Research Article **CODEN: AJPAD7** **ISSN: 2321-0923**

Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry

Journal home page: www.ajpamc.com

A FACILE METHOD FOR THE SYNTHESIS OF OXOKETENE N, S-ACETALS/AMINALS FROM THE REACTION OF AMINO COMPOUND WITH OXOKETENE DITHIOACETALS

Rachna Mishra*[1] and Dharma Kishore[1]

*[1]Department of Chemistry, Banasthali University, Banasthali, Rajasthan-304022, India.

ABSTRACT

Oxoketene dithio acetals **(4)** reacted with cyclic secondary amine namly N-methyl piperazine to produce oxoketene N,S-aminal **(5)** in good yield. This research work explores the synthetic utility of oxoketene-*N*, *S*-acetals derived from oxoketenedithioacetals in the synthesis of a wide variety of heterocyclic compounds of potential biological interest.

KEY WORDS

Cyclic secondary amine, N, S-aminal, N-methyl piperazine and Oxoketenedithio-acetals.

Author of correspondence:

Rachna Mishra,

Department of Chemistry,

Banasthali University,

Banasthali, Rajasthan-304022, India.

Email: racshukla@gmail.com.

INTRODUCTION

α-Oxoketene N, S-aminal (1.001), N, N-aminal (1.002) and N, O-aminal (1.003) are useful intermediates for the synthesis of a wide range of five and six membered heterocycles[1-3] (Figure No.1). These compounds can behave either as enaminones providing C-C-N component in the product the heterocycles[4] or act as 1, 3- bielectrophilic component in their reactions with bifunctional heteronucleophiles furnishing various annulated heterocycles[5].

In which Oxoketene-*N*, *S*- acetals (1.001) are highly versatile synthons for heterocyclic synthesis[1,6] and are quite stable and can be stored indefinitely without any decomposition and exhibit the nucleophilic displacement reactions by various

binucleophiles followed by intramolecular cyclisation leading to the formation of cyclic compounds (such reactions are characteristics of enamines)[1,6]. Junjappa and coworkers prepared a series of functionalized heterocycles by treating them with binucleophiles like hydrazines, hydroxylamines, guanidines, cyanoacetamides, and so forth[7-9], They have also prepared functionalized quinolines from *α*-oxoketene-*N,S*-acetals employing Vilsmeier-Haack reaction[10]. A similar strategy was reported for the synthesis of quinoxalines from nitroketene-*N, S*-acetals and for important benzoheterocycles displaying a broad spectrum of biological activities. My research work explores the synthetic utility of oxoketene-*N, S*-acetals derived from oxoketenedithioacetals in the synthesis of a wide variety of heterocyclic compounds of potential biological interest.

The *α*-oxoketene-*N, S*-acetals are generally prepared by the direct amination reactions of oxoketene-*S, S*-acetals by appropriate amines which result in a mixture of oxoketene-*N, S*-acetals and –*N, N*-acetals in most of the cases. Several synthetic methods for N, N-keteneacetals and N, S-keteneacetals derived from primary alkyl amines and aromatic amines are available. However, the synthetic methods for heterocyclic ketene N, N-, N, O- and N,S-acetals are found to be less explored. The ketene-dichlorides which were used extensively for the synthesis of heterocyclic keteneacetals, are not very stable compounds. The synthetic methods reported earlier have one or more disadvantages such as the lack of the easy of availability and preparation of necessary starting materials. We report herein an easy and efficient synthesis of the heterocyclic ketene acetals by direct displacement of the thiomethyl functional groups of ketene dithioacetals by conjugate addition elimination reaction with various binucleophiles.

Oxoketene-N, S- and N, N-acetals have been used as versatile three-carbon synthons for the synthesis of various heterocyclic compounds[11-20]. These intermediates are generally prepared by nucleophilic addition elimination reactions of oxoketene dithioacetals with amines in boiling solvents such as absolute ethanol[21], a mixture of xylene and DMF[22-23], and ethanoic acid or propanoic[24] acid. Likewise, aromatic amine derivatives are prepared by heating dithioacetals with the appropriate aromatic amine at 150-160 ºC in the absence of solvent or by conversion of the amine into its N-anion by reaction with n-BuLi in THF at -78 ºC[25]. In these reactions, generally a mixture of oxoketene-N, S- and N, N-acetals are obtained[25, 26]. This gives rise to a low yield of the desired product and uses severe work up procedures. Due to the importance of these synthons in synthesizing complicated compounds, development of a facile and selective method to synthesize these intermediates and improve the total yields of the target molecules would be very advantageous. Herein, we wish to report a very convenient and selective method to prepare a newly developed, practical version of these synthons under moderate conditions from oxoketene dithioacetals derived from isatin.

RESULTS AND DISCUSSION

In the present work, the synthesis of oxoketene N, S-aminal (5) was carried out by the oxoketenedithioacetals 4 (a-d) from its reaction with N-methyl piperazine, which in turn was realized in three steps from isatin (1) following the procedure that has been reported in the literature for such reactions on other related substrates. The proposed synthesis in its first step had propelled forward with the formation of compound 2(a-d) which resulted from the reaction of isatin (1) with formaldehyde and secondary amines effecting the reaction under the conditions of Mannich's reaction.

It has been shown in our laboratory that microwave induced reaction of isatin provided an elegant way for the preparation of Mannich's bases of isatin. The same methodology was applied in the conversion of 1 to 2 (a-d) (R= pyrrolidinyl, piperidinyl, morpholinyl, and 1- methyl piperazinyl). The literature is replete with examples showing that incorporation of the bioactive pharmacophores such as pyrrolidine, piperidine, morpholine, N-substituted piperazines provided a beneficial effect on the overall efficacy of the parent drug molecules. This prompted us to incorporate the Mannich's base

fragments on the lactam nitrogen of isatin molecule. Treatment of 2 (R= piperidinyl) with ethylacetoacetate under the condition of Claisen condensation produced 3. Carbonyl compounds containing an adjacent CH_2 or CH_3 group have been known in the literature to undergo a facile reaction with CS_2 and CH_3I in presence of a base, to form the corresponding oxoketene dithioacetal derivatives. This strategy was applied on 2.096 (a-d) to form the oxoketenedithioacetal derivatives 4 (a-d) from 3 (a-d) [Scheme. 1-2].

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. Purity of compounds was monitored on silica gel 'G' coated TLC plates. IR spectra were recorded on Schimadzu FTIR-8400S Spectrometer in KBr, ^{1}HNMR spectra were taken in CDCl3+DMSOd6 on BRUKER AVANCE II 400 NMR Spectrometer using TMS as an internal standard and Mass spectra were recorded on a Joel SX-102 mass spectrometer.

1-(Pyrrolidin-1-ylmethyl) indoline-2,3-dione.(2a)

To a suspension of isatin **(1)** (2.94 g., 0.02 mol.) in ethanol was added pyrrolidine (1.42 g., 0.02 mol.) and 37% formaldehyde (0.5 ml). The mixture was irradiated in a microwave oven at an intensity of 80% with 30 s/cycle. The completion of the reaction was checked by TLC. The solution was kept at °C for 30 min. and the resulting precipitate was collected and recrystallized from a mixture of DMF and water to give **2 a** (3.22 g.): Same procedure was applied for the preparation of 2 (b-d).

Z)-Ethyl 3-oxo-2-(2-oxo-1-(pyrrolidin-1-ylmethyl) indolin-3-ylidene)butanoate.(3a)

A mixture of 2 a (1.15 g., 0.005 mol.) and acetoacetic ester (0.65 g., 0.005 mol.) was dissolved in ethanol (20 ml) and piperidine (1ml) was added. The mixture was allowed to stand 15 days at room temperature the yellow needles formed were recrystallized from ethanol to give 3a (1.19 g.): Same procedure was applied for the preparation of 3 (b-d).

(Z)-Ethyl 5,5-bis(methylthio)-3-oxo-2-(2-oxo-1-(pyrrolidin-1-ylmethyl)indolin-3-ylidene) pent-4-enoate(4a)

suspension of potassium-ter-butoxide (0.672 g., 0.006 moles) in dry benzene (15 ml) and DMF (10ml) and the reaction mixture (3a) was allowed to stand at room temperature for 4 h., then methyl iodide (0.45 g., 0.006 mol.) was gradually added with stirring and external cooling (exothermic reaction). The reaction mixture was allowed to stand for 2 h. at room temperature with occasional shaking and then refluxed on water bath for 3 h. The mixture was poured on crushed ice and the benzene layer was separated. The aqueous portion was extracted with benzene and was washed with water and dried over sodium sulphate and the solvent was removed by distillation. The product obtained was purified by crystallization with ethanol water mixture to give 4a (1.17 g.): Same procedure was applied for the preparation of 4 (b-d).

(2Z, 4E)-Ethyl 5-(4-methylpiperazin-1-yl)-5-(methylthio)-3-oxo-2-(2-oxo-1-(pyrrolidin-1-ylmethyl)indolin-3-ylidene) pent-4-enoate(5a)

A mixture of compound 4a (1.19 g., 0.0024 mol.) and 1-methyl piperazine (.073g., 0.0073 mol.) in toluene (10 ml) was heated to reflux for 2 h. Solvent and excess 1-methyl piperazine was removed under vacuum and the residue was triturated with a mixture of ethyl acetate and ether (1:3) to give 5a (0.75 g.) as yellow crystals: Same procedure was applied for the preparation of 5 (b-d).

Interpretation of spectral data

Structure of all the compounds were established on the basis of their elemental analysis, IR, ^{1}HNMR and MS spectral data. Physical data of all the compounds were found to be consistent to the structures assigned to these molecules. As a representative case the spectral characteristics of 2a, 3a, 4a and 5a are discussed below. The microanalysis and spectral data (IR, ^{1}HNMR and MS) of all the compounds are given in Table No.1 and 2 respectively.

Infrared spectrum of compound 2a on KBr exhibited peaks at 3010 cm^{-1} [C-H], 1155 cm^{-1}[C=C], 1721cm^{-1}[C=O, carbonyl], 1668 cm^{-1} [C=O,

amide], 1403[C-N]. Disappearance of peaks for [C=O, carbonyl] and appearance of ester [C=O] at 1737 in 3a provided a clear evidence for the formation of ester group, Along with this, IR spectrum of 3a also exhibited band at 2962[C-H methyl], 1010 [C-N, indole]. Appearance of Me-S [C-S] at 645 gave a clear evidence for the formation of 4 from 3a Along with this, IR spectrum also exhibited band at 2912[C-H methyl], 1720 [C=O carbonyl], 1587[C=C str. ArH]. Compound 5a exhibited peaks at 1715 cm^{-1}[C=O, carbonyl], 1455 cm^{-1} [C=C str. ArH], 750 cm^{-1} [C-N], 645 cm^{-1} [C-S]. Similar interpretations established the formation of compound 2-5 (b-d).

^{1}HNMR spectrum of compound 2a in $CDCl_3$+DMSO-d_6 displayed signals for presence of 14 protons and 3a displayed signals for presence of 26 protons, 5a displayed signals for presence of 34 protons in which all protons were bounded to carbon atoms (as no protons exchanged with D_2O). Compound 2a exhibited sharp singlet at δ 4.03 which were assigned to two proton of CH_2 group. One multiplet at δ 7.89-7.38 was assigned to 4 protons of benzene ring. One multiplet at δ 2.51-1.68 was due to eight protons for pyrrolidine ring. A distinguishing feature in ^{1}HNMR spectrum of 3a which established its formation from 2a was the appearance of a quartet for 2H at δ 4.20 and a singlet at δ 2.27attributable to the presence of methylene and methyl group respectively. Compound 4a exhibited a sharp singlet at δ 6.09 which were assigned to one of vinyl CH proton. One multiplet at δ 8.76-7.14 was due to four protons of benzene ring. One triplet at δ 1.29 was alterbutalets the methyl groupA distinguishing feature in ^{1}HNMR spectrum of 5a which established its formation from 4a was the appearance of a multiplet at δ 2.79-2.73 which was due to the eight protons of piperazine ring.In a likewise manner the formation of compound 2(b-d)-5(b-d) were established on the basis of ^{1}HNMR spectrum.

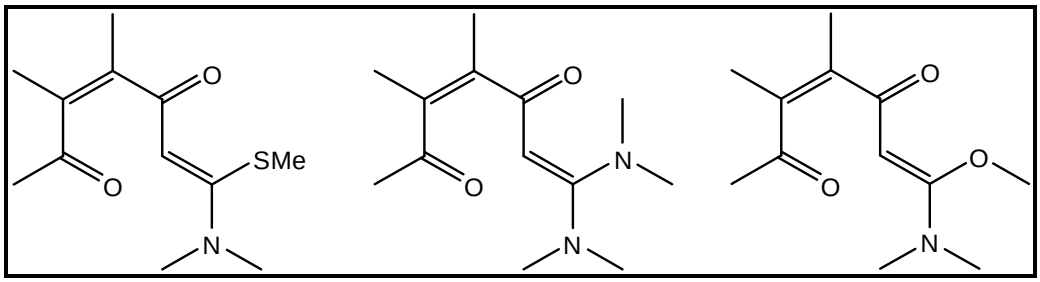
Table No.1: Physical and analytical data of the compounds 2-5(a-d)

S.No	Compound No.	Molecular Formula	Molecular Weight	Yield (%)	M.P.(°C)	Elemental Analysis	
						(Cal. /exp.) N	(Cal. /exp.) S
1	2a	$C_{13}H_{14}N_2O_2$	230.26	71%	116-118	12.10/12.17	-
2	2b	$C_{14}N_{16}N_2O_2$	244.29	71%	100-102	11.41/11.47	-
3	2c	$C_{13}H_{14}N_2O_3$	246.26	71%	100-101	11.31/11.38	-
4	2d	$C_{15}H_{18}N_2O_2$	258.32	70%	108-110	10.82/10.84	-
5	3a	$C_{19}H_{22}N_2O_4$	342.39	69%	130-132	8.12/8.18	-
6	3b	$C_{20}H_{24}N_2O_4$	356.42	65%	125-126	7.79/7.86	-
7	3c	$C_{19}H_{22}N_2O_5$	358.39	65%	120-121	7.76/7.82	-
8	3d	$C_{20}H_{25}N_3O_4$	371.43	67%	120-122	11.25/11.31	-
9	4a	$C_{22}H_{26}N_2O_4S_2$	446.13	71 %	125-127	6.20/6.27	14.32/14.36
10	4b	$C_{23}H_{28}N_2O_4S_2$	460.61	71 %	130-132	6.04/6.08	13.89/13.92
11	4c	$C_{22}H_{26}N_2O_5S_2$	462.58	79 %	125-126	5.98/6.06	13.80/13.86
12	4d	$C_{23}H_{29}N_3O_4S_2$	475.62	74 %	110-112	8.78/8.83	13.40/13.48
13	5a	$C_{26}H_{34}N_4O_4S$	498.64	65 %	120-122	11.16/11.24	6.38/6.43
14	5b	$C_{27}H_{36}N_4O_4S$	512.66	69 %	109-110	10.89/10.93	6.20/6.25
15	5c	$C_{26}H_{34}N_4O_5S$	514.64	68 %	132-133	10.82/10.89	6.19/6.23
16	5d	$C_{27}H_{37}N_5O_4S$	527.68	71 %	114-115	13.21/13.27	6.03/6.08

Table No.2: Spectral data of compound 2-5 (a-d)

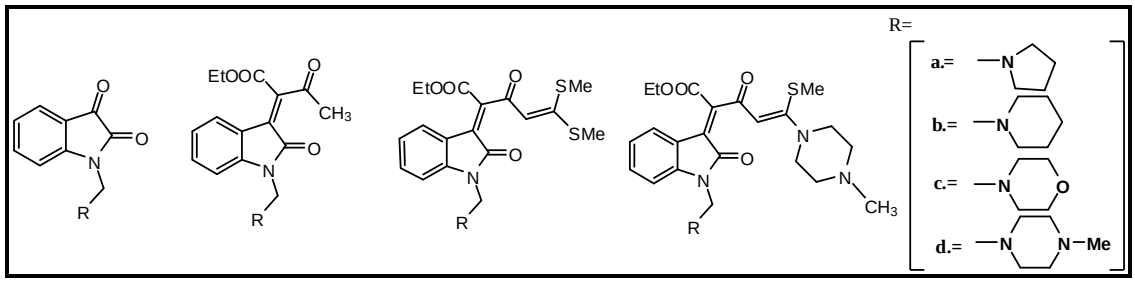
S.No	Compound No.	IR(KBr)CM^{-1}	^{1}HNMR
1	2a	3010[C-H ArH] 1555[C=C str. ArH] 1721[C=O carbonyl] 1403 [C-N]	7.89-7.38[4H, m, Ar-H], 4.03[2H, s, CH_2], 2.51-1.68[8H, m, pyrrolidine-H]
2	2b	3016[C-H ArH] 1550[C=C str. ArH] 1720[C=O carbonyl] 1400 [C-N]	7.89-7.38[4H, m, Ar-H], 4.03[2H, s, CH_2], 2.45-1.53[8H, m, piperidine-H]
3	2c	3018[C-H ArH] 1543[C=C str. ArH] 1705[C=O carbonyl] 1399 [C-N]	7.89-7.38[4H, m, Ar-H], 4.03[2H, s, CH_2], 3.65-2.50[8H, m, morpholine C-H]
4	2d	3025[C-H ArH] 1588[C=C str. ArH] 1723[C=O carbonyl] 1408 [C-N]	7.89-7.38[4H, m, Ar-H], 4.03[2H, s, CH_2], 2.35[8H, m, piperazine C-H], 2.26[3H, s, CH_3]
5	3a	2962[C-H methyl] 1737 [C=O ester] 1450[C=C str. ArH] 1010 [C-N, indole]	8.76-7.31[8H, m, Ar-H], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.27[3H, s, CH_3], 2.51-1.68[8H, m, pyrrolidine C-H], 1.29[3H, t, CH_3]
6	3b	2954[C-H methyl] 1736 [C=O ester] 1454[C=C str. ArH] 1131 [C-N, indole]	8.76-7.31[8H, m, Ar-H], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.27[3H, s, CH_3], 2.45-1.53[10H, m, piperidine C-H], 1.29[3H, t, CH_3]
7	3c	2927[C-H methyl] 1723 [C=O ester] 1471[C=C str. ArH] 1113 [C-N, indole]	8.76-7.31[8H, m, Ar-H], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.27[3H, s, CH_3], 3.65-2.50[8H, m, morpholine C-H], 2.27[3H, s, CH_3], 1.29[3H, t, CH_3]
8	3d	2923[C-H methyl] 1735 [C=O ester] 1466[C=C str. ArH] 1110 [C-N, indole]	8.76-7.31[8H, m, Ar-H], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.27[3H, s, CH_3], 2.35[8H, m, piperazine C-H], 2.26[3H, s, CH_3], 1.29[3H, t, CH_3]
9	4a	2912[C-H methyl] 1720 [C=O carbonyl] 1587[C=C str. ArH] 645 [C-S]	8.76-7.14[4H, m, Ar-H], 6.09[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.80[3H, s, CH_3], 2.51-1.68[8H, m, pyrrolidine C-H], 1.29[3H, t, CH_3]
10	4b	2930[C-H methyl] 1728 [C=O carbonyl]	8.76-7.14[4H, m, Ar-H], 6.09[1H, s, CH],

		1497[C=C str. ArH] 625 [C-S]	4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.80[3H, s, CH_3], 2.45-1.59[10H, m, piperidine C-H], 1.29[3H, t, CH_3]
11	4c	2922[C-H methyl] 1717 [C=O carbonyl] 1537[C=C str. ArH] 689 [C-S]	8.76-7.14[4H, m, Ar-H], 6.09[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.80[3H, s, CH_3], 3.65-2.50[8H, m, morpholine C-H], 1.29[3H, t, CH_3]
12	4d	2924[C-H methyl] 1722 [C=O carbonyl] 1577[C=C str. ArH] 620 [C-S]	8.76-7.14[4H, m, Ar-H], 6.09[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.80[3H, s, CH_3], 2.35[8H, m, piperazine C-H], 2.26[3H, s, CH_3], 1.29[3H, t, CH_3]
13	5a	1715[C=O, carbonyl] 1455[C=C str. ArH] 750[C-N] 645[C-S]	8.74-7.14[4H, m, Ar-H], 5.24[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.79-2.13[8H, m, piperazine C-H], 2.51-1.68[8H, m, pyrrolidine C-H], 2.43[3H, s, CH_3], 2.26[3H, s, CH_3], 1.29[3H, t, CH_3]
14	5b	1705[C=O, carbonyl] 1450[C=C str. ArH] 728[C-N] 643[C-S]	8.74-7.14[4H, m, Ar-H], 5.24[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.79-2.13[8H, m, piperazine C-H], 2.45-1.53[10H, m, piperidine C-H], 2.43[3H, s, CH_3], 2.26[3H, s, CH_3], 1.29[3H, t, CH_3]
15	5c	1712[C=O, carbonyl] 1450[C=C str. ArH] 754[C-N] 659[C-S]	8.74-7.14[4H, m, Ar-H], 5.24[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.79-2.13[8H, m, piperazine C-H], 3.65-2.50[8H, m, morpholine C-H], 2.43[3H, s, CH_3], 2.26[3H, s, CH_3], 1.29[3H, t, CH_3]
16	5d	1718[C=O, carbonyl] 1440[C=C str. ArH] 744[C-N] 610[C-S]	8.74-7.14[4H, m, Ar-H], 5.24[1H, s, CH], 4.20[2H, q, CH_2], 4.03[2H, s, CH_2], 2.79-2.13[8H, m, piperazine C-H], 2.35[8H, m, piperazine C-H], 2.43[3H, s, CH_3], 2.26[3H, s, CH_3], 1.29[3H, t, CH_3]



1.001 **1.002** **1.003**

Figure No.1: *α*-Oxoketene N, S-aminal (1.001), N, N-aminal (1.002) and N, O-aminal (1.003)



1 **2** **3** **4** **5**

Figure No.2: Structure of compounds whose synthesis is described in this research paper

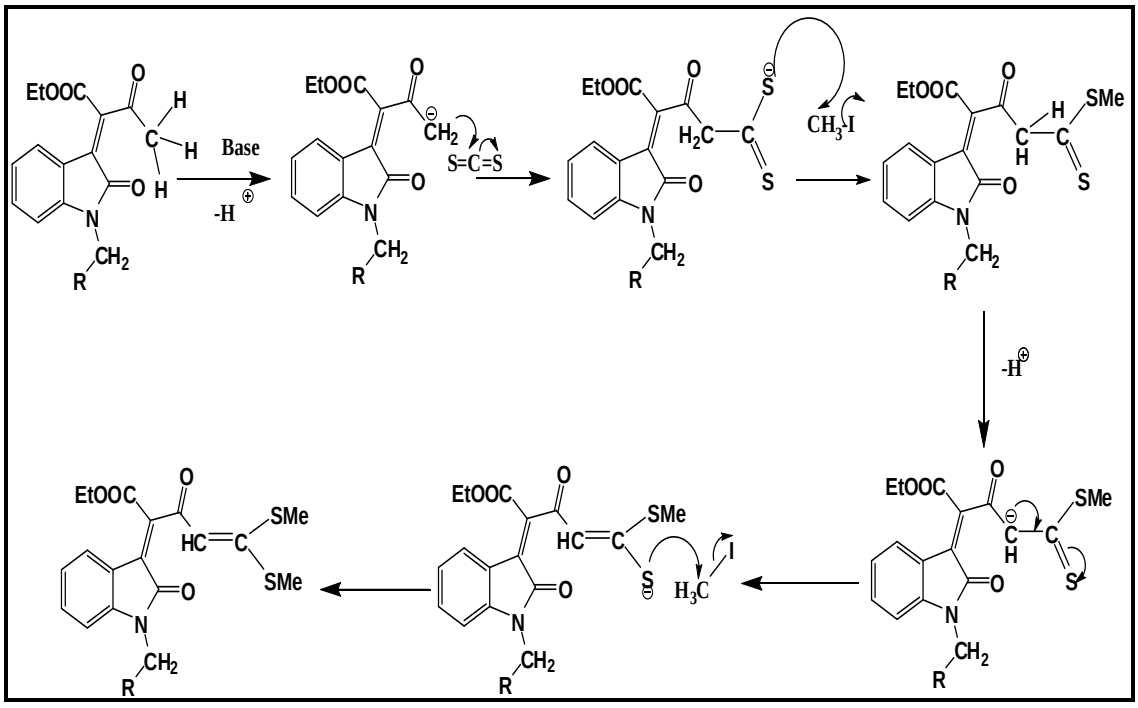


Figure No.3: General mechanism of formation of 4(a-d) from 3(a-d)

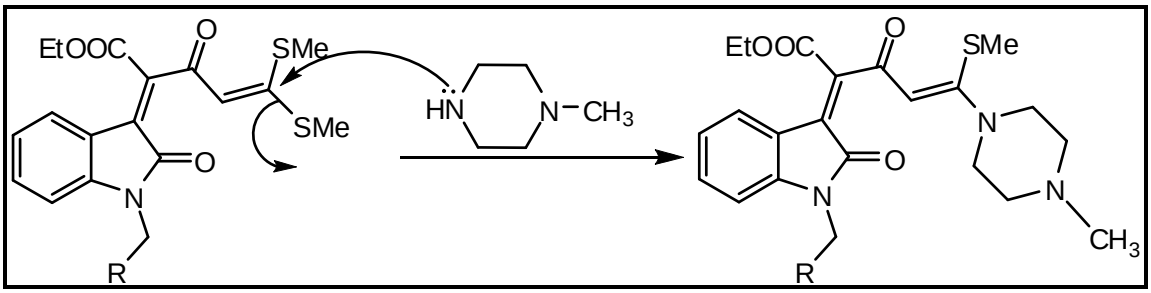
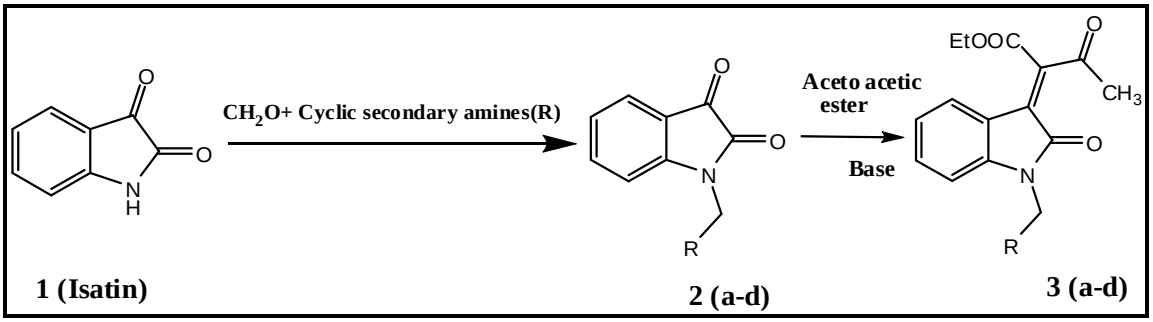
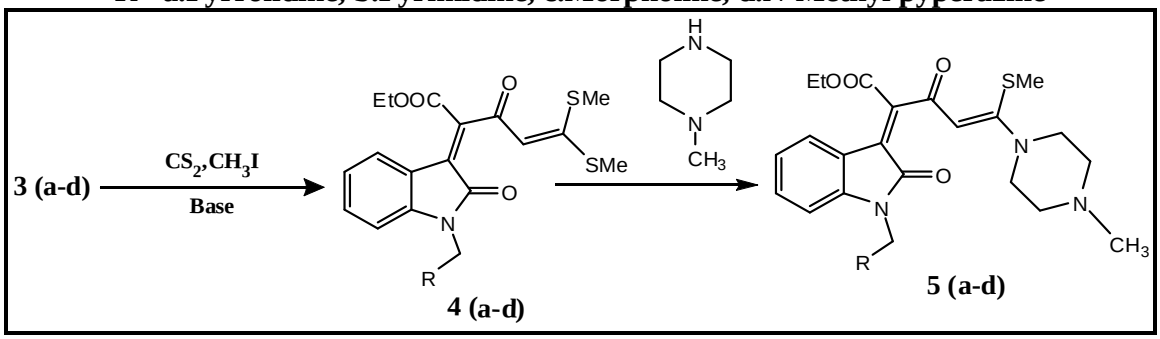


Figure No.4: General mechanism of formation of 5(a-d) from 4(a-d)



Scheme-1

R= a.Pyrrolidine, b.Pyrimidine, c.Morpholine, d.N-Methyl pyperazine



Scheme-2

CONCLUSION

In conclusion, several novel intermediates 5(a-d) used many important chemical reactions and useful in synthesis of many medicinal compounds having important biological activity as antibacterial, anti-fungal have been synthesized in this paper. The study provided an elegant method for the synthesis of N, S- aminal derivatives 5(a-d) of biological interest from the corresponding oxoketene dithioacetals 4(a-d).

ACKNOWLEDGEMENT

The authors are thankful to the Director SAIF, Punjab University Chandigarh (India) for providing spectral and analytical data of compounds and to the Department of Science and Technology (DST), New Delhi (India) for providing the financial assistance to 'Banasthali Center for Education and Research in Basic Sciences' under their CURIE (Consolidation of University Research for Innovation and Excellence in Women Universities) Programme. We are also thankful to Department of Biotechnology of Banasthali University for providing help in carrying out the antimicrobial screening.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Junjappa H, Ila H, Asokan C V. Alpha.-Oxoketene-S,S-, N,S-and N,N-Acetals: Versatile Intermediates in Organic Synthesis, *Tetrahedron*, 46, 1990, 5423-5506.
2. Zhao Y, Zhang W, Wang S and Liu Q. Ethynyl ketene-S,S-acetals: the highly reactive electron-rich dienophiles and applications in the synthesis of 4-functionalized quinolines via a one-pot three-component reaction, *J. Org. Chem.*, 72, 2007, 4985-3.
3. Moussounga J, Bouquant J and Chuche J. Chem Inform Abstract: A New Two-Step Synthesis of α-Oxo Ketene O, N-Acetals, *Synthesis*, 72, 1994, 483-485.
4. Mahata P K, Venkatesh C, Syam Kumar U K, Ila H and Junjappa H. A facile method for the synthesis of oxoketene-N, S- and N-N acetals from reactions of amino compounds, *J. Org. Chem*, 68, 2003, 3966-3975.
5. Sommen G, Comel A and Kirsch G. Preparation of thieno [2,3-b]pyrroles starting from ketene-N,S-acetals, *Tetrahedron*, 59, 2003, 1557-1564.
6. Ma Y, Wang M, Li D, Bekturhun B, Liu J and Liu Q. *α*-Alkenoyl ketene S, S-acetal-based multicomponent reaction:an efficient approach for the selective construction of polyfunctionalized cyclohexanones, *Journal of Organic Chemistry*, 74(8), 2009, 3116-3121.
7. Rahman A, Vishwakarma J N, Yadav R D, Ila H and Junjappa H. Reaction of *α*-ketoketene *S, N*-acetals with Hydroxylamine: a facile general route to 5-aryl-3-(*N*-arylamino, *N*-alkylamino, or *N*-azacycloalkyl)-isoxazoles, *Synthesis*, 247, 1984, 2169-2179.
8. Aggarwal V, Singh G, Ila H and Junjappa H. Reaction of *a*-ketoketene *S, N*-acetals with cyanoacetamide: a new general method for substituted and fused 4-(*N*-alkylamino-, *N*-arylamino-, or *N*-morpholino)-3-cyano-2(1*H*)-pyridones, *Synthesis*, 214, 1982, 3116-3121.
9. Chauhan S M S and Junjappa H. A novel one step synthesis of 5(3)-methylthio-, alkoxy-, amino- and hydroxypyrazoles using *α*-ketoketene-S, S-diacetals", *Synthesis*, 12, 1975, 798-801.
10. Mahata P K, Venkatesh C, Syam Kumar U K, Ila H and Junjappa H. Reaction of *α*-oxoketene-N,S-arylaminoacetals with Vilsmeier reagents: an efficient route to highly functionalized quinolines and their benzo/hetero-fused analogues, *Journal of Organic Chemistry*, 68(10), 2003, 3966-3975.
11. Junjappa H, Ila H and Asokan C V. α-Oxoketene-, S-, N,S- and N,N-acetals: Versatile intermediates in organic synthesis, *Tetrahedron*, 46, 1990, 5423.
12. Huang Z T and Shi X. Synthesis of heterocyclic ketene N, S-acetals and their reactions with ester of α, β unsaturated acids, *Synthesis*, 1990, 162.
13. Hojo M, Masuda R, Okada E, Yamamoto H, Morimoto K, Okada K. One pot synthesis and conformational features of N, N^1- disubstituted ketene aminals, *Synthesis*, 1990, 195.
14. Ren Z X, Wang L B, Li Z J, Huang Z T. Stereo selective synthesis of O-galactosides of benzoyl-substituted heterocyclic ketene aminals, *Carbohydrate Research*, 309(3), 1998, 251-259.
15. Zhao M X, Wang M X and Huang Z T. Examination of an unusal substituent effect on the reaction of heterocyclic ketene aminals with ethyl propiolate, *Tetrahedron*, 58, 2002, 1309-1316.
16. Li Z J, Yang Q, Chen X M and Huang Z T. Nitration of Benzoyl-Substituted Ketene Dithioacetals and Heterocyclic Ketene Aminals, *Synthesis*, 1999, 231.
17. Nie X P, Wang M X and Huang Z T. Reaction of heterocyclic ketene aminals with alpha-bromoketones: A convenient synthesis of pyrrole-fused 1,3-diazaheterocycles, *Synthesis*, 2000, 1439.
18. Barun O, Mohanta P K, Ila H and Junjappa H. An efficient general synthesis of novel functionalized tetrahydroisoquinoline derived

enamines via polarized ketene N, S-acetals *Synlett*, 2000, 653.
19. Loghmani Khouzani H, Sadeghi M M and Ghorbani M H. A Convenient Synthesis of Some-Oxoketene-*N,S*- and *N,N*-Acetals, *Journal of the Iranian Chemical Society*, 3(4), 2006, 360-366.
20. Chakrabarti S, Panda K, Ila H and Junjappa H. Synthesis of functionalized 1,2,3,4-tetrahydro-β-carboline derived enamines through bischler-napieralski type cyclization of polarized ketene N, S-acetals, *Synlett Synlett*, 309, 2005, 244-253.
21. Kumar A, Aggarwal V, Ila H and Junjappa H. A novel and convenient synthesis of 2-amino-4-(N-alkyl-N-arylamino)-pyrimidines using polarized ketene S,S- and S,N-acetals Synthesis, *Synthesis*, 41, 1980, 748.
22. Huang Z T and Wang M X. The reaction of benzoyl-substituted heterocyclic ketene aminals with aryl azides, *J. Org. Chem*., 57, 1992, 184.
23. Huang Z T and Wang M X. The synthesis and tautomerization of ketene aminals with benzimidazoline ring, *Tetrahedron*, 48, 1992, 2325.
24. Wang M X, Liu Y and Huang Z T. Novel and convient synthesis of polyfunctionalized quinolines quinolones and their annilation reaction, *Tetrahedron Lett.*, 42, 2001, 2553.
25. Mahata P K, Venkatesh C, Syam Kumar U K, Ila H, Junjappa H. Reaction of alpha-oxoketene-N,S-arylaminoacetals with Vilsmeier reagents: an efficient route to highly functionalized quinolines and their benzo/hetero-fused analogues, *J. Org. Chem*., 68, 2003, 3966.
26. Mahata P K, Syam Kumar U K, Sriram V, Ila H and Junjappa H. 1-Bis(methoxy)-4-bis(methylthio)-3-buten-2-one: useful three carbon synthon for synthesis of five and six membered heterocycles with masked (or unmasked) aldehyde functionality, *Tetrahedron*, 59, 2003, 2631.

Please cite this article in press as: Rachna Mishra and Dharma Kishore *et al.*, A Facile Method for the Synthesis of Oxoketene N, S-Acetals/Aminals from the Reaction of Amino Compound with Oxoketenedithioacetals, *Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry*, 2(4), 2014, 258 - 267.