

SYNTHESIS AND REACTIONS OF 2-THIOPHENE-CARBOXYLIC ACID AZIDE

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ABSTRACT

2-Thiophenecarboxylic acid chloride reacted with sodium azide to give the corresponding 2-thiophenecarboxylic acid azide 1, which decomposed with water to give sym-N-N'-di-thienylurea 3. Reaction of 1 with aromatic amines proceeded either via Curtius rearrangement yielding the corresponding urea derivatives 4a-e or via azido-group displacement to give the corresponding Anilide derivatives 5a-e. The reaction of 5e with phenylisocyanate or phenylisothiocyanate gave the corresponding semicarbazide derivatives 6a,b. Cyclization of 6a,b through boiling with 2N NaOH afforded the triazole derivatives 7a,b, respectively.

INTRODUCTION

Phenylurea derivatives are known for their larvicidal activity and are found to be stable in soil and water¹⁻⁴. Semicarbazide derivatives have been reported to be antitubercular⁵, fungicides⁶, bactericides⁷. As an extension to previous investigations⁸⁻¹⁰, special attention was drawn to 2-thiophenecarboxylic acid azide and its reactions. to prepare a series of new urea derivatives containing thiophene moiety.

2-Thiophenecarboxylic acid azide **1** was prepared by reaction of 2-thiophene-carboxylic acid chloride with sodium azide. Acid azide **1** underwent hydrolysis on boiling with water to give sym-N-N'-di[2-thienyl] urea **3**, those infrared spectrum showed γ_{NH} at 3300-3270 cm^{-1} and $\gamma_{\text{C=O}}$ diarylurea¹¹ at 1640-1630 cm^{-1} .

¹H-NMR spectrum of **3** showed signals at $\delta = 6.5$ (t, 2H, C-4, C-4', protons of thiophene ring), 6.7-6.8 (m, 4H, C-3, C-5, C-3', C-5', thiophene protons), 9.7 (s, 2H, 2NH).

On boiling **1** with dry benzene for 2 h, the isocyanate **2** was formed. Treatment of **2** with aniline, p-touldine, p-anisidine, p-chloro-aniline or hydrazine hydrate gave the corresponding N,N'-aryl-thienyl-urea derivatives **4a-e**, respectively.

The infrared spectra of **4a-e** revealed γ_{NH} at 3300-3260 cm^{-1} , $\gamma_{\text{C=O}}$ in diarylureas¹¹ at 1650-1630 cm^{-1} .

¹H-NMR spectrum of **4b** showed $\delta = 2.3$ (s, 3H, CH₃), 6.5 (t, 1H, C-4, thiophene proton), 6.7-7.1 (m, 4H, aromatic protons), 7.3-7.5 (m, 2H, C-3, C-5, thiophene protons), 8.2 (s, 1H, NH) and 9.5 (s, 1H, NH).

¹H-NMR of **4c** showed signals at $\delta = 3.7$ (s, 3H, OCH₃), 6.5 (t, 1H, C-4), 6.7-6.9 (m, 4H, aromatic protons), 7.4-7.6 (m, 2H, C-3, C-5), 8.5 (s, 1H, NH) and 9.5 (s, 1H, NH).

Synthesis and reactions of.....

¹H-NMR of **4d** showed signals at $\delta = 6.6$ (t, 1H, C-4), 6.7-6.9 (m, 2H, C-3, C-5), 7.2-7.5 (m, 4H, aromatic), 8.8 (s, 1H, NH) and 9.6 (s, 1H, NH).

The base catalyzed decomposition of **1** with aromatic amines namely aniline, p-toluidine, p-anisidine, p-chloroaniline and hydrazine hydrate afforded the corresponding anilides **5a-c** and the thienoyl hydrazide **5e**. The structure of **5a-e** was established by comparison with authentic samples prepared via reaction of 2 thiophenecarboxylic acid chloride with the above mentioned amino compounds.

The infrared spectra of **5a-e** showed γ_{NH} at 3340-3300 cm^{-1} and $\gamma_{\text{C=O}}$ at 1640-1630 cm^{-1} . The acid hydrazide **5e** reacted with phenylisocyanate and phenylisothiocyanate to give the semicarbazide derivatives **6a,b** which cyclized to corresponding triazoles¹² **7a,b** through boiling with 2N NaOH.

I.R spectrum of compound **6a** showed γ_{NH} at 3300-3270 cm^{-1} and $\gamma - \overset{\text{O}}{\parallel}{\text{C}} - \text{NH}$ at 1680-1670 cm^{-1} .

I.R spectrum of **6b** showed γ_{NH} at 3300-3270 cm^{-1} and $\gamma_{\text{C=S}}$ at 1500-1480 cm^{-1} .

I.R spectrum of compound **7a** showed γ_{NH} at 3200-2850 cm^{-1} and $\gamma_{\text{C=O}}$ at 1650-1620 cm^{-1} , while I.R spectrum of **7b** showed $\gamma_{\text{C=S}}$ at 1460-1440 cm^{-1} , and $\gamma_{\text{C=N}}$ at 1510 cm^{-1} , and γ_{NH} at 3300-3230 cm^{-1} .

¹H-NMR of **7b** showed signals at $\delta = 6.3$ (t, 1H, C-4, thiophene proton), 7.2-7.3 (m, C-3, C-5, thiophene protons) and 7.4-7.6 (m, 5H aromatic protons).

Table 1 Characterization Data of the Synthesized Compounds

Comp. No.	Mol. Formula	m.p. °C	Yield %	Analysis Calc./Found			
				C%	H%	N%	S%
3	C ₉ H ₈ N ₂ OS ₂ (224.3)	215-17	55	48.1	3.5	12.4	
				47.8	3.3	11.9	
4a	C ₁₁ H ₁₁ N ₂ OS (219.2)	218-20	74	60.2	5.05		
				60.1	4.9		
b	C ₁₂ H ₁₂ N ₂ OS (232.3)	196-8	73	62.04	5.2	12.05	13.8
				62.4	5.1	11.7	13.5
c	C ₁₂ H ₁₂ N ₂ O ₂ S (247.2)	182-3	70	58.3	4.8	11.3	
				57.8	4.6	10.8	
d	C ₁₁ H ₉ ClN ₂ OS (252.7)	220-2	72	52.2	3.5		
				53.0	3.3		
e	C ₅ H ₇ N ₃ OS (157.1)	232-5	60	38.2	4.4		
				37.6	4.1		
5a	C ₁₁ H ₉ NOS (203.2)	123-5	73	65.02	4.4	6.8	
				65.0	4.3	6.5	
b	C ₁₂ H ₁₁ NOS (217.2)	155-7	65	66.3	5.10		14.7
				65.8	5.2		14.3
c	C ₁₂ H ₁₁ NO ₂ S (233.2)	135-7	68	61.8	4.7		
				61.2	4.6		
d	C ₁₁ H ₈ ClNOS (237.7)	158-60	75	55.5	3.3		13.4
				55.1	3.1		13.1
c	C ₅ H ₆ N ₂ OS (142.1)	225-7	78	42.2	4.2		
				41.9	3.9		
6a	C ₁₂ H ₁₁ N ₃ O ₂ S (261.3)	218-20	85	55.1	4.2		
				54.8	3.8		
b	C ₁₂ H ₁₁ N ₃ OS ₂ (277.3)	180-20	87	51.9	3.9	15.1	
				51.3	3.3	14.6	
7a	C ₁₂ H ₉ N ₃ OS (243.2)	>300	42	59.2	3.7		
				58.4	3.6		
b	C ₁₂ H ₉ N ₃ S ₂ (259.3)	148-50	35	55.5	3.4		
				55.1	3.1		

EXPERIMENTAL

All melting points are uncorrected. The IR-spectra were measured on Perkin-Elmer spectrophotometer 297 using KBr water technique, analysis, $^1\text{H-NMR}$ and mass spectra were carried out by the Micro-Analytical Unit, Cairo University.

2-Thiophenecarboxylic acid azide 1

To a cold solution of 2-thiophenecarboxylic acid chloride in acetone (50 ml), sodium azide (0.015 mol), in the least amount of water, was added under stirring. The stirring was continued for half an hour. The reaction mixture was poured onto ice cold water. The obtained oil was extracted with benzene (50 ml). The extract was dried with anhydrous calcium chloride. The acid azide 1 extract was used directly for the following reactions.

Sym. $\text{N,N}'$ -di[2-thienyl] urea 3

The acid azide extract was treated with water (2 ml). The mixture was refluxed for one hour. After concentration, the solid formed was filtered off and recrystallized from methanol (Table 1).

Reaction of aromatic amines with isocyanat 2: Formation of urea derivatives 4a-e

The acid azide extract was boiled for two hours. To the boiled solution, the requisite amine (0.01 mol) was added. The solution was stirred at room temperature for 4 hrs. The solid product formed was filtered off and recrystallized from ethanol (Table 1).

Reaction of acid azide 1 with aromatic amines: Formation of anilides 5a-e

- a) A mixture of the acid azide extract **1**, and the requisite amines (0.01 mol) was boiled under reflux for 2 hrs. The solution was concentrated and the solid formed was filtered off and recrystallized from methanol (Table 1).
- b) To a solution of 2-thiophenecarboxylic acid chloride in benzene (30 ml), the appropriate amine (0.01 mol) and pyridine (2 ml) were added. The solution was refluxed for 2 hrs. After concentration and cooling the product was filtered off, washed with diluted HCl and crystallized from methanol to give **5a-e** [M.ps. undepressed when admixed with samples prepared by the method a].

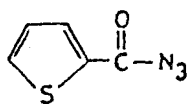
Reaction of 5e with phenylisocyanate and phenylisothiocyanate: Formation of semicarbazide derivatives 6a,b

To a solution of **5e** (0.01 mol) in 30 ml of absolute ethanol, the appropriate isocyanate (2 ml) was added dropwise. The reaction mixture was refluxed for 2 hrs. After cooling, the solid obtained was filtered off and recrystallized from ethanol (Table 1).

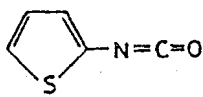
Formation of Triazoles 7a,b

A suspension of the semicarbazides **6a,b** (0.01 mol) in 15 ml 2N NaOH was refluxed for 6 hrs. The reaction mixture was cooled and then neutralized with dilute acetic acid. The solid formed was filtered off, washed with water and recrystallized from ethanol (Table 1).

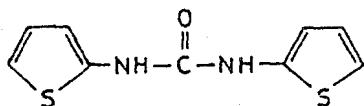
Synthesis and reactions of



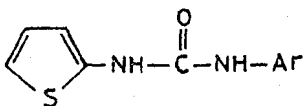
1



2

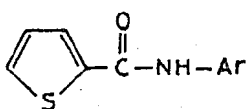


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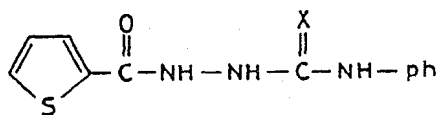


4

4,5	
a,	C ₆ H ₅ -
b,	C ₆ H ₄ ·CH ₃ (p-)
c,	C ₆ H ₄ ·OCH ₃ (p-)
d,	C ₆ H ₄ Cl (p-)
e,	NH ₂

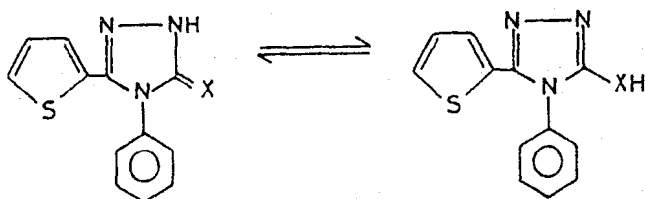


5



6

- a, X = O
b, X = S



7

Scheme (1)

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Synthesis and reactions of

تخليق وتفاعلات أزيد-٢-ثيوفين حمض الكربوكسيل

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ملخص البحث :

تم تحضير أزيد-٢-ثيوفين حمض الكربوكسيل بتفاعل كلوريد الحمض المقابل في محلول مائي من أزيد الصوديوم في الأسيتون . وعند غليان محلول الأزيد في البنزين مع قطرات من الماء يعطى ن-ثنائي ثينيل-يوريا - أيضا عند غليانه في البنزين الجاف لمدة ساعتان يتكون الأيزوسيانات المقابلة والتي تتفاعل مع مشتقات الأمينات مثل الأنلين ، بارا-تولودين ، بارا-أنزدين ، بارا-كلوروانلين والهيدرازين ليكون مشتقات اليوريا المقابلة . بتفاعل أزيد الحمض مع نفس الأمينات الأروماتية بتكون مشتقات الأنيليدات المقابلة والتي أمكن تحضيرها بتفاعل كلوريد الحمض المقابل مع الأمينات السابقة . عند تفاعل هيدرازين حمض الثيوفين مع فنييل أيزوسيانات وفينيل أيزوثيوسيانات ليكون مشتقات السيمكربازيدات المقابلة والتي تتحولق بغليانها مع محلول مائي من أيدركسيد الصوديوم وتكون مشتقات التريازول .

وقد تم إثبات التركيب الكيميائي بالتحليل الدقيق ، طيف الأشعة تحت الحمراء الرنين النووي المغناطيسي .