1582	500,402,222
d	p-Cl,m-$NO_2C_6H_3$	$C_{15}H_{11}ClN_4O_3$	202-204	29	3025	1710	1580	1580	510,414,248
e	o-$CH_3C_6H_4$	$C_{16}H_{16}N_3O$	180-182	25	3000	1730	1595	1595	500,395,215
f	C_5H_4N	$C_{15}H_{12}N_4O$	201-203	40	3010	1740	1580	1580	495,310,230

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