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Synthesis and semiempirical calculations of imidazolidine, isoxazolone and thiazoline thiol derivatives of acenaphthylene-1,2-dione

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A convenient synthesis of acenaphthylidene derivatives involving Knovenaegel type condensation of imidazolidine, oxazolidine and thiazolidine derivatives with acenaphthylene-1,2-dione has been described. The structures of newly synthesized products have been established by spectral technique. Exclusive formation of *anti*-monocondensation products has been explained on the basis of semiempirical calculations.

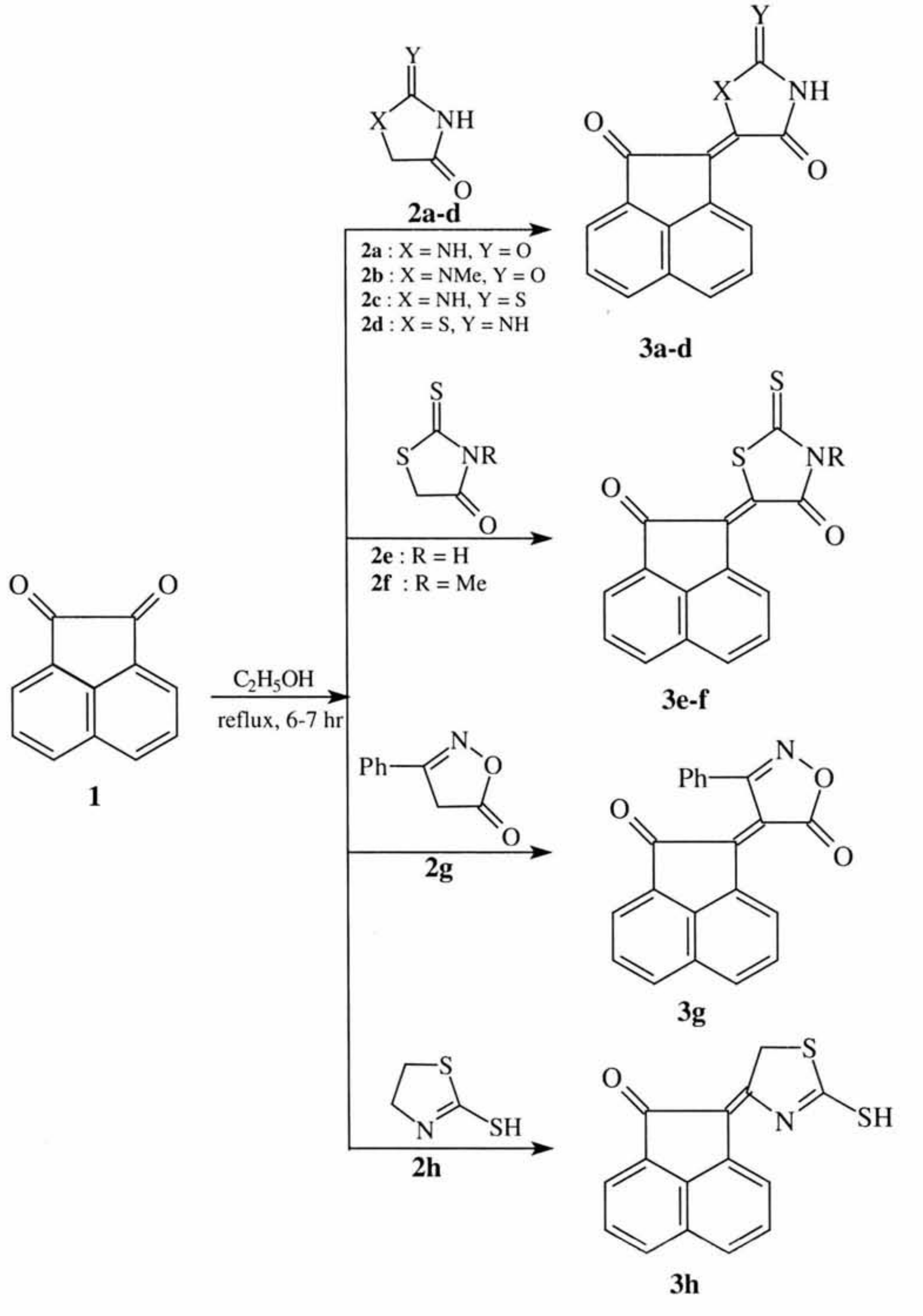
1,2-Dicarbonyl compounds are well-recognized for their versatility towards number of organic reactions[1,2] and possess a wide spectrum of biological activities[3,4]. In our laboratory we have investigated a variety of reactions of indol-2,3-diones *viz.* 1,3-dipolar cycloaddition reactions[5-7] with secondary cyclic α-amino acids, photochemical, thermal and basic reactions[8-10] with various five-membered active methylene heterocycles, etc. Acenaphthylene-1,2-dione is an α-diketone having tricyclic symmetrical structure. Both the keto groups are chemically equivalent. Literature survey revealed that cyclocondensation reactions[11], Diels-Alder reactions[12] and 1,3-dipolar cycloaddition reactions[13] have been examined. It has been reported earlier by Karishin *et al.*[14] that one of the carbonyl group of dihalo derivative of acenaphthylene-1,2-dione condenses with active methylene of 2-imino-4-thiazolidinone. In the light of the above results and prompted by our earlier studies we have extended this work to the reactions of acenaphthylene-1,2-dione with several active methylene heterocycles. These heterocycles are found in various natural products having medicinal and pharmacological properties[15-17] and hence the resulting products would be of significant medicinal importance.

The stereochemistry of the products has been ascertained by semiempirical molecular orbital calculations where *anti*-monocondensation product is favoured and is supplemented by experimental work. The results are presented herein.

The reaction of acenaphthylene-1,2-dione **1** and five-membered heterocycles **2a-h** have been carried out in equimolar ratio in refluxing ethanol for 6 hr whereby it afforded 1′,5-dehydro{imidazolidine-2,4-dione}acenaphthylen-2′-one **3a-h** (**Scheme I**). The structures of the products were ascertained from their spectral features. The IR spectrum of typical **3f** showed absorption bands at 2900 and 1700 cm^{-1} assignable to aliphatic C-H and >C=O vibrations, fairly strong bands at 1270 and 710 cm^{-1} were due to >C=S group and C-S-C vibration, respectively. Its ^1H NMR spectrum showed singlet at δ 2.50 for N-CH_3 protons along with a multiplet in the region of δ 7.78-8.18 (6ArH), signal for imino proton appeared at δ 10.14 ppm. Typical ^{13}C NMR spectrum of **3f** displayed signal for N-methyl carbon at δ 36.09, olefinic carbons at δ 109.65 and 108.90, aromatic carbons in the region of 122.86-142.04, thiocarbonyl carbon at δ 167.23, carbonyl carbons at δ 178.96 and 184.32 ppm. Additional evidence was gathered from the mass spectrum. The mass spectrum of **3f** showed [M^+] peak at m/z 311 (60%) confirming the formation of only monocondensation product. The other prominent peaks were seen at m/z 210 (100%) [M^+-C_3H_3NOS], 182 (50%) [M^+-C_3H_3NOS, -CO], 150 (7%) [M^+-C_3H_3NOS, -S], 138 (20%) [M^+-CO, -$C_4H_3NOS_2$]. Physical and spectral data have been tabulated in **Table I** and **Table II,** respectively.

Semiempirical Calculations

In order to ascertain the configuration of condensation products, semiempirical calculations were performed using MOPAC6 program. The results are compiled in **Table III**. It may be noticed from **Table III** that the heat of formation of the monocondensation products is much lower than the



Scheme I

corresponding biscondensation products, suggesting their feasibility and thermodynamic stability. The monocondensation products may exist in two configurations *viz. syn* and *anti*. Out of these which isomer predominates can be explained by ΔH_f, electronic and steric factors. The difference between the heats of formation between **3a** (*anti-syn*) is about 111 Kcal/mol whereas in case of **3c** this difference is 24 Kcal/mol. In case of imidazolidinone derivatives **3a,c**, the favourable isomer is *anti*. It may be attributed to the formation of hydrogen bond between the imino proton and carbonyl group of acenaphthene

Table I — Physical and analytical data of acenaphthylidene derivatives **3a-h**

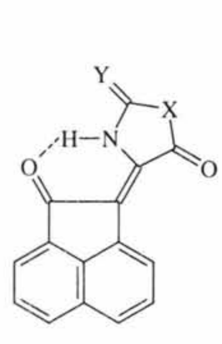
Compd	Physical state	m.p. °C	Mol. formula	Yield (%)	Found % (Calcd) C	H	N
3a	Yellow fibrous solid	280	$C_{15}H_8N_2O_3$	82	68.04	2.89	10.47
					(68.18	3.03	10.06)
3b	Bright orange solid	240	$C_{16}H_{10}N_2O_3$	88	69.04	3.61	9.94
					(69.07	3.60	10.07)
3c	Orangish brown solid	160 (dec.)	$C_{15}H_8N_2O_2S$	76	64.35	2.80	10.89
					(64.29	2.86	10.0)
3d	Buff solid	210	$C_{15}H_8N_2O_2S$	87	65.33	2.73	11.31
					(64.29	2.86	10.0)
3e	Orange powder	310	$C_{15}H_7NO_2S_2$	90	60.21	2.38	4.91
					(60.61	2.36	4.71)
3f	Bright orange solid	270 (dec.)	$C_{16}H_9NO_2S_2$	80	61.88	2.75	4.52
					(61.74	2.89	4.50)
3g	Chocolate brown powder	130	$C_{21}H_{11}NO_3$	78	77.54	3.39	4.31
					(76.13	3.32	4.22)
3h	Yellow rods	210	$C_{15}H_9NOS_2$	82	63.68	3.04	4.85
					(63.60	3.18	4.95)

Table II— Spectral data of acenaphthylidene derivatives **3a-h**

Compd	IR (cm^{-1})	^1H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
3a	3360-3100 (NH), 3050 (C-H_{aro}), 1720 (>C=O), 1620 (NH_{def})	7.89-8.46 (m, 6ArH), 10.39 (s, NH), 10.62 (s, NH)	-
3b*	3300-3190 (NH), 3100 (C-H_{aro}), 2890 (C-H_{ali}), 1725 (>C=O), 1420 (C-N)	2.81 (s, NCH_3), 7.56-8.39 (m, 6ArH), 10.46 (brs, NH)	189.75 (>C=O), 171.05 (NMeCO), 169.75 (NHCO), 144.16-118.67 (10 ArC), 109.10, 108.73 (C=C), 28.34 (NCH_3)
3c	3300-3100 (NH), 3050 (C-H_{aro}), 1700 (>C=O), 1390 (C-N), 1250 (>C=S)	7.51-8.22 (m, 6ArH), 9.76 (s, NH), 10.56 (s, NH)	189.35, 175.42 (>C=O), 169.13 (>C=S), 140.77-121.49 (10 ArC), 107.33, 104.04 (C=C)
3d	3300 (NH), 3010 (C-H_{aro}), 1710 (>C=O), 1600 (C=N), 700 (C-S-C)	3.90 (s, >C=NH), 7.65-8.26 (m, 6ArH), 8.96 (s, NH)	-
3e	3350-3250 (NH), 3060 (C-H_{aro}), 1710 (>C=O), 1270 (>C=S), 700 (C-S-C)	7.12-8.19 (m, 6ArH), 9.19 (s, NH)	-
3f	2900 (C-H_{ali}), 1700 (>C=O), 1270 (>C=S), 710 (C-S-C)	2.50 (s, NCH_3), 7.78-8.18 (m, 6ArH), 10.14 (s, NH)	184.32, 178.96 (>C=O), 167.23 (>C=S), 142.04-122.86 (10 ArC), 109.65, 108.90 (C=C), 36.09 (NCH_3)
3g	3090 (C-H_{aro}), 1710 (>C=O), 1610 (C=N), 1170 (C-O)	6.42-8.03 (m, 11ArH)	-
3h	3080 (C-H_{aro}.), 2750 (SH), 1700 (>C=O), 1590 (C=N), 695 (C-S-C)	2.50 (s, CH_2), 7.8-8.4 (m, 6 × ArH), 9.98 (s, NH)	187.13 (>C=O), 136.05-127.9 (10 ArC), 120.8 (C-SG), 118.7, 116.5 (C=C), 26.8 (CH_2)

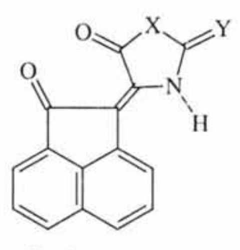
* Mass spectrum (m/z) of 3b: 278[$C_{16}H_{10}N_2O_3$]$^{+\cdot}$ [$M^{+\cdot}$] [42%], 235[$M^{+\cdot}$NHCO] [100%], [$M^{+\cdot}$NHCO,-CO] [42%], 178 [M $^{+\cdot}$NHCO,-CO,-NCH_3] (31%), 166 [M^+-$C_4H_4N_2O_2$] (38%).

nucleus leading to the formation of six membered chelate ring which greatly enhances the stability (**Figure 1**). The O-H bond distance in all the cases is in the expected range of 2.14-2.20 Å. On the contrary the relatively smaller stability of *syn*-isomer may be attributed to the repulsion between the O/O atoms. When this imino proton is substituted by a methyl group as in the case of **3b**, the possibility of hydrogen



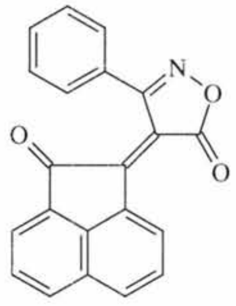
3a, 3c *anti*

3a : X = NH, Y = O
3c : X = NH, Y = S

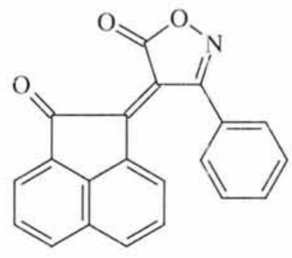


3a, 3c *syn*

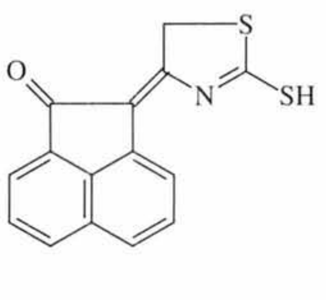
3a : X = NH, Y = O
3c : X = NH, Y = S



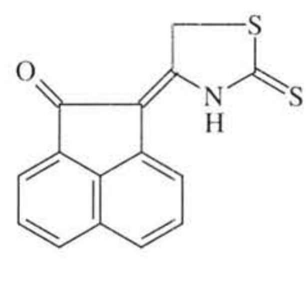
3g *anti*



3g *syn*



3h thiol-form



3h thioketo-form

Table III — Theoretical data of acenaphthylidene derivatives

Compd	ΔH_f (Kcal/mol)			O---H
	Mono (*anti*)	Mono (*syn*)	Bis	(Å)
3a	-34.70	77.06	52.33	2.14
3b	-31.68	-31.35	46.27	-
3c	32.10	56.28	81.58	2.20
3d	-29.88	49.29	221.17	-
3e	-7.09	48.92	111.31	-
3f	48.60	49.20	112.23	-
3g	26.88	70.81	78.71	-
3h	70.30	72.16	152.12	-

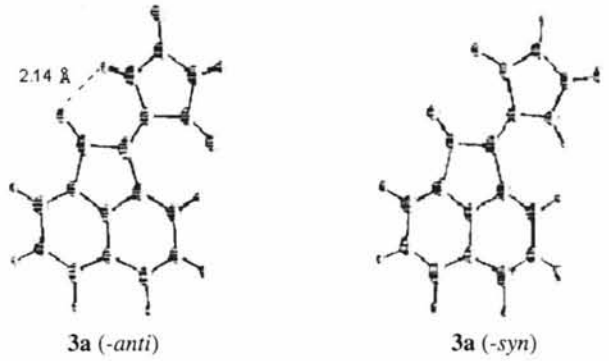
bonding is exhausted. Here both configurations have comparable heat of formation and thereby both are equally probable.

The preferential formation of *anti*-isomer in case of isoxazolone product **3g** could be attributed to the steric hindrance between the phenyl ring of isoxazolone moiety and acenaphthene nucleus as well as repulsion between the oxygen atoms in *syn*-isomer (**Figure 2**).

In the case of **3h**, thiol product is more favourable than the thioketo form because of extended π-conjugation.

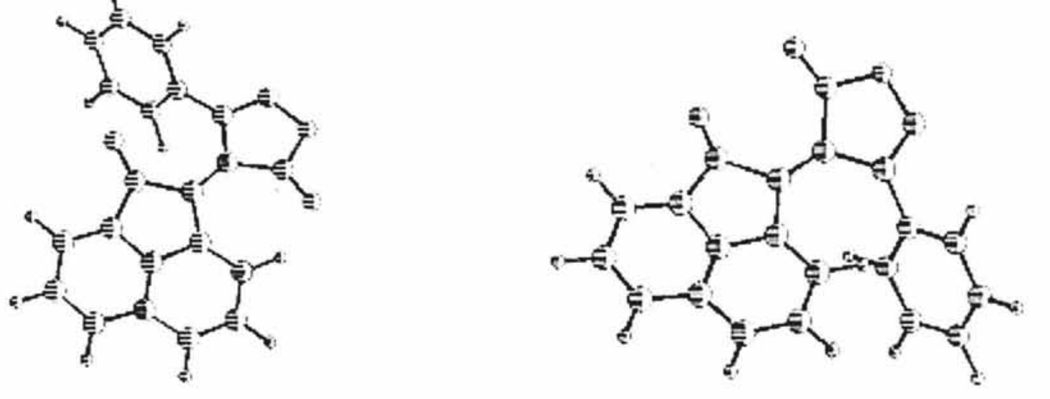
Experimental Section

All the reactions were carried out under nitrogen atmosphere. The melting points were taken in open glass capillaries and are uncorrected. The solvents were purified by standard procedures[18,19]. The IR spectra were recorded on a Nicolet Magna IR™ spectrometer model 550 in KBr pellets. The ^{1}H and



3a (-*anti*) 3a (-*syn*)

Figure 1 — *anti* and *syn* configuration of **3a**



3g (-*anti*) 3g (-*syn*)

Figure 2 - *anti* and *syn* configuration of **3g**

^{13}C NMR spectra were recorded on a Bruker 300 MHz and 75.47 MHz models respectively. Chemical shifts are reported in δ ppm downfield from TMS. Mass spectra were obtained from IICT, Hyderabad. Elemental analyses were performed on Perkin Elmer series C, H, N analyzer 2400. Column chromatography was performed with solvents of rising polarity using silica gel 60 mesh (Merck).

A typical method for the synthesis of acenaphthylene derivative 3a. A mixture of acenaphthylene-1,2-dione **1** (0.36 g, 2 mmoles) and imidazolidine-2,4-dione **2a** (0.40 g, 4 mmoles) was refluxed under nitrogen atmosphere for 6 hr in absolute ethanol. The completion of reaction was monitored by TLC. The crude product obtained was column chromatographed over silica gel whereby petroleum ether-chloroform (1:3) fraction afforded the compound **3a** as yellow fibrous solid, m.p. 280°C, yield 0.62 g (82%).

Acknowledgements

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