

SYNTHESIS AND CHARACTERIZATION A NEW THIADIAZEPINE COMPOUNDS FROM NEW BIS(4-AMINO-3-MERCPTO-1,2,4-TRIAZOL) DERIVATIVES

Atyaf A.Q. Younus^{1*} and Nasreen R. Jber²

¹Department of Chemistry, College of Education for pure Science, University of Al-Anbar, Ramadi, Iraq.

²Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, Iraq.

ABSTRACT

Synthesis of [1,2,4] triazolo [3,4-b] [1,3,4]thiadiazepines (T)₁₋₁₈ is described from new synthesis compounds containing amino group in (4) position of 4-Amino-3-mercpto-1,2,4-triazol and substituted chalcones (C)₁₋₁₅ in ethanol by reflux for 3-4 hrs. Characterization of the new compounds was established by FTIR, and some of them were characterized using ¹HNMR and Mass spectral data.

INTRODUCTION

1,2,4-Triazole system is an important starting material in the synthesis of biologically active heterocycles, which constitute an important class of organic compounds with diverse biological activities, including antiparasitic, analgesic, antibacterial and anti-inflammatory activities¹⁻³.

Thiadiazepines are not only known for their potent antimicrobial activities⁴ but they are also excellent charge generating agents⁵. They also act as intermediate for preparation of substituted caprolactams

Useful for treatment of HIV disease.

In this paper we describe the synthesis and structural characterization of a new series of Bis(3,4-b) 1,3,4-thiadiazepines. 4-amino-3-mercpto-1,2,4-triazole and chalcone derivatives were prepared as per the literature procedure.

Experimental

Succinic dihydrazide Preparation

Dimethyl succinate (5ml) in 25ml of ethanol was taken in round bottom flask. To that hydrazine hydrate (6ml) was added and refluxed for (4 hours). The solution was cooled in ice⁶. The solid crystals was precipitated out and recrystallized with ethanol to give compound [89%], yield, m.p.= 170-172°C.

Terephthalicdihydrazide Preparation

Dimethyl terephthalate (5g, mol) solved in (50 ml of ethanol absolute) was taken in round bottom flask. To that hydrazine hydrate (2ml) was added and refluxed for (4 hours). The solution was cooled in ice⁶. The solid crystals was precipitated out and recrystallized with ethanol to give compound [90%], yield 88%, mp.=132-135°C.

Succinic dihydrazide[Bis(potassium dithiocarbazinate)] Preparation

To a solution of potassium hydroxide (2.24g) in ethanol absolute (150ml), succinic dihydrazide (2.92g, 0.02mol) and carbon disulfide (3ml) were added as a drops and the mixture was stirred in ice bath (0-6 °c)⁶. The yellow solid was precipitated out and the potassium salt obtained in quantitative yield was directly used without purification.

Terephthalicdihydrazid[Bis(potassium dithiocarbazinate)] Preparation

To a solution of potassium hydroxide (1.75g) in ethanol absolute (150ml), terephthalicdihydrazide (3g, mol) and carbon disulfide (3ml) were added as a drops and the mixture was stirred in ice bath (0-6 °c)⁶. The yellow solid was precipitated out and recrystallized with ethanol to give compound [88%], yield 84%, mp.=320-321°C.

Bis[(3,3'-thio-4,4'-amino-1,2,4-triazole)-5-yl]ethane Preparation

Suspension of potassium salt was direct used because it was non stable, hydrazine hydrate (2 ml) and water (80 ml) was refluxed for 4 hrs. the color of the reaction mixture changed to green, hydrogen sulfide was evolved and a homogenous solution resulted. A white solid was precipitated by dilution with cold water (100 ml) and acidification with concentrated hydrochloric acid⁶. The product was filtered, washed with cold water (2×30 ml) and recrystallized from ethanol, compound [72%] yield 62%, mp.= 220-222°C.

Bis[(3,3'-thio-4,4'-amino-1,2,4-triazole)-5-yl]phenyl Preparation

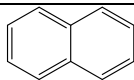
A suspension of potassium salt of terephthalicdihydrazide (2g, mol), hydrazine hydrate (2 ml, 0.04 mol) and water (100 ml) was refluxed for (3 hrs). the color of

the reaction mixture changed to light green, hydrogen sulfide was evolved and a homogenous solution resulted A solid was precipitated by dilution with cold water (100 ml) and acidification with concentrated hydrochloric acid⁶. The product was filtered, washed with cold water (2×30 ml) and recrystallized form ethanol.

General procedure for preparation of substituted benzylideneacetophenone(C)₁₋₁₅

To asolution of substituted aldehyde (0.01 mol) in ethanol (25 ml), a solution of NaOH (6 ml, 40%) was added. The reaction mixture was stirred at room temperature for (4 hr), diluted with water (100 ml) and acidified with dil. HCl. The product obtained was filtered, washed with water, and recrystallized form ethanol⁷.

Table 1: Physical properties of compounds (C)₁₋₁₅

Comp.No	X	Z	Molecular Formula	Molecular Weight	Solvent	Yield %	Color	mp.°C
C ₁	<i>P</i> -NH ₂	<i>P</i> -NO ₂	C ₁₅ H ₁₂ N ₂ O ₃	268	Ethanol absolute	85%	Orange	154-157
C ₂	<i>P</i> -OH	<i>P</i> -NO ₂	C ₁₅ H ₁₁ NO ₄	269	Ethanol absolute	77%	Dark Orange	107-110
C ₃	<i>P</i> -NH ₂	<i>P</i> -Br	C ₁₅ H ₁₂ NOBr	301.9	Ethanol absolute	73%	Yellow	175-178
C ₄	<i>P</i> -NH ₂	<i>m</i> -NO ₂	C ₁₅ H ₁₂ N ₂ O ₃	268	Ethanol absolute	69%	Orange	157-160
C ₅	<i>P</i> -NH ₂	<i>P</i> -CH ₃	C ₁₆ H ₁₅ NO	237	Ethanol absolute	72%	Yellow	118-120
C ₆	<i>P</i> -NH ₂	<i>P</i> -OCH ₃	C ₁₆ H ₁₅ NO ₂	253	Ethanol absolute	66%	Orange	121-123
C ₇	<i>P</i> -NH ₂	<i>P</i> -Cl	C ₁₅ H ₁₂ NOCl	257.5	Ethanol absolute	74%	Yellow	218-220
C ₈	<i>P</i> -NH ₂		C ₁₉ H ₁₅ NO	273	Ethanol absolute	82%	Yellow	148-150
C ₉	<i>P</i> -NH ₂	<i>P</i> -N-(CH ₃) ₂	C ₁₇ H ₁₈ N ₂ O	266	Ethanol absolute	62%	Orange	98-100
C ₁₀	<i>P</i> -NH ₂	<i>o</i> -NH ₂	C ₁₅ H ₁₅ N ₂ O	239	Ethanol absolute	70%	Brown	Over 300
C ₁₁	<i>P</i> -NH ₂	1,3-(OCH ₃) ₂	C ₁₇ H ₁₇ NO ₃	283	Ethanol absolute	67%	Yellow	100-103
C ₁₂	1,3-(OCH ₃) ₂	<i>P</i> -NO ₂	C ₁₇ H ₁₅ NO ₅	313	Ethanol absolute	77%	Orange	220-222
C ₁₃	1,3-(OCH ₃) ₂	<i>P</i> -Br	C ₁₇ H ₁₅ O ₃ Br	346.9	Ethanol absolute	82%	Pale yellow	117-120
C ₁₄	1,3-(OCH ₃) ₂	<i>P</i> -Cl	C ₁₇ H ₁₅ O ₃ Cl	302.5	Ethanol absolute	86%	Pale yellow	135-138
C ₁₅	1,3-(OCH ₃) ₂	<i>p</i> -N-(CH ₃) ₂	C ₁₉ H ₂₁ NO ₃	311	Ethanol absolute	73%	Orange	88-90

General procedure for preparation of substituted [1,2,4] triazolo [3,4-b][1,3,4] thiadiazepine

Amixture of triazole (0.001 mol) and the corresponding chalcones (0.002 mol) in

ethanol absolute (30 ml) was refluxed for (4 hr). reaction mixture on cooling was diluted with (500 ml) water and stile to night. The color solid was filtered and purified by recrystallization form (ethanol-water)⁸.

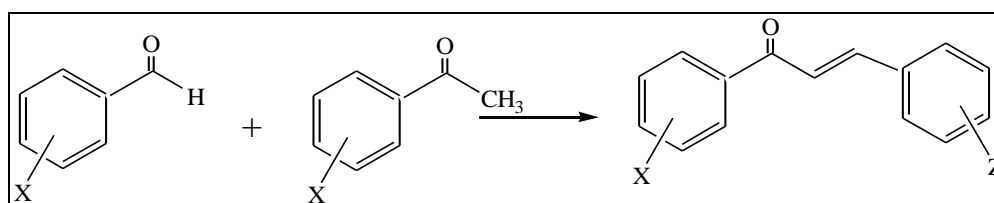
Table 2: Physical properties of compounds (T)₁₋₁₈

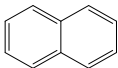
Comp No.	G	With C _n	Molecular formula	Molecular Weight	Solvent	Yield %	Color	mp.
T ₁	-Ph-	C ₂	C ₄₀ H ₂₄ N ₁₀ O ₆ S ₂	804	Ethanol absolute	69%	White	+340
T ₂	-Ph-	C ₃	C ₄₀ H ₂₆ N ₁₀ S ₂ Br ₂	869.8	Ethanol absolute	78%	Pale yellow	145-147
T ₃	-Ph-	C ₄	C ₄₀ H ₂₄ N ₁₂ O ₄ S ₂	800	Ethanol absolute	77%	Light brown	+340
T ₄	-Ph-	C ₅	C ₄₂ H ₃₂ N ₁₀ S ₂	740	Ethanol absolute	62%	White	+340
T ₅	-Ph-	C ₈	C ₄₈ H ₃₂ N ₁₀ S ₂	812	Ethanol absolute	55%	Red	130-133
T ₆	-Ph-	C ₉	C ₄₄ H ₃₈ N ₁₂ S ₂	798	Ethanol absolute	66%	Red	120-123
T ₇	-Ph-	C ₁₁	C ₄₄ H ₃₆ N ₁₀ O ₄ S ₂	832	Ethanol absolute	62%	Dark red	102-104
T ₈	-Ph-	C ₁₂	C ₄₄ H ₃₂ N ₁₀ O ₆ S ₂	892	Ethanol absolute	71%	Orange	148-150
T ₉	-Ph-	C ₁₅	C ₄₈ H ₄₄ N ₁₀ O ₄ S ₂	888	Ethanol absolute	68%	Dark brown	124-126
T ₁₀	-CH ₂ .CH ₂ -	C ₁	C ₃₆ H ₂₆ N ₁₂ O ₄ S ₂	754	Ethanol absolute	75%	Orange	198-221
T ₁₁	-CH ₂ .CH ₂ -	C ₃	C ₃₆ H ₂₆ N ₁₀ S ₂ Br ₂	821.8	Ethanol absolute	78%	White	174-176
T ₁₂	-CH ₂ .CH ₂ -	C ₇	C ₃₆ H ₂₆ N ₁₀ S ₂ Cl ₂	733	Ethanol absolute	71%	Light yellow	152-154
T ₁₃	-CH ₂ .CH ₂ -	C ₉	C ₄₀ H ₃₈ N ₁₂ S ₂	750	Ethanol absolute	68%	Brown	160-164
T ₁₄	-CH ₂ .CH ₂ -	C ₁₁	C ₄₀ H ₃₆ N ₁₀ O ₄ S ₂	784	Ethanol absolute	74%	Red	181-182
T ₁₅	-CH ₂ .CH ₂ -	C ₁₂	C ₄₀ H ₃₂ N ₁₀ O ₆ S ₂	844	Ethanol absolute	76%	Yellow	201-203
T ₁₆	-CH ₂ .CH ₂ -	C ₁₃	C ₄₀ H ₃₂ N ₈ O ₄ S ₂ Br ₂	911.8	Ethanol absolute	82%	White	214-216
T ₁₇	-CH ₂ .CH ₂ -	C ₁₄	C ₄₀ H ₃₂ N ₈ O ₄ S ₂ Cl ₂	823	Ethanol absolute	78%	White	222-225
T ₁₈	-CH ₂ .CH ₂ -	C ₁₅	C ₄₄ H ₄₄ N ₁₀ O ₄ S ₂	840	Ethanol absolute	71%	Green	90-92

RESULTS AND DISCUSSION

Synthesis of 4,4'-benzylideneacetophenone(C)₁₋₁₅

The title compound was prepared according to the following:

(C)₁₋₁₅

Z = *P*-NO₂, *P*-Br, *m*-NO₂, *P*-CH₃, *P*-OCH₃, *P*-Cl, , *P*-N(CH₃)₂,
o-NH₂, 1,3-(OCH₃)₂. X = *P*-NH₂, *P*-OH, 1,3-(OCH₃)₂.

Compounds (C)₁₋₁₅ were synthesized by the reaction of aromatic substituted benzaldehyde with substituted acetophenone to achieve calcones (C)₁₋₁₅.

The structures of all products were identified by using FT-IR and ¹H-NMR for some of

them. The purities of compounds were confirmed by using an elemental analysis. The elemental analysis of compounds (C)₁₋₈ are listed in Table (3). The observed values are in well agreement with theoretical values indicating structure of respective compounds.

Table 3: Elemental Analysis (CHNS-O) for compounds (C)₁₋₈

Comp. No.	Formula	%C		%H		%N	
		Calc.	Found	Calc.	Found	Calc.	Found
C ₁	C ₁₅ H ₁₂ N ₂ O ₃	67.16	67.35	4.47	5.16	10.44	9.80
C ₂	C ₁₅ H ₁₁ NO ₄	66.91	69.34	4.08	4.12	5.20	4.97
C ₃	C ₁₅ H ₁₂ NOBr	59.62	59.34	3.97	4.04	4.63	4.85
C ₄	C ₁₅ H ₁₂ N ₂ O ₃	67.16	66.82	4.47	4.30	10.44	11.01
C ₅	C ₁₆ H ₁₅ NO	81.01	81.63	6.32	7.31	5.90	5.84
C ₆	C ₁₆ H ₁₅ NO ₂	75.88	76.48	5.92	6.05	5.53	5.83
C ₇	C ₁₅ H ₁₂ NOCl	69.90	69.77	4.66	3.94	5.43	5.18
C ₈	C ₁₉ H ₁₅ NO	83.51	82.30	5.49	5.88	5.12	4.98

The spectroscopic observation of (C)₉ is given: FT-IR (KBr, cm⁻¹) figure (1): show the appearance of bands at 3413, 3334, 3143, 2975, 2891, 1682, 1631 and 847 which could be assigned to asymmetrical and symmetrical

stretching of amino group, ν C – H of ethylene group⁽⁹⁾, ν C –H aliphatic, ν (C = O), ν C = C and out of plane bending of *para*- disubstituted benzene ring.

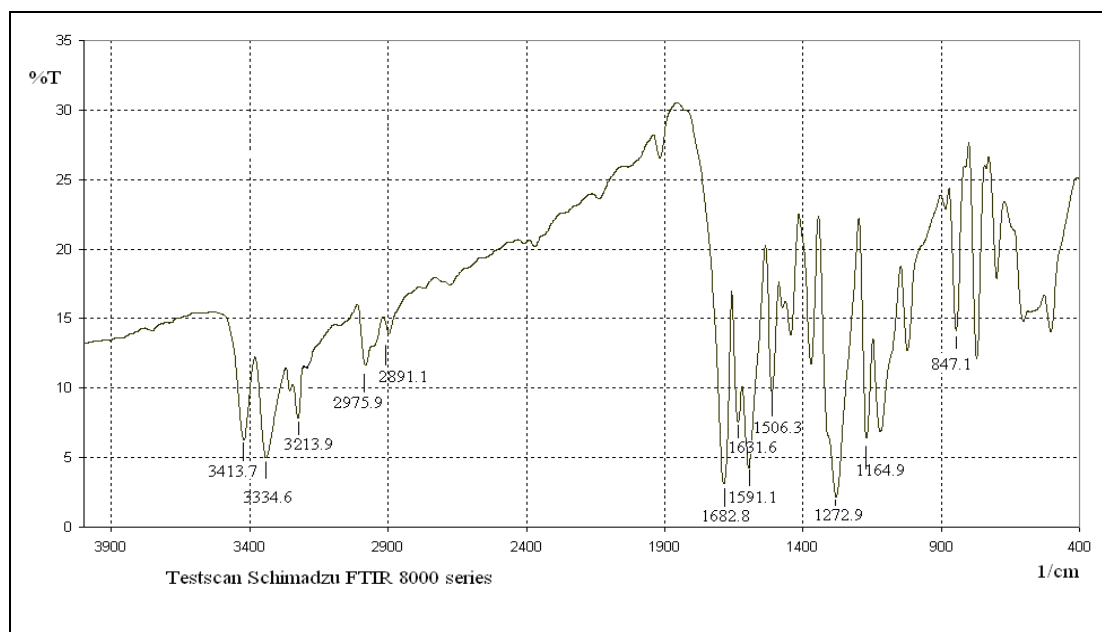


Fig. 1: FTIR spectrum of 4-N,N-dimethylaminobenzylidene-4'-aminoacetophenone(C)₉, ¹HNMR (DMSO-d₆), δ in ppm) figure (2) compound (C)₇: 6.9-8.1 (d-d, 8H, arom. H), 6.5 (s, 2H, CH = CH), 4.5 (s, 2 H, NH₂). Table (4) shows the FT-IR absorption bands for synthesizes compounds.

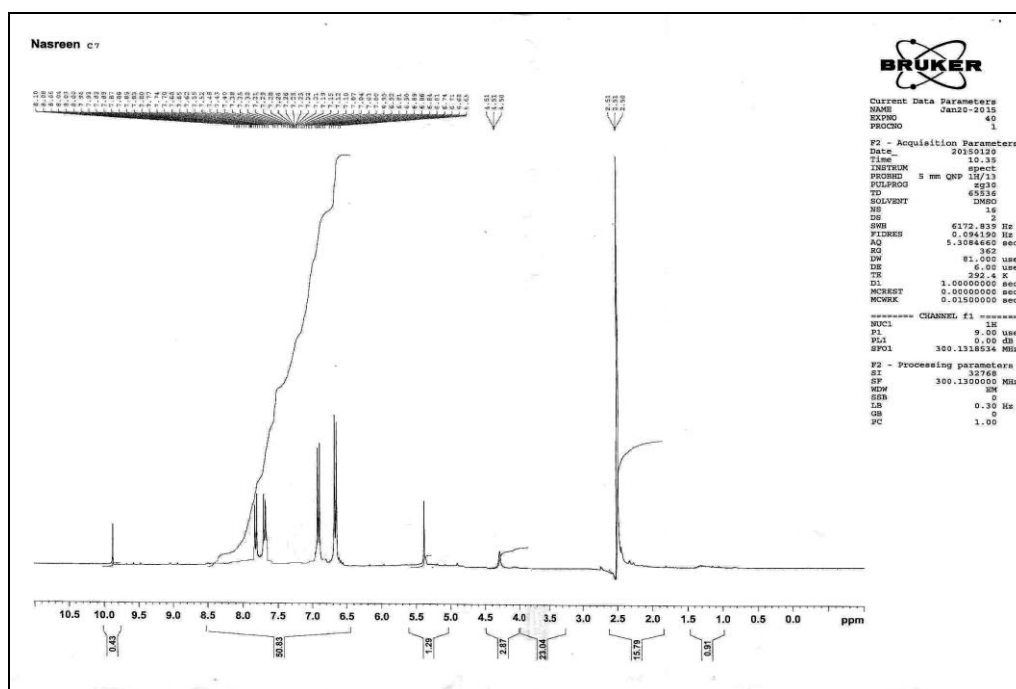
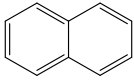


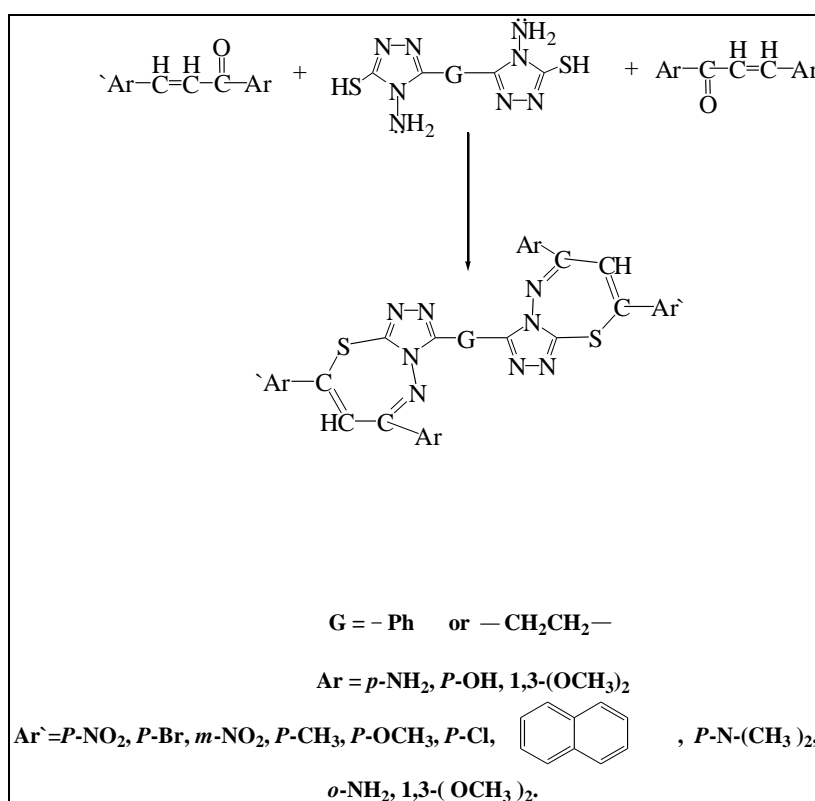
Fig. 2: ¹HNMR spectrum of 4-chlorobenzylidene-4'-aminoacetophenone(C)₇

Table 4: Characteristic FTIR absorption bands of synthesized compounds (S)₁₋₁₀

Comp. No.	X	Z	ν C = CH	ν C = O	ν C = C	γ para-Sub.	Other
C ₁	<i>P</i> -NH ₂	<i>P</i> -NO ₂	3107	1637	1589	825	3483, 3384 (ν NH ₂)
C ₂	<i>P</i> -OH	<i>P</i> -NO ₂	3207	1647	1591	834	3302 (ν O-H)
C ₃	<i>P</i> -NH ₂	<i>P</i> -Br	3198	1652	1600	841	3454, 3313 (ν NH ₂)
C ₄	<i>P</i> -NH ₂	<i>m</i> -NO ₂	3201	1657	1597	837	3457, 3320 (ν NH ₂)
C ₅	<i>P</i> -NH ₂	<i>P</i> -CH ₃	3178	1642	1602	829	3461, 3371 (ν NH ₂)
C ₆	<i>P</i> -NH ₂	<i>P</i> -OCH ₃	3176	1658	1595	842	3423, 3315 (ν NH ₂)
C ₇	<i>P</i> -NH ₂	<i>P</i> -Cl	3180	1639	1600	831	3419, 3376 (ν NH ₂)
C ₈	<i>P</i> -NH ₂		3217	1637	1584	829	3481, 3327 (ν NH ₂)
C ₉	<i>P</i> -NH ₂	<i>P</i> -N-(CH ₃) ₂	3213	1682	1631	847	3413, 3334 (ν NH ₂)
C ₁₀	<i>P</i> -NH ₂	<i>o</i> -NH ₂	3176	1663	1602	837	3404, 3310 (ν NH ₂)
C ₁₁	<i>P</i> -NH ₂	1,3-(OCH ₃) ₂	3242	1645	1591	827	3442, 3348 (ν NH ₂)
C ₁₂	1,3-(OCH ₃) ₂	<i>P</i> -NO ₂	3190	1652	1585	840	1514, 1342 (ν NO ₂)
C ₁₃	1,3-(OCH ₃) ₂	<i>P</i> -Br	3076	1652	1587	846	2941&2842 (ν CH - Aliphatic)
C ₁₄	1,3-(OCH ₃) ₂	<i>P</i> -Cl	3104	1647	1585	837	2987& 2850 (ν CH - Aliphatic)
C ₁₅	1,3-(OCH ₃) ₂	<i>p</i> -N-(CH ₃) ₂	3152	1645	1586	838	2935 (ν CH - Aliphatic)

Synthesis of substituted [1,2,4] triazolo [3,4-b] [1,3,4]thiadiazepines (T)₁₋₁₈:

The title compound was prepared according to the following scheme



Scheme. 1: The synthetic pathway for [1,2,4] triazolo [3,4-b] [1,3,4]thiadiazepines (T)₁₋₁₈

Compounds (T)₁₋₁₈ were synthesized by the reaction of chalcone compounds (C)₁₋₁₅ with Bis[(3,3'-thio-4,4'-amino-1,2,4-triazole)-5-yl]phenyl or ethane in absolute ethanol to give

[1,3,4]thiadiazepines (T)₁₋₁₈ derivatives compounds.

The structures of all products were identified by using FT-IR and ¹H-NMR for some of

theme. The purities of compounds were confirmed by using an elemental analysis. The

elemental analysis of compounds (T)₁₋₁₈ are listed in Table (5).

Table 5: Elemental Analysis (CHNS-O) for compounds (T)₁₋₁₈

Comp. No.	Formula	% C		% H		% N		% S	
		Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
T ₂	C ₄₀ H ₂₆ N ₁₀ S ₂ Br ₂	55.18	54.53	2.98	2.69	16.09	15.67	7.35	6.98
T ₃	C ₄₀ H ₂₄ N ₁₂ O ₄ S ₂	60.00	58.88	3.00	2.43	21.00	22.49	8.00	7.34
T ₄	C ₄₂ H ₃₂ N ₁₀ S ₂	68.10	65.12	4.32	3.96	18.91	20.04	8.64	8.91
T ₆	C ₄₄ H ₃₈ N ₁₀ S ₂	66.16	64.30	4.76	3.90	17.54	18.74	8.02	9.03
T ₈	C ₄₄ H ₃₄ N ₁₀ O ₈ S ₂	59.19	60.89	3.81	3.65	15.69	16.64	7.17	8.45
T ₉	C ₄₈ H ₄₆ N ₁₀ O ₄ S ₂	64.86	63.48	5.18	5.54	15.76	17.45	7.20	8.03
T ₁₁	C ₃₆ H ₂₆ N ₁₀ S ₂ Br ₂	52.56	53.46	3.16	3.50	17.03	16.90	7.78	8.28
T ₁₃	C ₄₀ H ₃₈ N ₁₂ S ₂	64.00	62.94	5.06	5.37	22.40	20.07	8.53	9.07
T ₁₅	C ₄₀ H ₃₄ N ₁₀ O ₈ S ₂	56.87	55.42	4.02	5.01	16.58	18.00	7.58	8.82
T ₁₈	C ₄₀ H ₃₄ N ₆ O ₄ S ₂ Br ₂	57.14	58.78	4.04	4.98	13.33	14.71	7.61	9.00

Spectroscopic observation of (T)₁₁ for example is given: FT-IR (KBr, cm⁻¹) figure (3): 3477 and 3384 (NH₂ asymmetrical and symmetrical stretching), 3074 (Ar-H), 2974–2874 (ν C-H, aliphatic stretching), 1624 (ν CH=N), 1614 (ν C=C) and 822 (out of plane bending for *para*-substituted benzene ring).

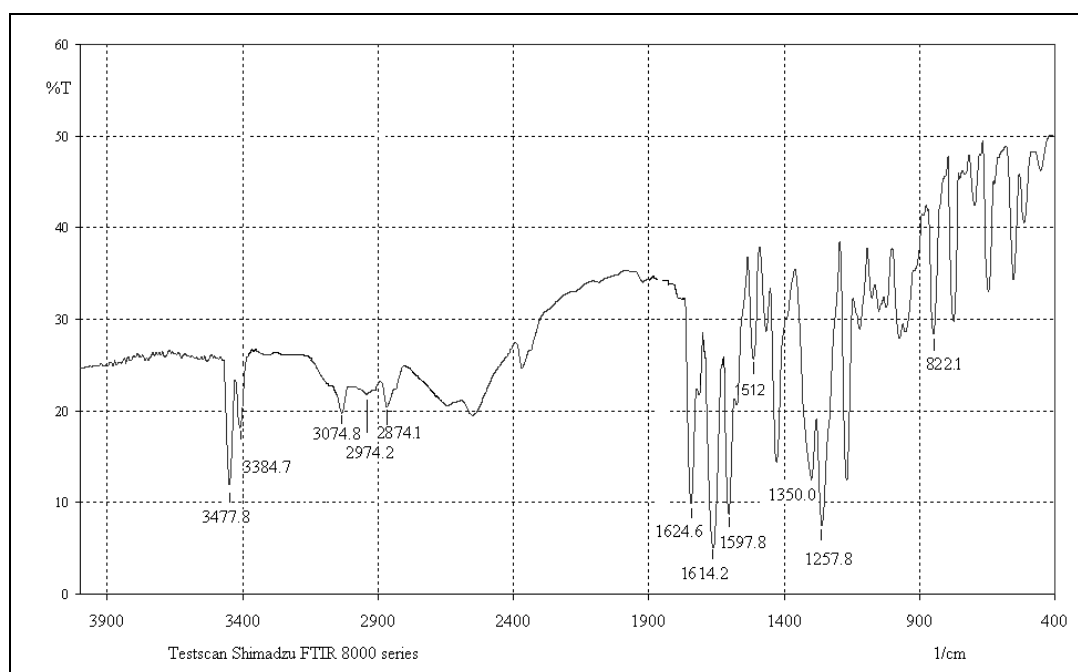
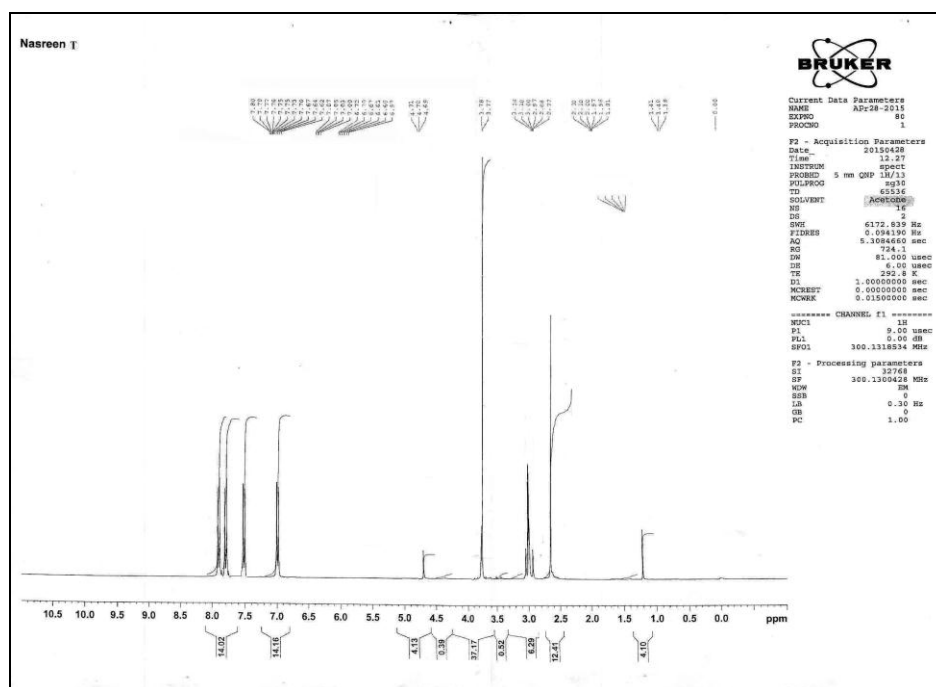


Fig. 3: FTIR spectrum of compound (T)₁₁

¹HNMR spectrum of compound (T)₁₃ (Acetone-d₆, δ in ppm) figure (4): 6.57-7.807.90 (d-d, 16H, arom. H), 4.47 (4H, NH₂), 2.8(s, 12H, N(CH₃)₂), 3.0(t, 4H, CH₂ – CH₂), 1.3 (s, 2 H, CH (thiadiazepine ring). Table (6) shows the FT-IR absorption bands for synthesized compounds.

Fig. 4: ¹H NMR spectrum of compound (T)₁₃Table 6: Characteristic FTIR absorption bands of synthesized compounds (T)₁₋₁₈

Comp.No.	ν NH ₂	ν Ar - H	ν C = N	ν C = C	γ <i>para</i> -Sub.	Other
T ₁	-	3056	1621	1593	827	1563, 1394 (NO ₂) & 3203 (O- H)
T ₂	3324 & 3223	3057	1632	1598	833	-
T ₃	3423 & 3315	3072	1622	1585	820	1555 1398 (NO ₂)
T ₄	3342 & 3218	3072	1640	1599	823	2962 & 2856 (C-H Aliphatic)
T ₅	3434 & 3335	3074	1633	1602	846	-
T ₆	3356 & 3281	3068	1628	1604	842	2973 & 2871 (C-H Aliphatic)
T ₇	3356 & 3281	3043	1624	1601	840	2981 & 2879 (C-H Aliphatic)
T ₈	-	3064	1631	1610	836	1553, 1357 (NO ₂), 2986 & 2877 (C-H Aliphatic)
T ₉	-	3058	1629	1603	827	2971 & 2891 (C-H Aliphatic)
T ₁₀	3407 & 3299	3061	1632	1598	838	1551, 1361 (NO ₂)
T ₁₁	3477 & 3384	3074	1624	1614	822	2974 & 2874 (C-H Aliphatic)
T ₁₂	3435 & 3321	3065	1621	1598	824	2962 & 2885 (C-H Aliphatic)
T ₁₃	3469 & 3369	3064	1630	1602	820	2912 & 2804 (C-H Aliphatic)
T ₁₄	3378 & 3251	3076	1633	1612	831	2973 & 2871 (C-H Aliphatic)
T ₁₅	-	3041	1628	1610	840	1535, 1334 (NO ₂), 2966 & 2851 (C-H Aliphatic)
T ₁₆	-	3053	1627	1597	842	2973 & 2871 (C-H Aliphatic)
T ₁₇	-	3061	1630	1602	838	2951 & 2854 (C-H Aliphatic)
T ₁₈	-	3050	1639	1608	818	2906 & 837 (C-H Aliphatic)

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