Synthesis of Dispiro 1,3-Oxazepine-4,7-Diones

Dr. Ali H. Samir
(Ibn AL-Haitham)/University of Baghdad

Abstract

Dispiro-1,3-oxazepine-4,7-diones can be synthesized by reaction of thiosemicarbazide with carbon disulphide in alcoholic anhydrous sodium carbonate gives 2-amino-5-mercapto-1,3,4-thiadiazole (I). Compound (II) were synthesized by the reaction of compound (I) with methyl iodide, this product has been oxidized to sulphone derivatives. The Schiff's bases of the compounds(IVa,IVb) were synthesized by condensation of different aromatic aldehydes with sulphone derivatives, the Schiff' bases were cyclized with pyromelitic dianhydride to give dispiro-1,3-oxazepine -4,7-diones as shown in scheme[1]. The new compounds were characterized by physical properties and spectral data (FT-IR).

Introduction

Among azoles, thiadiazole and its derivatives continue to draw the attention of synthetic organic chemists due to large group of compounds possessing a wide spectrum of uses[1]. Heterocyclic compounds possessing 1,3,4-thidiazole ring system showed antifungal and anthelmintic effects[1,2]. Compounds containing the above ring also exhibit anti-inflammatory, antimicrobial properties[3] and the depression effect on the central nervous system[4]. Also heterocycles have been used in the chemistry of disperse dyes[5].

Diels-Alder's reaction was the only widely useful example of the So-called cycloaddition reactions[6]. The addition of carbenes and nitrenes to unsaturated centers has extended the series to include three, four, five, and six membered ring systems[7]. Condensation of Schiff bases with anhydrides (maleic, phthalic, nitrophthalic, succinic) give corresponding cycloaddition products including 1,3-oxazipenes . The reaction of these anhydrides with Schiff's bases is classified as a 5+2→7, implying 5-atom component plus 2-atom component leading to 7-membered cyclic ring[8]. Some of these compounds showed biological activity like ASENDIN which is an antipressant agent of the dibenzonazepine calss. ASENDIN is an antidepressant with a mild sedative component to it's action[9].

The aim of the present study is to synthesize some new 1,3-oxazepine derivatives.

Experimental

Chemicals: all the chemicals which used were supplied from Aldrich , Merck and BDH chemicals Co. and were used as received.

Techniques: melting points were determined using an (Electrothermal) melting point apparatus and are uncorrected. FTIR spectra were recorded with SHIMADZU FTIR-4800S. Infrared spectrophotometer as (KBr)disc.

Synthesis of 2-amino-5-mercapto-1,3,4-thidiazole[I].

A mixture of (2 g,0.02 mol.) of thiosemicarbazide and (2.33 g, 0.02 mol) of anhydrous sodium carbonate was dissolved in 25ml. abs. ethanol. To this solution (3.2 g, 0.04 mol.) of carbon disulphide was added.

The resulting mixture was heated under reflux for 7 hrs. the reaction mixture was then allowed to cool down to room temperature. Most of solvent was removed under reduced pressure and the residue was dissolved in 20 ml distilled water and then acidified with cold concentration hydrochloric acid to give pale yellow precipitate. The crude product was filtered and washed with cold water, recrystallized from ethanol to give yellow product m.p(230-231)$^{\circ}$ C[10].

Synthesis of Thioether Compound [II] [11].

Compound (I) containing (-SH) group (0.001 mol.) dissolved in (10 ml.) dioxan, which contained (0.001 mol.) potassium hydroxide. Methyl iodide (0.001 mol.) was added using separating funnel dropwise with stirring. The reactants were refluxed for 2 hrs. The solvent was evaporated under redued pressure, water was added, and the crude product was extracted with ethyl acetate and dried with anhydrous magnesium sulphate.

Remove the solvent by distillation from a water bath (rotary evaporator) gave solid products, which recrystallized from dioxan to give the desired product, yield (70%), m.p (157-159)$^{\circ}$ C.

Synthesis of Sulphone Compound [III] [12].

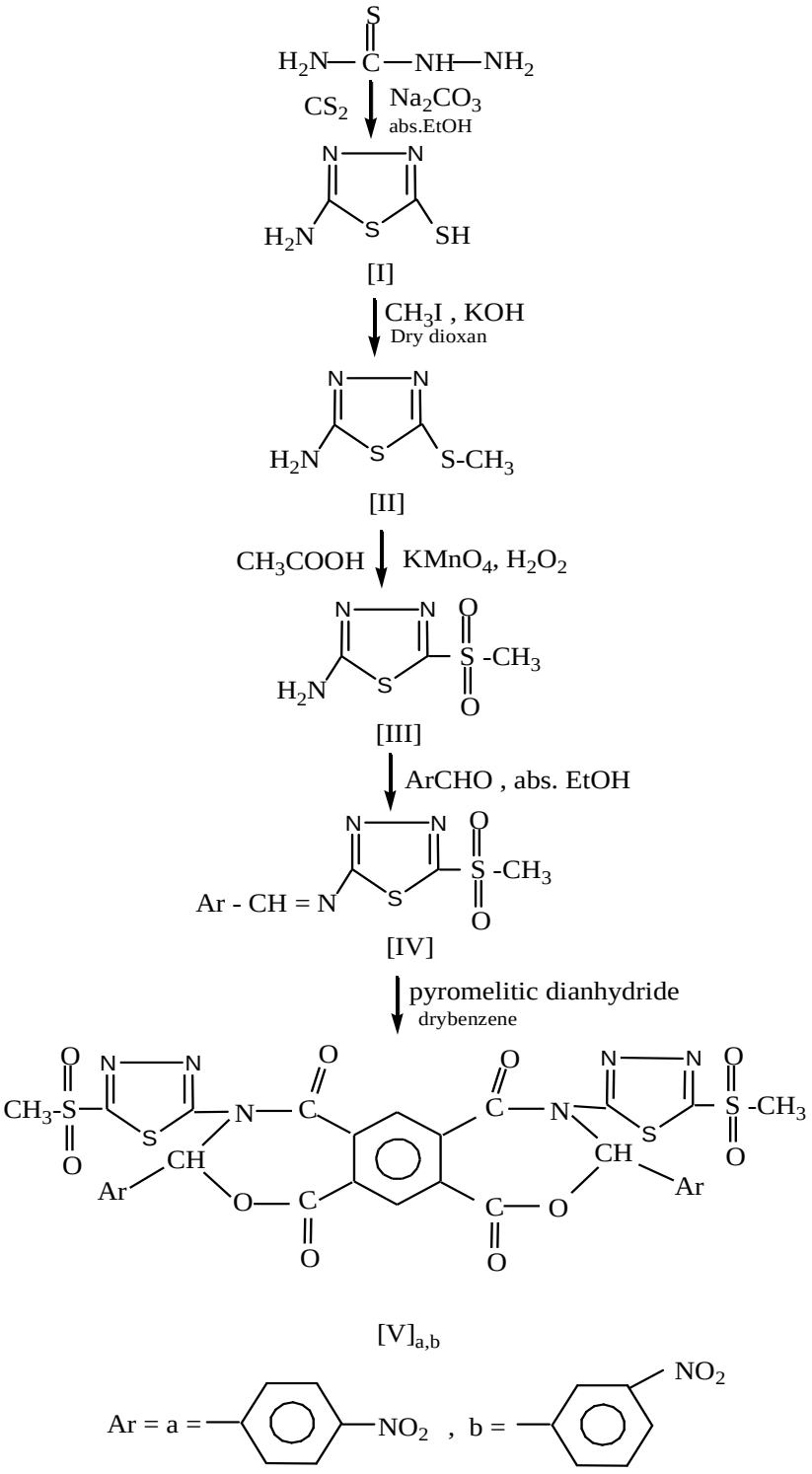
Methylthioether (II) (0.001 mol.) was dissolved in 80% aqueous acetic acid. To this solution, potassium permanganate (0.002 mol.) in water (5 ml.) was added during a period of 30 minutes at 5° C. After 1 hr., 30% hydrogen peroxide was added in quantity sufficient to discharge the color, work up by neutralization with 10% sodium hydrogen carbonate solution, extraction with ethyl acetate and evaporation of the organic extract yield the compound with m.p (191-193)$^{\circ}$ C.

Synthesis of Sciff's Bases Compounds [IV] [13].

A mixture of compound (III) (0.001 mol.), absolute ethanol and appropriate aromatic aldehyde (0.001 mol.) in acidic condition(3 drops of acetic acid) was refluxed in water bath for 4 hrs. The reaction mixture was then allowed to cool at room temperature, and the precipitate was filtered and dried, recrystallized from ethanol (50%) to give colored crystals. Table (1) shows the m.p, yield and synthesized compounds IVa and IVb.

Synthesis of Oxazepine Compounds[V]:

A mixture of (0.06 mol.) of Schiff's bases and (0.03 mol.) of pyromelitic dianhydride dissolved in (30 ml.) dry benzene which was refluxed in water bath for 5 hrs. The solvent was removed and the resulting colored crystalline solid was recrystallized from dioxane to give [V_a, V_b]. Table (2) shows the m.p and yield percent,



Scheme -1-

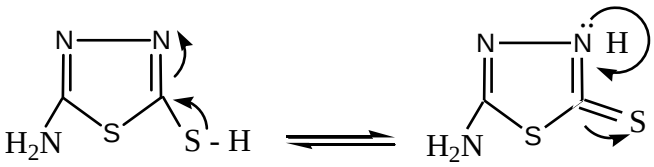
Results and Discussion

Compound [1] 2-amino-5-mercapto-1,3,4-thiadiazole was prepared through the reaction of thiosemicarbazide with carbon disulphide in the presence of anhydrous sodium carbonate in absolute ethanol.

The structure of compound [I] was identified by it's melting point and FT-IR spectroscopy. The FT-IR spectrum of compound [I] shows the following characteristic bands, two bands at 3414 cm^{-1} and 3236 cm^{-1} were due to asymmetric and symmetric stretching vibration of ($-NH_2$) group respectively, an absorption band at 3070 cm_{-1} was due to the (N-H) stretching (tautomeric form).

The (-SH) stretching band found as very weak shoulder at 2550 cm^{-1}, aband at 1570 cm^{-1} was due to (C=N) stretching of the thiadiazole ring moiety. The sharp band at 1527 cm^{-1} and 1369 cm^{-1} are due to the (N-H) bending and (C-N) stretching vibration respectively.

Also, the absorption band at 1064 cm^{-1} for the (C=S) group which gives an evidence that compound [I] can exist in two tautomeric forms, thiol (A) and thione form (B) [10].



(A) **(B)**

Compound [II] were synthesized by the reaction of compound [I] with methyl iodide in the presence of potassium hydroxide in dry 1,4-dioxan. The mechanism of the alkylations were explained by the nucleophilic attack of sulphide ion on the methyl iodide and remove the iodide ion as KI [14].

The FT-IR of this compound showed disappearance band of which is due to (C=S). Also the disappearance of very week band at (2400-2500)cm^{-1} due to (S-H) group, and remaining of the two functional group due to (C=N) exocyclic, (C=N) endocyclic, at (1605-1630)cm^{-1}, (1550-1585)cm^{-1} respectively [15], and the appearance of band at (1346-1343) cm^{-1} due to ($S-CH_3$) [16].

Compound [III] were obtained by regioselective complete S-oxidation of corresponding methyl sulphids by treatment with hydrogen peroxide and potassium permanganate.

The FT-IR spectrum of compound [III] showed two bands at (1280-1380)cm^{-1} and (1110-1160)cm^{-1} were due to asymmetric and symmetric stretching vibration of (SO_2) group respectively[17].

The condensation reaction of equimolar quantity of primary amine with aromatic aldehydes was the major method to prepare Schiff's bases.

FT-IR spectrum of compound [IV] showed the disappearance of two absorption band due to the ($-NH_2$) stretching of amino group.

On the other hand, the FT-IR spectra showed bands for olefinic (C-H), aromatic(C=C), endocyclic (C=N) and exocyclic imine (C=N) group stretching vibrations [10]. FT-IR absorption for these compounds are show in table (3).

Compounds [V_a, V_b] were synthesized by the reaction of compounds containing azomethene group with pyromelitic dianhydride in presence of dry benzene, the compounds were identified by m.p. and FT-IR spectra.

The FT-IR spectra of compounds (V_a, V_b) showed disappearance of the band due to (C=N) exocyclic group and appearance band due to (C=O) Lactone, Lactam. Other data of functional group are shown in table (4).

References :

1- P. K. Sengupta,M. R. Ray and S. S. Chakravorti, Indian J. Chem.16,(1978), P 231.

2- A. H. El-Masry ,H. H. Fahmy and S. H. Ali Abed Al-Wahed ,Molecules, 5,(2000) ,p 1429.

3-A. S. Orabi ,M. A. Moneim E. El –Din Salem and M. El Din Abdel- Fattah ,Polish J. Chem. ,74,(2000), P 1675.

4- C. Colotto ,F. Varano , L. Cecchi,G. Filacchioni ,A Galli,C. Costagli and V. Carla ,J.Med. Chem. ,43,(2000), P 3824.

5- H. R. Maradiya, J. Serb Chem. Soc. ,67(11),(2002),P 709.

6-A.Francis Carey,6th ed,Organic Chemistry,McGraw Hill, Inc, New York, (2006) ,P430-433.

7-Morrison Boyd ,"Organic Chemistry ",6th ed ,Prentice Hall International,Inc.,NewYork,(2000) ,P 1013-1024.

8- F. A. Hussein ,Iraqi J. Chem., 27(4),(2001),P 77.

9- A. Grand ,J. of Ethnopharmacology, 22(1988), P 25-31.

10-A.S. Nadia,Ph.D. Thesis,College of Science,Al-Nahrain University, Iraq, (2005).

11-M.J. Mahmoud,I.F. Mustafa,Mutah Journal for Research and Studies,11 (5),(1996), P1022,P 6804.

12-Y. Watanabe,T. Numata ,S. Oae,Synthesis ,81,(1981), P 204.

13-M. J. Mahmoud,Z. M. Al-Rubaiy,R. K. Al-Kubaisy,M. M. Al-Najafi,H. M. Al-Jumaily,Ibn Al- Haitham ,J. for Pure and Appl. Sci.,17(1),(2004),P 103-110.

14-Z. M. Al-Rubaiy, M.Sc. Thesis,College of Education,Baghdad University,Iraq,(1998).

15-A. A. Aly and R. El-Ayed,Chem.,60(1),(2006), P 56-60.

16-I. F. Mustafa ,Mu'tah Journal for Research and Studies,12(3),(1997), P144.

17-D. H. Williams and I. Fleming "Spectroscopic Methods in Organic Chemistry",2nd ed. , McGraw-Hill,London,(1973).

Table (1): The physical properties of compounds [IV_a, IV_b].

Comp. No.	Molecular formula	m.p/ ° C	Yield%
IV_a	$C_9H_6O_2N_4S_2$	112-114	65%
IV_b	$C_9H_6O_2N_4S_2$	197-199	68%

Table (2): The physical properties of compounds V_a and V_b.

Comp. No.	m.p/ ° C	Yield%	Molecular Formula
V_a	186-188	85%	$C_{30}H_{18}O_{14}N_8S_2$
V_b	190-192	70%	$C_{30}H_{18}O_{14}N_8S_2$

Table (3): Characteristic FT-IR absorption bands (cm^{-1}) of compounds (IV_a, IV_b).

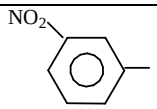
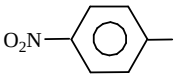
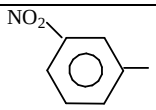
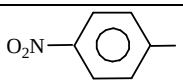
Comp. No.	Ar.	C=N str. Exocyclic cm^{-1}	C=N str. Endocyclic cm^{-1}	S=O cm^{-1}	C-H Aromatic cm^{-1}	C=C Aromatic cm^{-1}
IV_a		1604	1570	(1280-1380) asy.	3070	1446,1527
IV_b		1635	1590	(1110-1160)sym.	3051	1438,1516

Table (4): Characteristic FT-IR absorption bands (cm^{-1}) of compounds (V_a,V_b)

Comp. No.	Ar.	C=N str. Endocyclicc cm^{-1}	C=O str. Lactone cm^{-1}	C=O str. Lactam cm^{-1}	C-O str. lactone cm^{-1}	C-NO_2 cm^{-1}
V_a		1592	1714	1640	1270	1527,1354
V_b		1586	1698	1668	1254	1532,1393

تحضير مركبات ثنائي سبايرو ٣،١- اوكسازبين ٧،٤- دايون

د.علي حمادي سمير
قسم الكيمياء / كلية التربية –ابن الهيثم/ جامعة بغداد

الخلاصة :

تضمن هدا البحث تحضير مركبات ثنائي سبايرو -٣،١- اوكسازبين -٧،٤- دايون بتفاعل الثايوسيميكاربازايد مع ثنائي كبريتيد الكاربون في وسط قاعدي لتعطي المركب ٢- امينو -٥-مركبتو -٤،٣،١- ثياديازول [I] ،اما المركب [II] فقد حضر من مفاعلة المركب [I] مع يوديد المثيل بوجود هيدروكسيد البوتاسيوم ، ومن اكسدة المركب [II] باستخدام برمنكنات البوتاسيوم في الوسط الحامضي تم الحصول على مشتقات السلفون [III] . اما قواعد شف [IVa,IVb] فقد حضرت بتكاثف الالديهايدات الاروماتية مع مشتقات السلفون في البنزين الجاف ،ومن مفاعلة قواعد شف الناتجة مع انهيدريدات البايروماليتيك تم الحصول على مركبات ثنائي سبايرو-٣،١- اوكسازبين -٧،٤-دايون[Va,b] . شخصت هده المركبات من خلال القياسات الطيفية والفيزياوية .