

Synthesis and identification of a new series of sultams derived from 2- amino 5-(4- substituted phenyl)1,3,4-thiadiazole

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Abstract

A new series of sultams have been synthesized from the reaction of sultone(4,6-dimethy 3,5-butadiene 1,2-sultone) with a new series of heterocyclic primary amines containing 1,3,4-thiadiazole unit(2-amino 5-(4-substituted phenyl)thiadiazole).The intermediate compounds (amines) and final compounds have been characterized by IR, ¹H-nmr and ¹³C-nmr spectroscopy

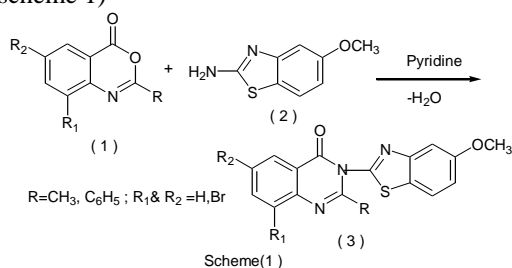
Keywords :sultone, saltam, aminothiadiazoole

Introduction

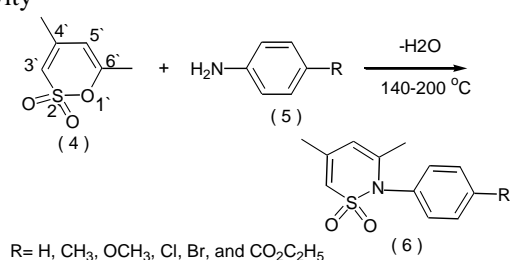
The structure^[1] of (4,6-dimethy 3,5-butadiene 1,2-sultone)(4) composed of a conjugated diene system attached at one end to SO₂ group while its other end is attached to oxygen atom.

Unsaturated sultones^[2] are cyclic esters derived from hydroxyl sulfonic acid which are analogous to the lactones of hydroxyl carboxylic acids.

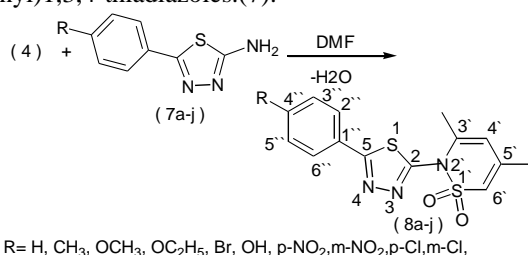
In the following^[3] reaction of substituted unsaturated lactones (1) with 2-amino-5-substituted benzo thiazole(2),the nitrogen atom of amino group take place the oxygen position of the lactone(1) to give compound (3) (scheme 1)



In 1961, Helferich et. al ^[4] prepared unsaturated sultams(6), through the condensation of (4,6-dimethy 3,5-butadiene 1,2-sultone)(4) with primary aromatic amines(5).Most sultams were found to posses antibacterial activity ^[5-8]



The present work involves synthesis of a new series of heterocyclic sultams(8) from the reaction of compound (4)with the prepared-2- amino-5-(4-substituted-phenyl)1,3,4-thiadiazoles.(7).



Experimental:

Melting points were determined using an Electrothermal melting point apparatus ,IR spectra were recorded on a Bio-rad Merlin FT-IR spectroscopy Mod FTS 3000, using KBr disc. ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker(300MHz) with TMS as internal reference in(Jordon) :

Synthesis^[9] of [2-amino 5-(4-substituted phenyl) thiadiazoles] (7):

The mixture of 0.01 mole of substituted benzoic acid, 0.01mole thiosemicarbazide and 3.5ml of POCl₃(phosphorousoxychloride) was refluxed gently for 30 minutes,cooled to room temperature ,then10 ml of water added drop by drop and refluxed for 4 hours, cooled and the precipitate was filtered washed with 5% Na₂CO₃, H₂O and recrystallized in DMSO,water.The yields, melting points and IR data were summarized in table(2).

Synthesis of (4,6-dimethy3,5-butadiene1,2-sultone)(4).

Detailed procedure is described in reference(2).

Synthesis^[10],of [5-(4-substituted -phenyl)thiadiazoles]-2,4-dimethyl 1,3-butadiene 1,4-sultams(8)

The substituted amines (0.01_mole were dissolved in 10 ml of DMF and mixed with 0.01 mole sultone(4) which dissolved in 10 ml of DMF and refluxed for 2 hours then poured into water (20)ml the precipitate was filtered off and recrystallized from methanol. The yields ,melting points and IR data of the prepared sultams were summarized in table(3)

Results and Discussion

The structures of the synthesized sultams (8a-i) was characterized by IR,¹H-nmr and ¹³C-nmr spectroscopy. The IR spectrum^[11] of the compound (4) shows the band for the conjugated diene at (1575 and 1605)

cm⁻¹and characteristic bands for the SO₂ group at (1160 and 1315) cm⁻¹.

Further support comes from the comparison of the IR absorptions spectra of the products(8)with starting materials (7),in which the two bands of NH₂ group of the heterocyclic amines(7) are disappeared, the SO₂ groups gave two bands at (1181-1305) cm⁻¹ which indicate that the NH₂ group of the compound (7) reacts with sultone(4) and the H₂O was expelled out and forms the heterocyclic sultams (8).

The ¹H-n.m.r spectrum of compound(4) shows that the proton at C₃ has a chemical shift at a further down field than that of C₅ table(1),also the protons of the methyl group at C₆ position showed at lower field than those of the C₄ methyl group, because of the deshielding effect of the

oxygen atom attached to C-6, which agreed with that reported in literature^[12].

In the ¹H-n.m.r spectrum of 5-(4-chlorophenyl) 2-amino thiadiazole(7g) there are signals for the aromatic protons at (7.3-8.0)ppm with two signals for the two protons of NH₂ group at (11.0 – 11.2)ppm. While in the ¹H-n.m.r spectrum of the compound (8g) (fig. 1) shows that there are two signals for the two methyl groups at(2.01and 2.1)ppm of C₃ and C₅ positions respectively ,and signals of the two proton of (C₄ and C₆) of the sultam ring appear at(5.96- and 6.9)ppm. respectively, with the signals of the aromatic proton at (7.3-8.06) ppm and two doublet signals for protons of para substituted of phenyl group, the signals of NH₂ group was disappeared.

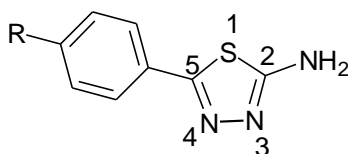
In the ¹³C-n.m.r, chemical shifts of the compound (8g)(fig 2) there are two signals at (19.9 and 21.36) ppm for two

methyl groups ,and (106,113,)ppm signals for C₄ and C₆ position and 147ppm for C₃,₅ of the heterocyclic part. Other signals of the aromatic and thiadiazole ring carbons are appeared as C₂,₆:127.32 ; C₃,₅:128.92 ;C₄: 129.7; C₁: 130.38 , C₅: 113 and C₂:156.64 ppm.

Table(1):¹H-nmr data for compound (4).

Position	Chemical shifts ppm
H ₃	6.2
H ₅	5.62
C ₄ -CH ₃	2.03
C ₆ -CH ₃	2.15

Table (2); Yields, Melting points and IR (Cm⁻¹) data of heterocyclic amines(7) .



Comp.	formula	R	Yield%	M.P. °C	NH str	cyclicC=N	C=C str
7a	C ₈ H ₇ SN ₃	4-H	40.5	174-176	3261,3108	1662	1608
7b	C ₉ H ₉ SN ₃	4-CH ₃	82	214-216	3278,3094	1634	1609
7c	C ₉ H ₉ SN ₃ O	4- OCH ₃	56.5	228-230	3250,3190	1645	1612
7d	C ₁₀ H ₁₁ SN ₃ O	4-OC ₂ H ₅	62	238-240	3240,3180	1675	1608
7e	C ₈ H ₆ SN ₄ O ₂	4-NO ₂	55	226-228	3430,3230	1626	1595
7f	C ₈ H ₆ SN ₄ O ₂	3- NO ₂	62.2	220-222	3283,3153	1614	1594
7g	C ₈ H ₆ SN ₃ Cl	4-Cl	80	180-182	3397,3273	1682	1620
7h	C ₈ H ₆ SN ₃ Cl	2-Cl	58	220-222	3340,3260	1646	1623
7i	C ₈ H ₆ SN ₃ Br	4-Br	84	231-233	3272,3128	1680	1618
7j	C ₈ H ₇ SN ₃ O	4-OH	50	232-234	3264,3067	1634	1604

Table (3); Yields, Melting points and IR(Cm⁻¹) data of prepared sultams(8)

Comp.	formula	R	Yield%	M.P; °C	S=O	C=C str. Ar, sultam	Comp.
8a	C ₁₄ H ₁₄ S ₂ N ₃ O ₂	4-H	60	197-199	1140,1310	1610	8a
8b	C ₁₅ H ₁₆ S ₂ N ₃ O ₂	4-CH ₃	59	205-207	1140,1320	1600	8b
8c	C ₁₅ H ₁₆ S ₂ N ₃ O ₃	4- OCH ₃	60	240-242	1150,1310	1603	8c
8d	C ₁₆ H ₁₈ S ₂ N ₃ O ₃	4-OC ₂ H ₅	60	215-217	1150,1300	1615	8d
8e	C ₁₄ H ₁₃ S ₂ N ₄ O ₄	4-NO ₂	46	210-212	1150,1320	1600	8e
8f	C ₁₄ H ₁₃ S ₂ N ₄ O ₄	3- NO ₂	46	185-187	1145,1300	1600	8f
8g	C ₁₄ H ₁₃ S ₂ N ₃ O ₄ Cl	4-Cl	59	175-177	1100,1300	1610	8g
8h	C ₁₄ H ₁₃ S ₂ N ₃ O ₄ Cl	2-Cl	59	230-232	1150,1315	1600	8h
8i	C ₁₄ H ₁₃ S ₂ N ₃ OBr	4-Br	48	245-247	1150,1300	1610	8i
8j	C ₁₄ H ₁₄ S ₂ N ₃ O ₅	4-OH	45	205-207	1160,1310	1600	8j

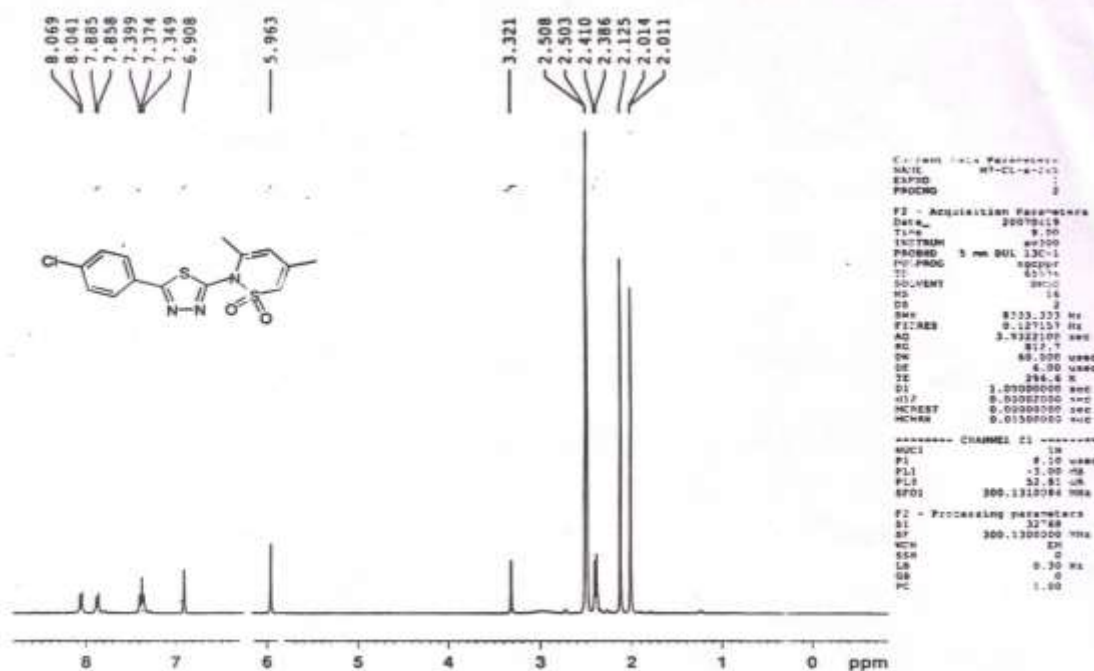


Figure 1 : ¹H-nmr spectrum for compound (8g).

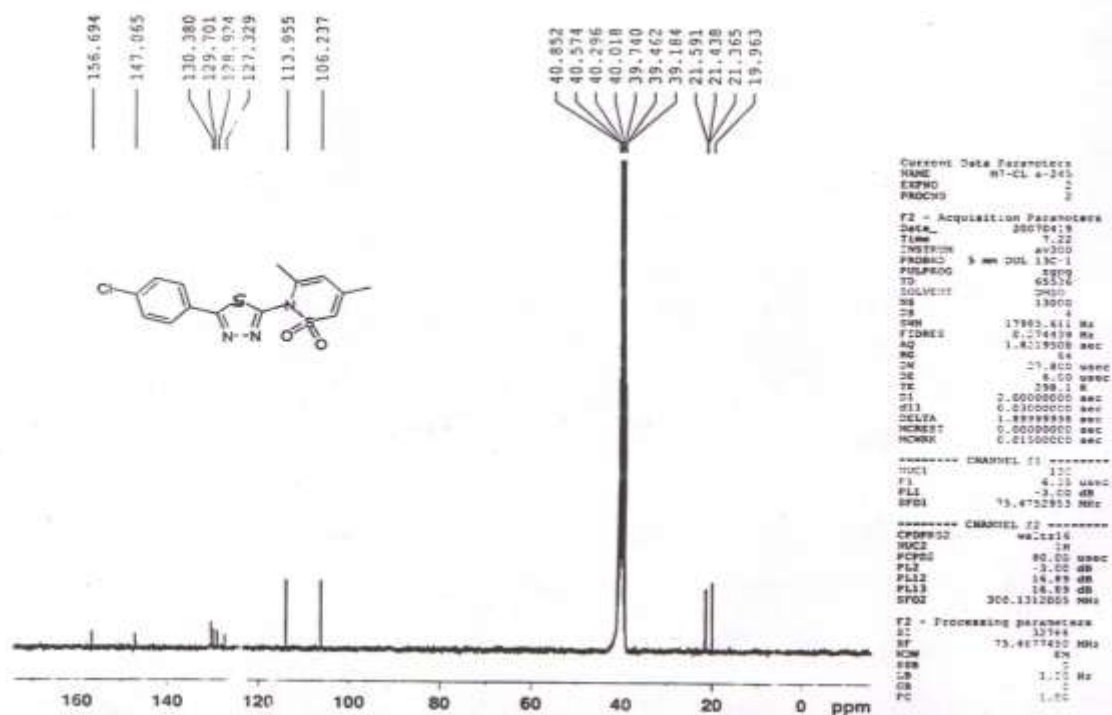


Figure 2 : ¹³C-nmr spectrum for compound (8g).

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تحضير و تشخيص سلسلة جديدة من مركبات السلتام المشتقة من

(٢-أمينو ٥-(٤-فنييل المعوض) ١و٣و ٤ ثايدايازول)

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(تاريخ الاستلام: ٢٤ / ٧ / ٢٠٠٨ ، تاريخ القبول: ٢٧ / ١١ / ٢٠٠٧)

الملخص

تم تحضير سلسلة جديدة من مركبات السلتام من تفاعل السلتنون (٤و٦-ثنائي مثيل ٣و٥-بيوتادين ١و٢-سلتنون) مع سلسلة جديدة من أمينات أولية تحتوي على وحدة ١و٣و٤-ثايدايازول[٢-أمينو ٥-(٤-فنييل المعوض) ١و٣و ٤ ثايدايازول] وتم تشخيص المركبات ألوسطية والنهائية (الأمينات و السلتام) بواسطة طيف الأشعة تحت الحمراء وطيف ألرنين ألنووي ألمغناطيسي للبروتون وطيف ألرنين ألنووي ألمغناطيسي للكربون ١٣.