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### SYNTHESIS AND SEMIEMPIRICAL CALCULATIONS OF THIAZOLIDINONE AND IMIDAZOLIDINONE DERIVATIVES OF $\alpha$ -DIONES

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## SYNTHESIS AND SEMIEMPIRICAL CALCULATIONS OF THIAZOLIDINONE AND IMIDAZOLIDINONE DERIVATIVES OF $\alpha$ -DIONES

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*The condensation reactions of  $\alpha$ -diones with rhodanine and creatinine to give acenaphthylidene, isatylidene and thioisatylidene derivatives, which may act as potential bioactive compounds, are described. The synthesized compounds have been characterized by elemental analysis and spectral studies, as well as by molecular modelling using PCWIN model.*

**Keywords:** Acenaphthylidene; creatinine; isatylidene and thioisatylidene derivatives; rhodanine; semiempirical calculations; spectral characterization

## INTRODUCTION

Heterocyclic compounds derived from  $\alpha$ -diones are important organic compounds that are found in various natural products as fundamental nuclei and are well recognized for their pharmacological and biochemical uses.<sup>1,2</sup> For the present study we have chosen three  $\alpha$ -diones, viz. acenaphthacene- $\alpha$ -dione (**I**), 1H-indol-2,3-dione derivatives (isatins) (**IIa–c**), and 5-methyl-benzo[b]thiophene-2,3-dione (thioisatin) (**III**), because of their high reactivity profile in condensation and 1,3-dipolar cycloaddition reactions. Acenaphthacene- $\alpha$ -dione, a tricyclic symmetrical molecule, undergoes a variety of reactions.<sup>3,4</sup> Isatin<sup>5</sup> and

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thioisatine<sup>6</sup> derivatives also undergo various reactions, including condensation reactions. Recently we have reported 1,3-dipolar cycloaddition reactions of these  $\alpha$ -diones with various cyclic secondary amino acids.<sup>7–9</sup> However, their condensation reactions with several five-membered heterocyclic systems containing two hetero-atoms have remain unexplored. For example, 2-thioxo-4-thiazolidinone (rhodanine) and its derivatives are unique heterocyclic molecules possessing amide and keto groups. In addition, it has an active methylene group. These functional characteristics play an important role in governing their condensation reactions.<sup>10</sup> Furthermore, rhodanine-incorporating toxophores such as C=O and C=S are expected to display strong biological activities.<sup>11,12</sup> Similarly, N-methyl-2-imino-4-imidazolidinone (creatinine) also possess pronounced antifungal activities<sup>13</sup> and undergoes several condensation reactions.<sup>14</sup> Thus in continuation of our work on the 1,3-dipolar cycloaddition and condensation reactions of  $\alpha$ -diones, we herein report the coupling of these  $\alpha$ -diones with 5-membered heterocyclic systems to get new heterocyclic compounds of better biological activity.

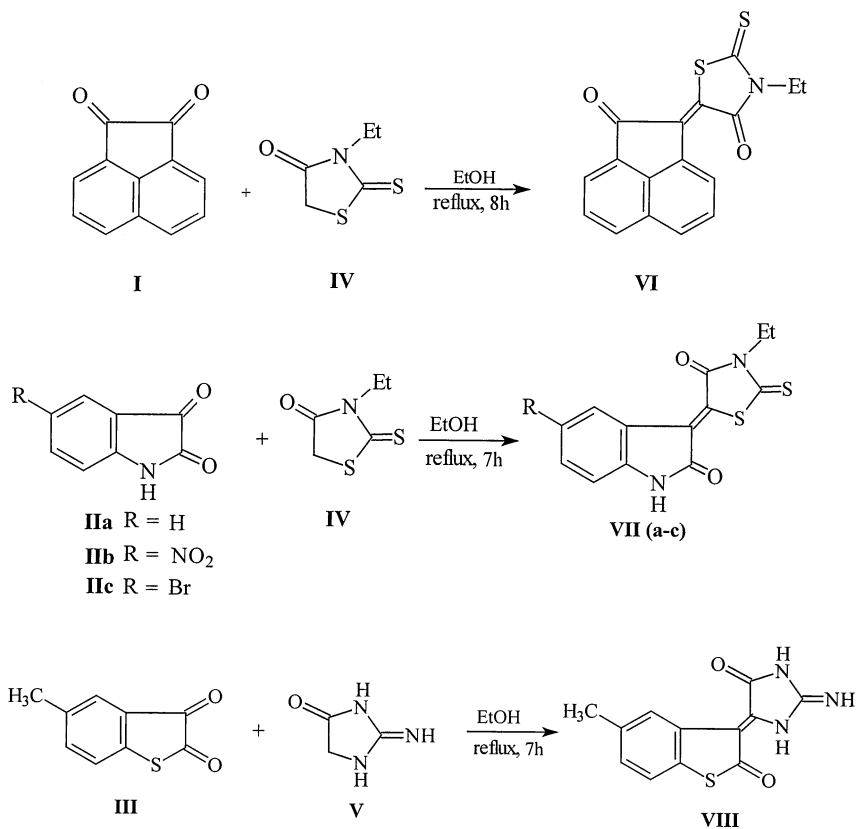
## RESULTS AND DISCUSSION

The reaction of acenaphthacene-1,2-dione (**I**) with 3-ethylrhodanine (**IV**) was carried out in the molar ratio of 1:1 in refluxing absolute ethanol for 8 h, whereby 5, 1'-dehydro[3-ethyl-2-thioxo-4-thiazolidinone]acenaphthylene-2'-one (**VI**) was produced in 74% yield (Scheme 1). Similarly, isatin, and its derivatives (**IIa–c**) with 3-ethylrhodanine (**IV**) afforded isatylidine derivatives (**VIIa–c**) in 62–80% yield. Analogous reaction of thioisatin (**III**) was carried out with creatinine (**V**), and the product 5,3'-dehydro 1-methyl-2-imino-4-imidazolidinone]-5-methylbenzo[b]thiophene-2'-one (**VIII**) was isolated in 70% yield. All the products were purified by column chromatography and recrystallization. Physical properties and analytical data of the condensation products are given in Table I.

The formation of a monocondensation product in all of the above reactions may be explained by the Knoevenagel-type condensation of active methylene heterocycles with the keto group of the  $\alpha$ -diones and is in conformity with the previously reported reactions of dihalo derivatives of acenaphthacene-1,2-dione with pseudothiohydantoin by Karishin and Samusenko.<sup>15</sup> These observations have been further supplemented by semiempirical calculations.

**TABLE I** Physical and Analytical Data of Compounds

Compound no.	Physical state	Molecular formula	m.p. (C)	Yield (%)	Elemental analysis calcd. (found)		
					C	H	N
<b>VI</b>	Bright orange crystals	$C_{17}H_{11}NO_2S_2$	210	74	62.77 (62.71)	3.38 (3.35)	4.30 (4.28)
<b>VIIa</b>	Dark orange feathers like	$C_{13}H_{10}N_2O_2S_2$	260	75	53.89 (53.74)	3.45 (3.42)	9.65 (9.61)
<b>VIIb</b>	Shiny maroon crystals	$C_{13}H_9N_3O_3S_2$	280	62	46.56 (46.53)	2.68 (2.62)	12.53 (12.5)
<b>VIIc</b>	Dark magenta colored crystals	$C_{13}H_9N_2O_2S_2Br$	298	80	42.27 (42.22)	2.44 (2.41)	7.58 (7.55)
<b>VIII</b>	Light yellow powder	$C_{13}H_{11}N_3O_2S$	110	70	57.59 (57.57)	4.02 (4.00)	15.38 (15.36)

**SCHEME 1**

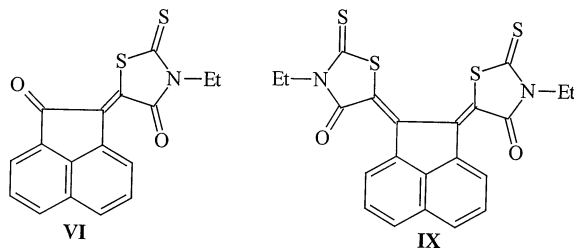


FIGURE 1

## SEMIEMPIRICAL CALCULATIONS

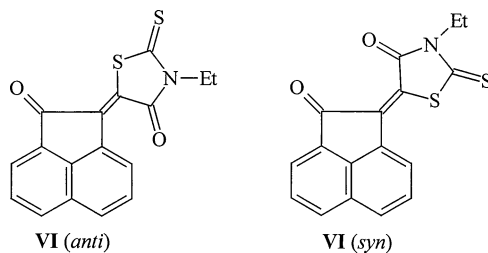
The formation of monocondensation product under experimental conditions has been further supplemented by semiempirical molecular methods using Mopac 6.0 programme with AM1 hamiltonians. The condensation of active methyl heterocycles with  $\alpha$ -diones, may take place in two manners. One in which the active methylene group condenses with only one of the two carbonyl groups of  $\alpha$ -diones, giving rise to monocondensation product (**VI**), and the other in which both the carbonyl groups of  $\alpha$ -dione condenses to produce biscondensation product (**IX**) (Figure 1).

The experimental observation, i.e., the exclusive formation of the monocondensation product, is supported by theoretical studies. The results are given in Table II. It may be noticed from the table that the heat of formation of the monocondensation product is lower than the corresponding biscondensation product, suggesting their feasibility and thermodynamic stability, thereby ruling out the formation of biscondensation product. The monocondensation product may exist in two configurations, viz. (**VI**) *syn* and (**VI**) *anti* (Figure 2).

Out of these the predominant isomers may be explained by  $\Delta H_f$  and electronic factors (Table II). The formation of *anti* isomer may be attributed to the relaxation from O—O repulsion in contrast to *syn*

TABLE II  $\Delta H_f$  (K.cal./mole) of Compounds

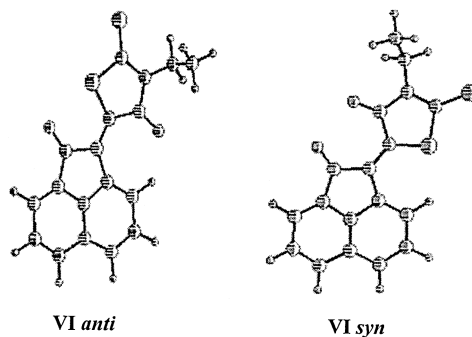
Compound no.	Mono (anti)	Mono (syn)	bis
<b>VI</b>	48.0137	48.4175	97.9891
<b>VIIa</b>	26.1426	26.5196	61.6526
<b>VIIb</b>	30.8918	31.0322	66.6076
<b>VIIc</b>	31.7626	32.0154	67.4164
<b>VIII</b>	37.68	39.72	108.40

**FIGURE 2**

isomer. Optimized geometries of *syn* and *anti* isomers are given below in Figure 3.

## SPECTRAL STUDIES

In the infrared (IR) spectrum of a typical compound (**VI**) the carbonyl group appeared at  $1700\text{ cm}^{-1}$ , C=S group at  $1250\text{ cm}^{-1}$ , C=C at  $1640\text{ cm}^{-1}$ , and C-H<sub>aro</sub> at  $3000\text{ cm}^{-1}$ . In its  $^1\text{H}$  NMR spectrum a triplet appeared at  $\delta$  1.2 due to  $-\text{CH}_3$  protons, a quartet at  $\delta$  4.2 due to N-CH<sub>2</sub> group, two doublets at  $\delta$  7.2 and  $\delta$  7.7, and two triplets at  $\delta$  7.9 and  $\delta$  8.0 ppm appeared due to aromatic protons. In the  $^{13}\text{C}$  NMR spectrum signals appeared at  $\delta$  197.3 and  $\delta$  195.2 due to  $>\text{C}=\text{O}$  carbons, at  $\delta$  167.7 due to  $>\text{C}=\text{S}$ , at  $\delta$  142.2–127.9 due to aromatic carbons, at  $\delta$  122.6 and  $\delta$  126.8 due to olefinic carbons, at  $\delta$  39.5 due to N-CH<sub>2</sub>, and at  $\delta$  12.4 ppm due to  $-\text{CH}_3$  carbons. Finally, conclusive evidence has been gathered from its mass spectrum in which it showed a molecular ion peak at  $m/z$  325 (90%). The spectral data of all novel heterocycles have been summarized in Table III.

**FIGURE 3**

**TABLE III** Spectral Data of Compounds

Compound no.	IR (cm <sup>-1</sup> )	<sup>1</sup> H δ (ppm)	<sup>13</sup> C δ (ppm)
<b>VI</b>	3000, 1700, 1640, 1250, 780	1.2(t), 4.2(q), 7.2(d), 7.7(t), 7.9(t) 8.0(d)	12.4, 39.5, 122–142, 167.7, 197.3
<b>VIIa</b>	3200, 1700, 1650, 1250, 750	1.3(t), 4.2(q), 6.9(d), 7.0(t), 7.3(t), 7.5(d), 10.6(s)	—
<b>VIIb</b>	3200, 1700, 1600, 1450, 1350, 1250, 750	1.3(t), 4.2(q), 7.1(d), 7.4(s), 8.3(d), 11.5(s)	11.9, 39.0, 123.5, 127.7, 168, 185
<b>VIIc</b>	3300–3100, 1700, 1630, 1250, 780, 550	1.3(t), 4.2(q), 6.8(d), 7.5(d), 7.6(s), 9.1(s),	—
<b>VIII</b>	3200, 2950, 1750, 1550	2.2(s), 3.4(s), 4.2(s), 7.3(m), 8.6(s)	—

## EXPERIMENTAL

All the reactions were carried out under a nitrogen atmosphere. Ethanol was dried by refluxing with anhydrous calcium oxide. Melting points of newly synthesized compounds were determined in open glass capillaries and are uncorrected. The IR spectra were recorded on a Nicolet Magna IR<sup>TM</sup> spectrometer model on KBr pellets. The <sup>1</sup>H NMR spectra were recorded on a Bruker 300 MHz model using tetramethylsilane as an internal standard. The <sup>13</sup>C NMR spectra were recorded on a Bruker 300 MHz model. Chemical shifts are given in δ ppm values. Mass spectra were recorded on a JEOL-SX 102 (FAB). Most of the spectra were recorded in CDCl<sub>3</sub> at CDRI, Lucknow, India. Elemental analysis were performed by Perkin Elmer series C, H, N, and S analyzer-2400.

A representative method for the synthesis of compound (**VI**) is described herein.

A reaction mixture of acenaphthacene-1,2-dione (**I**, 0.364 g; 2 mmol) and 3-ethylrhodanine (**VI**, 0.266 g; 2 mmol) in the equimolar ratio was refluxed for 6 h in absolute ethanol (40 ml). The reaction was monitored by TLC till complete consumption of the reactants. The crude product was subjected to column chromatography using silica gel column using solvents of rising polarity. The compound (**VI**) was obtained from pet ether-chloroform (1:2) mixture as orange solid (0.48 g, 74% yield). It was recrystallized from chloroform-n-hexane (1:5) as orange needles, m.p. 210°C.

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