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SYNTHESIS AND SPECTROSCOPIC STUDIES OF SOME 2-AMINOTHIOPHENE DYE PRECURSORS

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ABSTRACT

Some novel 2-aminothiophenes were prepared from cyanoacetates and a range of 1, 3-dicarbonyl compounds such as, o-acetoacetotoluidide, 4-chloroacetoacetanilide, and o-acetoacetanisidide using the Karl-Gewald one-pot technique. The 2-aminothiophenes are the major precursors for a number of dyestuff syntheses. The strategically located cyano, methyl ester, ethyl ester groups in the 3-position of the thiophene moiety was intended to confer a range of desirable properties on disperse dyes produced from the amines. The beauty of the technique is its simple work-up. However the yield was lower than expected. Detailed spectroscopic investigations (1H-NMR, MS and IR) of the obtained compounds are presented. The IR spectra of aminothiophene intermediates 1, 4, and 7 showed absorption peaks in the range 2203-2214 cm^{-1} due to the presence of cyano group. The amino group absorption for 1-9 appeared in the range of 3555-3260 cm^{-1} while the carbonyl absorption showed up in the range 1630-1664 cm^{-1}. The mass spectra and the HNMR of the intermediates are presented and validated their structures. The Karl-Gewald chemistry has been used successfully in the synthesis of a number of 2-aminothiophenes. Azo dyes derived from thiophene moiety have many advantages, such as a colour deepening effect as an intrinsic property of the thiophene ring, small molecular structure leading to better dye ability and heterocyclic nature of the thiophene ring resulting in excellent sublimation fastness on the dyed fibers.

Keywords: Karl-Gewald, 2-aminothiophene, 1, 3-dicarbonyl compounds, o-acetoacetotoluidide, intermediates.

INTRODUCTION

Many methods of synthesis of 2-aminothiophenes have been published in the last two decades. 2-Aminothiophenes attract special attention because of their applications in pharmaceutical, agriculture, pesticides and dyes. A series of reviews have been published dealing with the latest accomplishments of 2-aminothiophenes, [1-3]. The chemistry of 2-aminothiophenes has received much attention because of the convenient availability through the most versatile, synthetic method developed by Karl Gewald.

Sabnis *et al* [4] listed the various existing preparative methods which can be summarized as follows: reduction of the nitro group, nucleophilic displacement of the hydroxyl, mercapto, halo, methoxy, p-nitrophenoxy, and benzenesulfonyl groups, the Beckman rearrangement, the Hofmann reaction, the Schmidt reaction, the Curtius rearrangement, and the cyclization of thioamides and their S-alkylates.

Stacy and Eck [5, 6] equally reported a multistep synthetic route for 2-aminothiophenes in their classic work in the 60s. Other workers also experimented with the condensation of ethyl chloroacetoacetate with isothiocynates in the presence of sodium hydride to give 2-aminothiophenes. All the above synthetic routes involved difficult preparation of the starting materials and multistep synthesis. These routes did not always produce good yields and high purity. The key intermediates for the synthesis of 2-aminothiophenes by the above routes were also generally expensive.

Gewald [7] devised the most facile and promising set of synthetic routes leading to 2-aminothiophenes with electron withdrawing substituents such as cyano, carbethoxy, carboxamido etc in the 3 positions and alkyl, aryl, cycloalkyl, and hetaryl groups in the 4- and 5-positions. This method offers considerable improvements over existing synthetic methods for aminothiophenes.

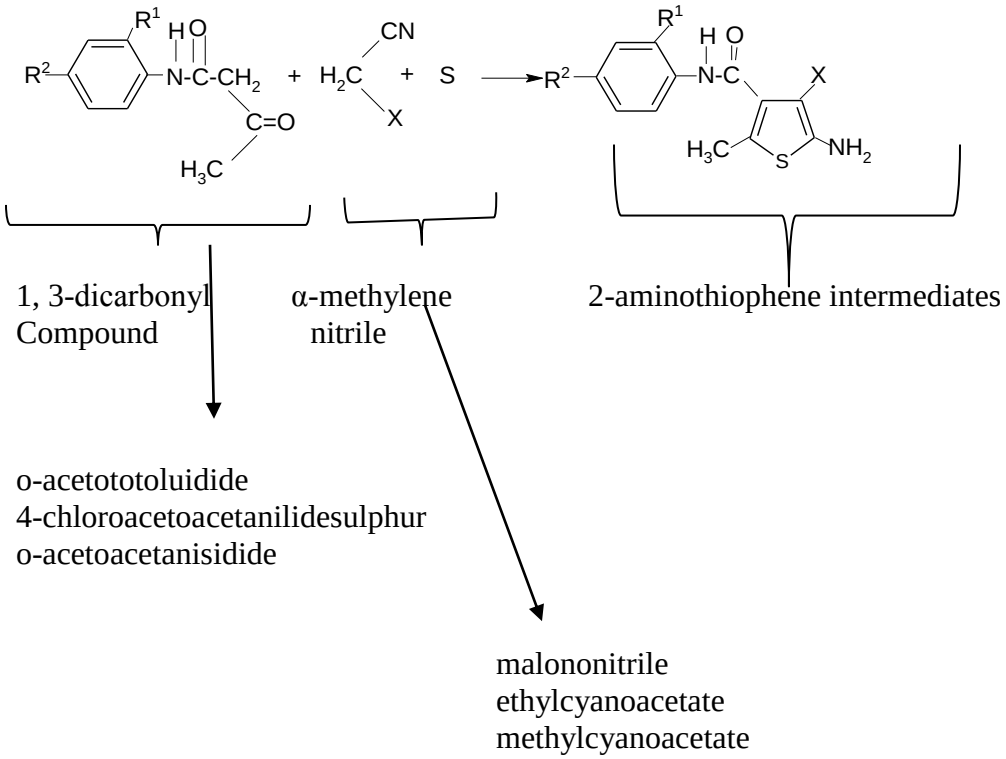
The most elegant and simpler version of the Gewald reaction was introduced a few decades ago. This convenient technique includes the condensation of aldehydes, ketones or 1,3-dicarbonyl compounds with activated nitriles such as malononitrile, cyanoacetic esters, cyanoacetamide and its N-substituted derivatives, heteroarylacetonitriles, α-cyanoketones and sulphur in the presence of amine at room temperature. Ethanol, dimethylformamide, dioxane, excess ketone such as methyl ethyl ketone, or cyclohexanone are preferred solvents and amines like diethylamine, morpholine, or triethylamine have been employed.

In this study, a number of aminothiophene intermediates designated as 1-9 were prepared using the Gewald's methodology. This convenient methodology included the condensation of the 1,3-dicarbonyl compounds, o-acetoacetotoluidide, 4-chloroacetoacetanilide, and o-acetoacetanisidide with the activated nitriles such as malononitrile, methylcyanoacetate and ethylcyanoacetate in the presence of sulfur in ethanol/basic media. These 2-aminothiophenes are the major precursors for a number of dyestuff syntheses.

EXPERIMENTALS

SYNTHESIS OF AMINOTHIOPHENE INTERMEDIATES

The aminothiophene intermediates were synthesized following methods reported in the literature [7], and as shown in the scheme below:



Scheme 1: Synthesis of Aminothiophene Intermediate

Aminothiophene Intermediate 1

O-Acetoacetotoluidide [20.15 g, 0.1 mol], malononitrile [6.96 g, 01 mol], and sulphur [3.37 g, 0.1 mol] in ethanol were stirred in the presence of morpholine [8.7 g, 0.1 mol] at 60-70 ºC for 3

hours. The resulting thick dark solution was cooled and stored overnight in a refrigerator, followed by filtration, washing with ethanol and then ethanol/water (1/1) solution and dried. The grey powder obtained was recrystallized from ethanol.

Aminothiophene Intermediate 2

Ortho-Acetoacetotoluidide [20.15 g, 0.1 mol], ethylcyanoacetate [11.96 g, 0.1 mol], and sulphur 3.37 g, 0.1 mol] were stirred under reflux in ethanol at 55-65 ºC for 2 hours using morpholine [8.7g, 0.1mol]. The resulting dark solution was cooled and stored overnight in a refrigerator, followed by filtration, washing with a small amount of ethanol and then ethanol/water mixture and dried. The white powder was recrystallized from ethanol.

Aminothiophene Intermediate 3

Morpholine [8.7g, 0.1 mol] was added to a stirred mixture of ortho-acetoacetotoluidide [20.15 gm, 0.1 mol], methylcyanoacetate [10.38 g, 0.1 mol], sulphur 3.37 gm, 0.1 mol] and ethanol [20 ml] and held at 70 ºC for 3 hours. The resulting solution was cooled by adding crushed ice and placing it in a refrigerator overnight, followed by filtration, washing with water and drying. The white was recrystallized from ethanol.

Aminothiophene Intermediate 4

4-Chloroacetoacetanilide [21.16g, 0.1mol], malononitrile [6.96 g, 0.1 mol], and sulphur [3.37 g, 0.1mol] in ethanol were stirred in the presence of morpholine [8.97 gm, 0.1 mol] at 60-70 ºC] for 3 hours. The resulting thick dark solution was cooled and stored overnight in a refrigerator, followed by filtration, washing with ethanol and then ethanol/water (1/1) solution and dried. The grey powder was recrystallized from ethanol.

Aminothiophene Intermediate 5

Exactly 4-chloroacetotoluidide [21.16 g, 0.1 mol], ethylcyanoacetate [11.96 g, 0.1 mol] and sulphur [3.39g, 0.1g] were refluxed in ethanol at 55-65 ºC for 2 hours using morpholine [9.0 g, 0.1mol]. The resulting dark solution was cooled and stored overnight in a refrigerator, followed by filtration, washing with a small amount of ethanol, and then ethanol water mixture (1/1) and dried. The white powder was recrystallized from ethanol.

Aminothiophene Intermediate 6

Morpholine [8.92 g, 0.1 mol] was added to a mixture of 4-chloroacetoacetanilide [21.16 g, 0.1 mol], methylcyanoacetate [10.38 g, 0.1 mol], and sulphur [3.36 g, 0.1 mol and ethanol [20 ml] at 50ºC. The mixture was stirred at 70 ºC for 3 hours. The resulting solution was cooled by adding crushed ice and placing it in a refrigerator overnight, followed by filtration, washing, washing and drying. The white product was recrystallized from ethanol.

Aminothiophene Intermediate 7

Ortho-acetoacetanisidide [20.72 g, 0.1mol], malononitrile [6.96 g, 0.1 mol], and sulphur [3.37 g, 0.1mol] in ethanol were stirred in the presence of morpholine [8.7 g, 0.1mol] at 60-70 ºC for 3 hours. The resulting thick dark solution was cooled and stored overnight in a refrigerator, followed by filtration, washing with ethanol and then ethanol/water solution and dried. The grey powder was recrystallized from ethanol.

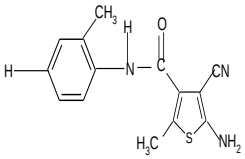
Aminothiophene Intermediate 8

Ortho-acetoacetanisidide [20.72 g, 0.1 mol], ethylcyanoacetate [11.96 g, 0.1 mol], and sulphur [3.36 g, 0.1 mol] were stirred under reflux in ethanol at 55-65 ºC for 2 hours using morpholine [8.7g, 0.1mol]. The resulting dark solution was cooled and stored overnight in a refrigerator, followed by filtration, washing with a small amount of ethanol and then ethanol/water mixture and dried. The white powder was recrystallized from ethanol.

Aminothiophene Intermediate 9

Morpholine [8.92 g, 0.1 mol] was added to a mixture of o-acetoacetanisidide [20.72 g, 0.1mol], methylcyanoacetate, [10.38 g, 0.1mol], sulphur [3.36 g, 0.1mol and ethanol [20 ml] at 50 ºC. The mixture was stirred at 70 ºC for 3 hours. The resulting solution was cooled down by adding crushed ice and placing it in a refrigerator overnight, followed by filtration, washing, washing and drying. A white product was obtained which was then recrystallized from ethanol.

STRUCTURES OF THE SYNTHESIZED INTERMEDIATES



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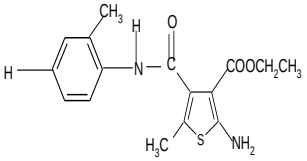

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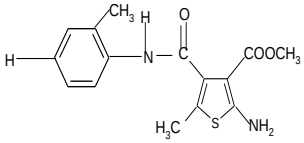

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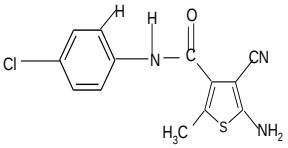

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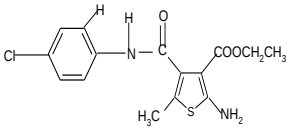

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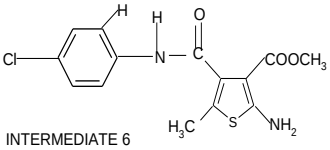

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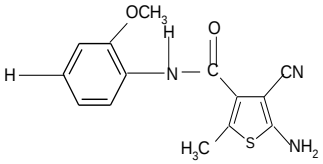

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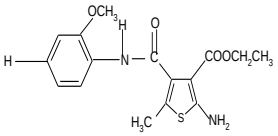

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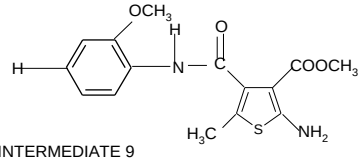


INTERMEDIATE 9

PROTON NMR DETERMINATION

^{1}H NMR spectra were recorded on a Mercury 300BB, in DMSO, using TMS as the internal standard and chemical shifts are given in δ (ppm), while coupling constants values were in Hz.

MASS SPECTRA DETERMINATIONS

Mass spectra were recorded on an Agilent Technologies 6460 mass spectrometer using the Electron Spray Ionization [ESI] technique. The data shows expected peaks at $[M+ H]^+$ and $[M + Na]^+$.

FT-IR DETERMINATIONS

FT-IR spectra were recorded on an Avatar OMNI-SAMPLER NEXUS 470 FT-IR spectrophotometer.

RESULTS AND DISCUSSION

The colour of the diazo compounds ranges from white to off-white, while intermediates 1, 4, and 7 with a cyano group gave a slightly brownish colour. The molecular mass of the intermediates is from 271-338, while the melting points were 128 ºC and 232 ºC for intermediates 9 and 4 respectively as shown in Table1 below.

Table 1: Molecular formula, molecular weight, melting point, yield (%), and appearance of aminothiophene intermediates 1-9

Intermediate	Molecular Formula	Molecular weight	Melt. Pt (ºC)	Yield %	Physical Appearance	R_f
1	$C_{14}H_{13}N_3OS$	271	220-222	49	Grey	0.45
2	$C_{16}H_{18}N_2O_3S$	318	132-133	56	White	0.56
3	$C_{15}H_{16}N_2O_3S$	304	128-129	14	Off-white	0.52
4	$C_{13}H_{10}ClN_3OS$	291	231-232	47	Light brown	0.48
5	$C_{15}H_{15}ClN_2O_3S$	338	161-162	34	White	0.62
6	$C_{14}H_{13}ClN_2O_3S$	324	165-167	58	White	0.55
7	$C_{14}H_{13}N_3O_2S$	287	204-206	55	Light brown	0.41
8	$C_{16}H_{18}N_2O_4S$	334	142-144	23	White	0.53
9	$C_{15}H_{16}N_2O_4S$	320	128-130	61	White	0.54

The yield of the intermediates can also be described as fair to poor. This is not surprising in view of the results from previous and similar works [4]. The R_f values of the aminothiophenes in Hexane: Ethyl acetate eluent (1:1) gave the results shown above. Intermediate 5 gave the highest value at 0.62 while intermediate 1 gave 0.45. The results are also in agreement with earlier work by Alaa and Tarek [8].

Table 2: Mass Spectra and Infra-Red Data (Cm^{-1}) of Aminothiophene Intermediates

	Mass m/z	**IR $v_{max}(cm^{-1})$**
INTERMEDIATE 1	272$(M+H)^+$, 294 $(M+Na)^+$	3365, 3325, 3217(NH), 2203 (CN), 1637 (CO)
INTERMEDIATE 2	319$(M+H)^+$, 341 $(M+Na)^+$	3396, 3263, 3152 (NH) 1648, 1626 (CO)
INTERMEDIATE 3	305$(M+H)^+$, 327 $(M+Na)^+$	3396, 3259, 3152 (NH) 1648, 1632 (CO)
INTERMEDIATE 4	292$(M+H)^+$, 314 $(M+Na)^+$	3365, 3309, 3198 (NH) 2204 (CN), 1642 (CO)
INTERMEDIATE 5	339$(M+H)^+$, 361 $(M+Na)^+$	3476, 3340, 3311 (NH) 1664, 1623 (CO)
INTERMEDIATE 6	325$(M+H)^+$, 347 $(M+Na)^+$	3376, 3342, 3312 (NH) 1665, 1624 (CO)
INTERMEDIATE 7	288$(M+H)^+$, 310 $(M+Na)^+$	3433, 3317, 3198 (NH) 2214 (CN), 1648 (CO)
INTERMEDIATE 8	335$(M+H)^+$, 357 $(M+Na)^+$	3465, 3429, 3337 (NH) 1661, 1641 (CO)
INTERMEDIATE 9	321$(M+H)^+$, 343 $(M+Na)^+$	3430, 3409, 3301 (NH) 1647, 1630 (CO)

The IR spectra of aminothiophene intermediates 1, 4, and 7 showed absorption peaks in the range 2203-2214 cm^{-1} due to the presence of cyano group. The amino group absorption for 1-9 appeared in the range of 3555-3260 cm^{-1} while the carbonyl absorption showed up in the range 1630-1664 cm^{-1}. The mass spectra data for the intermediates are presented in Table 2 and showed the relevant protonated peaks and the sodiated peaks i.e the $(M+H)^+$ and the $(M+Na)^+$. The peaks from intermediate 1 are observed at 272 and 294 corresponding to the $(M+H^+)$ and the $(M+Na^+)$. This is also the case for intermediates 2 and 3 where their peaks are shown at 319 and 341 and also at 305 and 327 respectively corresponding to the $(M+H^+)$ and the $(M+Na^+)$. The mass spectral data of aminothiophenes 4-9 are listed in Table 2 and followed the same patterns as for compounds 1-3 [8].

TABLE 3: ^{1}HNMR DATA OF THE AMINOTHIOPHENE INTERMEDIATES (DMSO) SOLVENT, TMS AS INTERNAL STD. δ (ppm) , J (HZ)

INTERMEDIATE 1: (DMSO, 300MHz) 2.19 (3H, s, CH_3); 2.39 (3H, s, CH_3); 7.11-7.36 (4H, m, ArCH); 7.731 (2H, br, s, NH_2); 9.07 (1H, s, NH)

INTERMEDIATE 2: (DMSO, 300MHz) 1.28 (3H, s, CH_3); 2.20 (3H, s, CH_3); 2.55 (3H, s, CH_3); 4.24 (2H, q, CH_2); 7.10-7.37 (4H, m, ArCH); 7.73 (2H, br. s, NH_2); 9.14 (1H, s, NH)

INTERMEDIATE 3: (DMSO, 300MHz) 2.19 (3H, s, CH_3); 2.54 (3H, s, CH_3); 3.74 (3H, s, CH_3); 7.10-7.55 (4H, m, ArCH); 7.74 (2H, b, s, NH_2); 9.14 (1H, s, NH)

INTERMEDIATE 4: (DMSO, 300MHz) 2.36 (3H, s, CH_3); 7.34 (2H, d , *J* = 8.7Hz, ArCH); 7.64 (2H, d, *J* = 9.0 Hz,); 7.79 (2H, br, s, NH_2); 9.70 (1H, s, NH).

INTERMEDIATE 5: (DMSO, 300MHz) 1.29 (3H, t, CH_3); 3.34 (3H, s, CH_3); 1.28 (3H, s, CH_3); 4.22 (2H, q, CH_2); 7.35 ((2H, d, *J* = 9Hz, ArCH); 7.64 ((2H, d, *J* = 9Hz, ArCH); 7.78 (2H, br, s, NH_2); 9.82 (1H, s, NH)

INTERMEDIATE 6: (DMSO, 300MHz) 2.48 (3H, s, CH_3); 3.76 (3H, s, CH_3); 7.36 (2H, d, *J* = 6.9Hz, ArCH); 7.64 (2H, d, *J* = 7.8Hz, ArCH); 7.78 (2H, br, s, NH_2) 9.81 (1H, s, NH).

INTERMEDIATE 7: (DMSO, 300MHz) 2.43 (3H, s, CH_3); 3.85 (3H, s, OCH_3,); 6.90-7.11 (3H, m, ArCH); 7.95 (1H, d, *J* = 9.3Hz, CH); 7.79 (2H, br, s, NH_2); 8.53 (1H, s, NH)

INTERMEDIATE 8: (DMSO, 300MHz) 1.27 (3H, t, CH_3); 2.59 (3H, s, CH_3); 3.86 (3H, s, OCH_3); 4.25 (2H, q, CH_2); 6.92 (1H, t, ArCH); 7.07, (2H, br, m, ArCH); 7.97 (1H, d, *J* = 7.8 ArCH); 7.80 (2H, br, s, NH_2); 8.54 (1H, s, NH)

INTERMEDIATE 9: (DMSO, 300MHz) 2.59 (3H, s, CH_3); 3.75 (3H, s, CH_3); 3.85 (3H, s, OCH_3); 6.94 (1H, ArCH); 7.01 (2H, br, m, ArCH); 7.96 (1H, d, *J* = 7.8, ArCH); 7.79 (2H, br, s, NH_2); 8.53 (1H, s, NH).
Abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m multiplet; br, broad.

The ^{1}H NMR spectrum of aminothiophene 1 showed singlets at 2.23 and 2.45 ppm due to the two methyl groups, one on the phenyl ring and the other attached to C-2 of the thiophene ring [9,10].The presence of a broad singlet at 7.75 ppm was attributed to the presence of NH_2group on the thiophene ring, while the NH group of the amide linkage is upfield shifted to 9.07 ppm, as compared to the starting o-acetoacetotoluidide that showed NH signal at 9.49 ppm. The formation of the thiophene intermediate 1 was evident by the disappearance of the CH_2 peak in the ^{1}H NMR of o-acetoacetotoluidide at 3.60 ppm (Table 3). As can be seen in Table 3, the

signals of the NH groups of aminothiophenes 1-9 shifted upfield as compared with their corresponding values for the starting materials (δ NH = 9.49, 10.21, 9.48, and 9.41 ppm for o-acetoacetotoluidide, 4-chloro-acetoacetanilide, and o-acetoacetanisidide). As an example, the NH group of 4-chloroacetoacetanilide appeared at 10.21 ppm is shifted to 9.68 ppm upon the formation of aminothiophene 4 [11, 12].

CONCLUSION

The Karl-Gewald chemistry has been used successfully in the synthesis of a number of 2-aminothiophenes [13]. The method offers an efficient and convenient approach to synthesis of aminothiophenes with short reaction times and fairly acceptable yield. The synthesized aminothiophenes are intended as precursors to a wide range of novel heterocyclic disperse dyes. Sabnis*et al* [4] have accomplished pioneering research on new dyestuffs from 2-aminothiophenes using the Gewald reaction [14]. Azo dyes derived from thiophene moiety have many advantages, such as a color deepening effect as an intrinsic property of the thiophene ring, small molecular structure leading to better dyeability and heterocyclic nature of the thiophene ring resulting in excellent sublimation fastness on the dyed fibers [15-17].

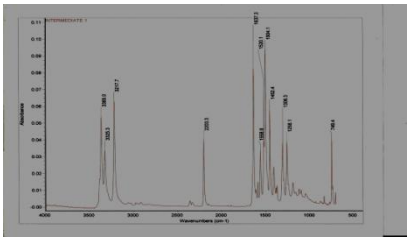
REFERENCES

1. Gronowitz, S. (1985). In Thiophene and its Derivatives, Part 1, S. Gronowitz,ed. John Wiley & Sons, New York, pp 1-213.
2. Norris, R. K. (1986). In Thiophene and its Derivatives, Part 2, S. Gronowitz, ed. John Wiley & Sons, New York, pp 631-799
3. Sabnis, R. W. (1994). The Gewald Synthesis, *Sulfur Rep*orts, **16 (**1), 1-17
4. Sabnis, R. W., Rangnekar, D. W., Sonawane, N. D. (1999), 2-Aminothiophenes by the Gewald Reaction. *J. Heterocycl. Chem.*, 36, 333-345.
5. Stacy, G. W. & Eck, D. L. (1967). 2-Aminothiophene. Heterocyclization of benzylthionitriles, *Tetrahedron Letters, 51, 5201-5204*
6. Stacy, G. W. & Eck, D L (1969). 2-Aminothiophene. Heterocyclization of benzylthionitriles. *J. Heterocyclic Chem., 6(2), 147-151*
7. Gewald, K. (1965). 2-Aminothiophenes: Chem Berlin. 98, 3571
8. Alaa, S. A. & Tarek, H.A. (2006). Novelazo disperse dyes derived from aminothiophenes*:* synthesis and UV-visible studies. *Dyes and Pigments, (70) 8-17.*

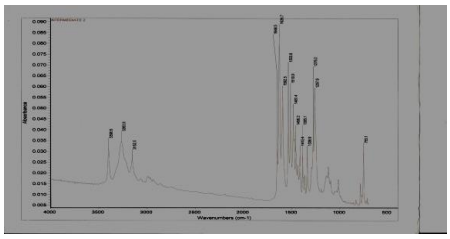
9. Hallas, G. & Towns, A.D. (1996a). A comparison of the properties of some 2-aminothiophene derived disperse dyes. *Dyes and Pigments 31 (4) 273-289.*
10. Hallas, G. & Towns, A.D. (1996b) Dyes derived from aminothiophenes. Part 1; synthesis of some heterocyclic disperse dyes using the Gewald reaction. *Dyes and Pigments 32 (3) 135-149.*
11. Jack, Jie Li (2005) *Name reactions in heterocyclic chemistry*. Hoboken NJ. Wiley InterScience. pp 180-285
12. Jae-Hong Choi, Sung-Hee Hong & Andrew D Towns, (1999). High fastness heterocyclicazo disperse dyes bearing ester functions. Coloration technology, 115(1), 32-37
13. Seferoglu, Z., Ertan, N., Tuncer, H. & Ertan, S. (2008). The synthesis, spectroscopic properties and crystal structure of novel bis-heterylazo disperse dyes. *Dyes and Pigments (77), 614-625*
14. Shuttleworth, L. & Weaver, M.A. (1990). Dyes for Polytester fibres In: *Chemistry and Application of Dyes*. Ed. Waring and Hallas. London. Plenum Press. Pp 130-149.
15. Hallas, G. & Towns A.D. (1997a). Dyes derived from aminothiophenes. Part 3: application of some disperse dyes derived from 2-aminothiophenes to hydrophobic fibres. *Dyes and Pigments (33), 215-228.*
16. Hallas, G. & Towns, A.D. (1997 b). Dyes derived from aminothiophenes. Part 4: Synthesis of some nitro-substituted thiophene-based azo disperse dyes. *Dyes and Pigments 33(4), 319-336*
17. Hallas, G. & Towns, A. D. (1997c). Dyes derived from aminothiophenes. Part 5: Properties of some Nitro-substituted Thiophene-based Azo Disperse Dyes. *Dyes and Pigments (34), 133*

INFRA-RED SPECTRA OF INTERMEDIATES 1-9

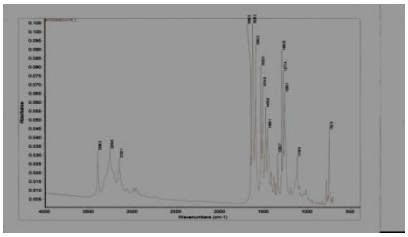
INTERMEDIATE 1



INTERMEDIATE 2



INTERMEDIATE 3



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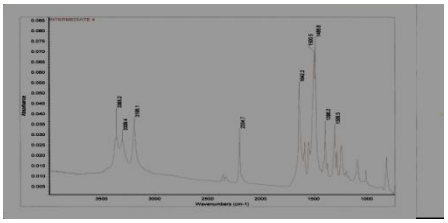

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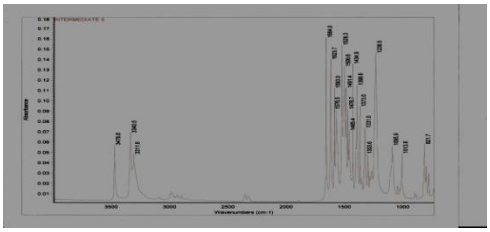

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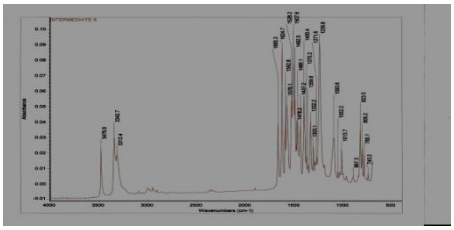

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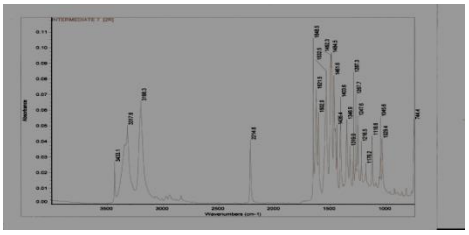

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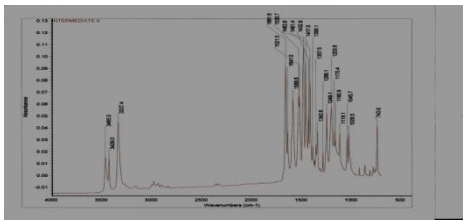
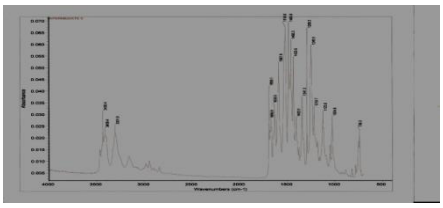
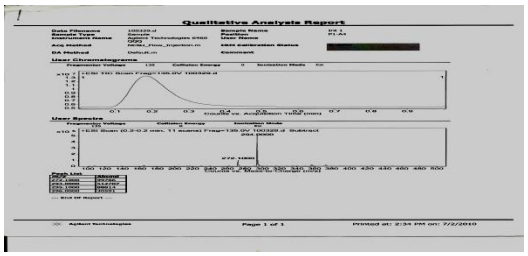


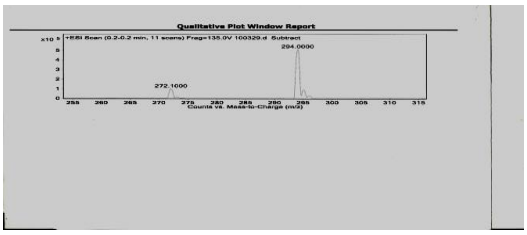
INTERMEDIATE 9



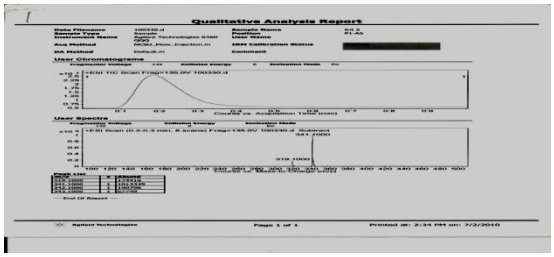
MASS- SPECTRA OF INTERMEDIATES 1-9

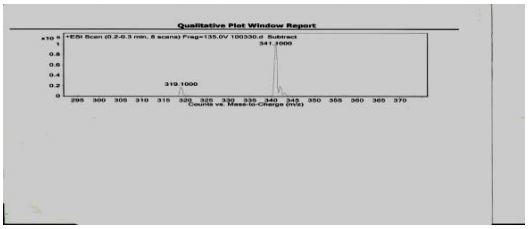
INTERMEDIATE 1



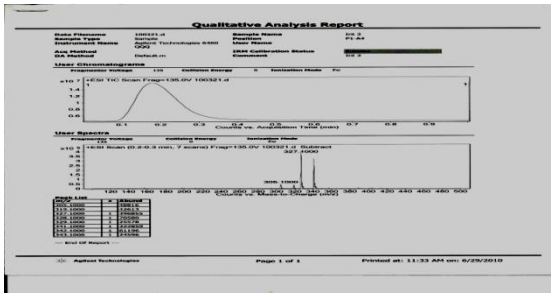


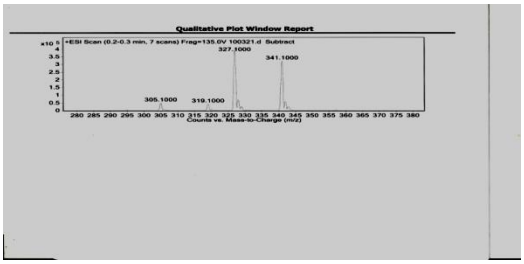
INTERMEDIATE 2





INTERMEDIATE 3





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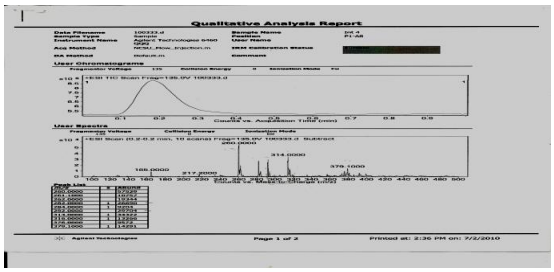
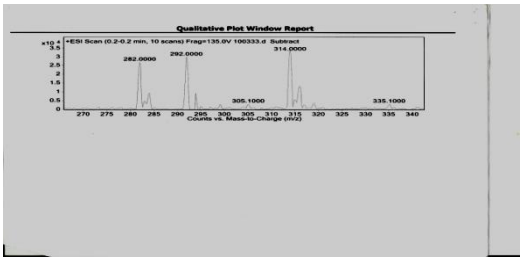
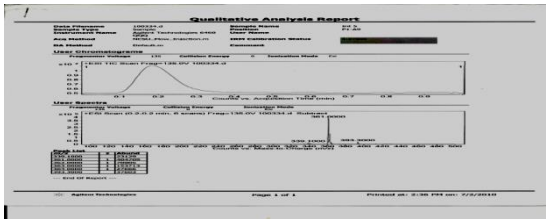
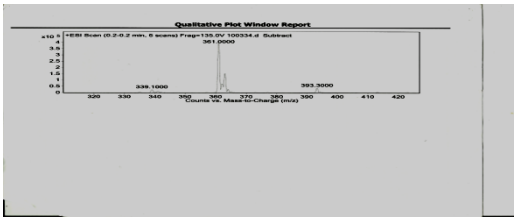


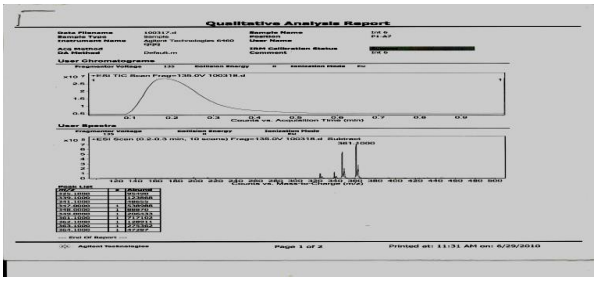


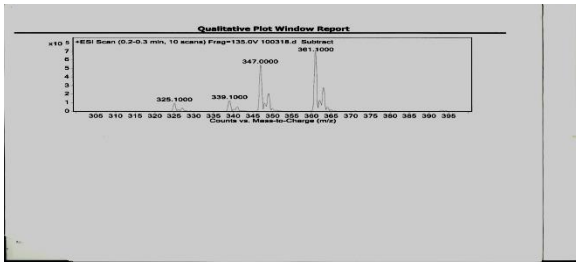
INTERMEDIATE 5





INTERMEDIATE 6





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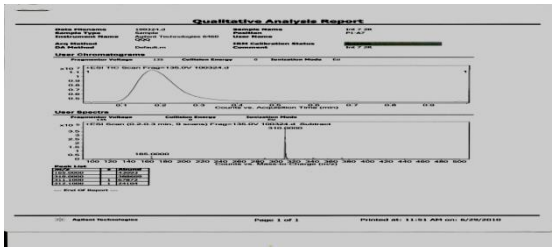
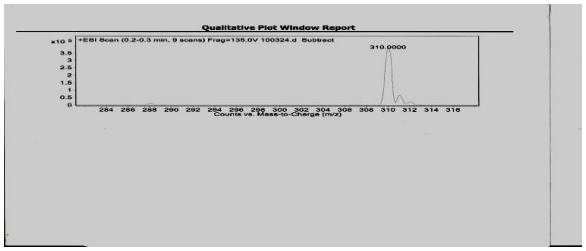
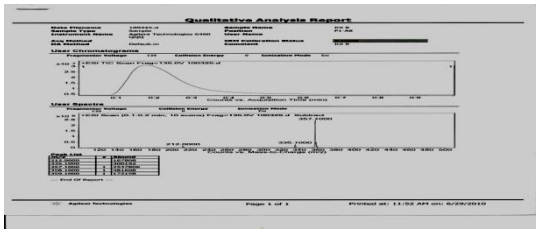
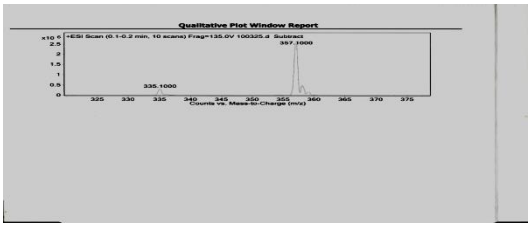


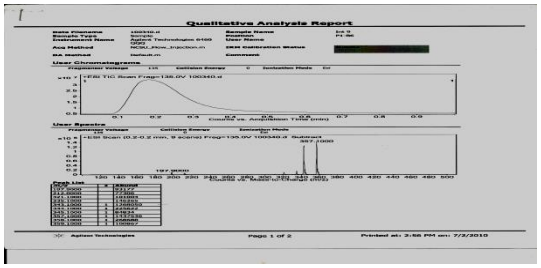


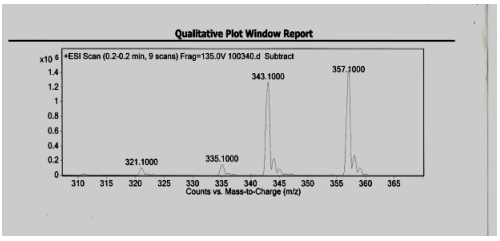
INTERMEDIATE 8





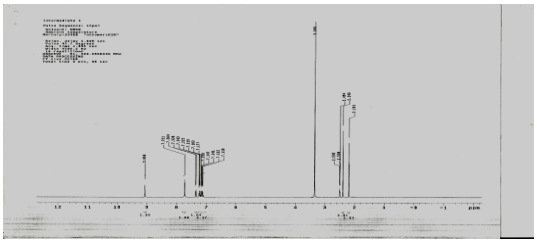
INTERMEDIATE 9



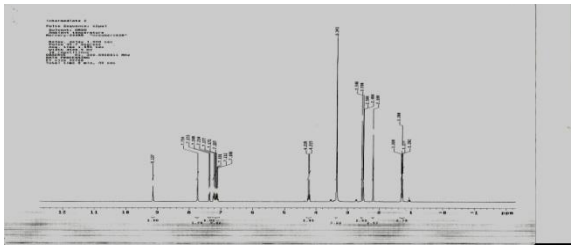


HNMR DATA OF INTERMEDIATES 1-9

INTERMEDIATE 1



INTERMEDIATE 2



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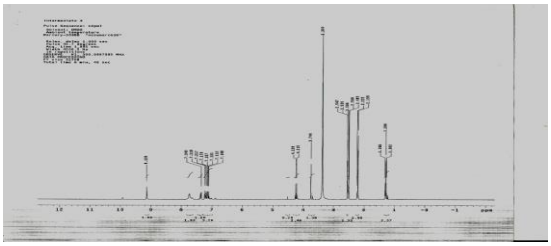
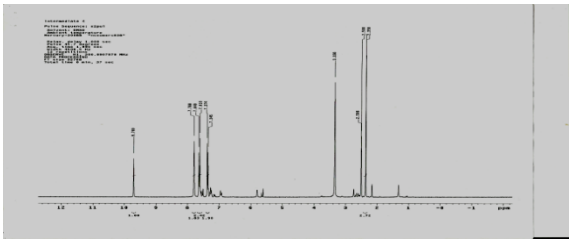


INTERMEDIATE 4



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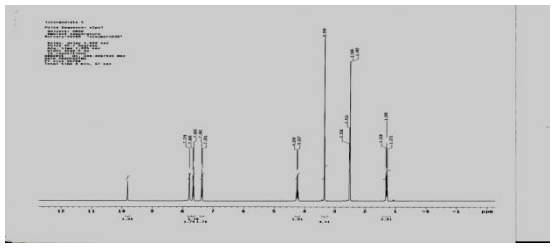

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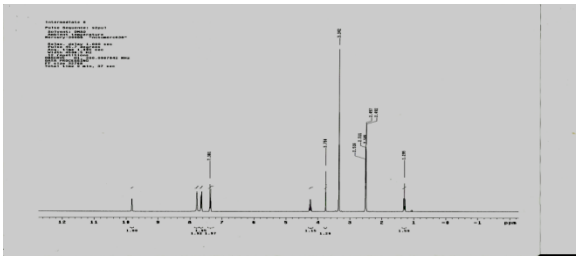

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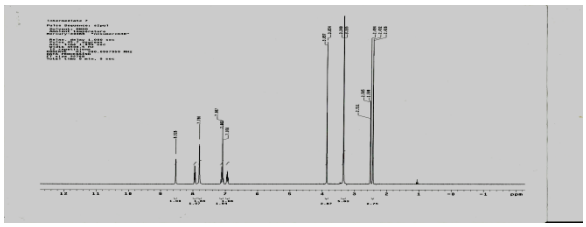

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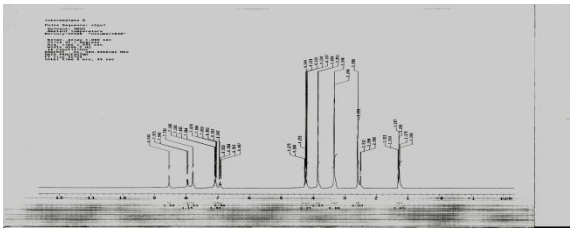

INTERMEDIATE 9