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CONDENSATION OF 4-AMINO-3-(2-METHOXY-4-PROPYLPHENOXYMETHYLENE)-(1H)-1,2,4-TRIAZOLE-5-THIONE WITH SOME AROMATIC ALDEHYDES

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SUMMARY

4-Amino-3-(2-methoxy-4-propylphenoxymethylen)-(1H)-1,2,4-triazole-5-thione was prepared from eugenol in Ocimum Sanetum L. essential oil. A series of 7 imines were synthesized from these key compounds by condensing it with different aromatic aldehydes. The structures of these imines were confirmed by EI MS, IR and NMR spectroscopy, in many cases 2D NMR spectra are also used.

I - INTRODUCTION

Eugenol is the main component of *Ocimum sanetum* L. essential oil, which is used in Vietnamese folk medicine. Recently the anticarcinogenic effect of eugenol has detected by a simplified short-term technique based on the inhibition of microsomal degranulation of rat liver microsomes, *in vitro* [1]. Many derivatives of eugenol, such as vanilin, O-methyleugenol and isoeugenol nicotinate are now widely applied in practical [2, 5].

During the last two decades, substituted 1,2,4-triazole and their derivatives are among the various heterocycles that have received considerable attention from chemists, due to their great potential biological activities, including antituberculosis, anticonvulsant, anti-inflammatory, insecticidal, antifungal, analgesic and antitumor properties [3]. It is our interest to combine the 1,2,4-triazole ring with a moiety of eugenol and to study spectroscopic and biological properties of the products.

In previous paper [4] we reported on the preparation and structure of 4-amino-3-(2-methoxy-4-propylphenoxymethylen)-(1H)-1,2,4-triazole-5-thione starting from eugenol, herein some imines derived from this compound are described.

II - EXPERIMENTAL

• *4-amino-3-(2-methoxy-4-propylphenoxy-methylen)-(1H)-1,2,4-triazole-5-thione (**K**)*

This compound was prepared according to the method reported in reference [4].

• *General procedure for preparation of imines **1 ÷ 7***

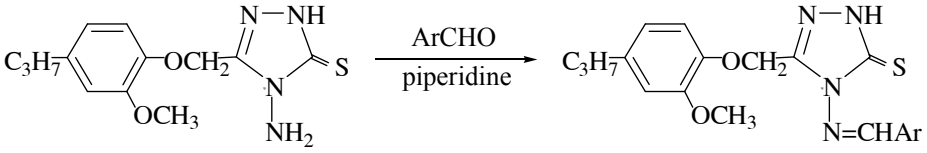
A mixture of (**K**) (0.72 g, 2.5 mmole), an aromatic aldehyde (2.5 mmole) and 2-3 drops of piperidine in a minimum amount of ethanol 99% was refluxed for 12 - 14 hours. The excess of ethanol was removed, the solid thus separated was filtered, washed with ethanol and recrystalized from ethanol or methanol. The results are given in table 1.

• *The IR spectra* were recorded in KBr discs at 400 - 4000 cm^{-1} on a *FTS 60000 Bio-Rad*. The NMR spectra were obtained at room

temperature on a *Bruker Avance 500 MHz* spectrometer in *DMSO-d_6* with TMS as the internal standard. The EI mass spectra were run on a *5989B Hewlett-Packard* mass spectrometer.

III - RESULTS AND DISCUSSION

The reported compounds were prepared from 4-amino-3-(2-methoxy-4-propylphenoxymethylen)-(1H)-1,2,4-triazole-5-thione (**K**) as following:



(K) **(1÷7)**

Results of synthesis of imines **1 ÷ 7** are given in table 1.

Table 1: Results of synthesis of imines **1 ÷ 7**

Compd.	Ar	Solvent for recrystallization	Form and color	Yield, %	M.p., °C	M MS/cal.
1	C_6H_5-	Ethanol	white needle crystals	43	142,2	382/382
2	2-$CH_3C_6H_4$-	Ethanol	white needle crystals	67	171,3	396/396
3	3-$CH_3C_6H_4$-	Methanol	white needle crystals	52	137,0	396/396
4	4-$CH_3C_6H_4$-	Ethanol	yellow needle crystals	50	153,5	396/396
5	2-FC_6H_4-	Ethanol	yellow needle crystals	70	163,0	400/400
6	2-ClC_6H_4-	Ethanol	white needle crystals	46	178,4	-
7	4-ClC_6H_4-	Ethanol	yellow needle crystals	68	161,0	-

The EI MS spectra of **1 ÷ 5** show peaks with m/z values that are in good agreement with their molecular weights (table 1). These compounds have nearly the same pattern of fragmentation in which the ions with m/z ***137*** or m/z ***166*** give the basic peaks.

The main IR bands are listed in table 2. The disappearance of the bands at 3332 and 3206 cm^{-1} on IR spectra of the imine series shows good agreement with the condensation reaction, in which the amino group of compound **K** become the imine group. The band about 3100 cm^{-1} which corresponds to the streching vibration of -NH-, indicating that compounds **1÷7** exist most the time in (1H)-1,2,4-triazole-5-thione form, but does not tautomerize into 3-mercapto-1,2,4-triazole form.

The chemical shifts of protons in eugenol and triazole moieties of **1 - 7** small change from one to another, so they are briefly listed as in figure 1.

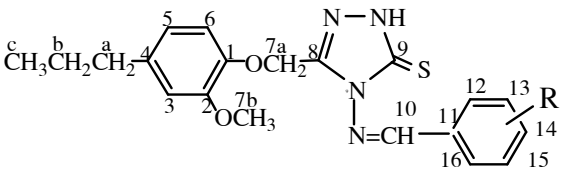


Figure 1: Resonance signals of ^{1}H NMR of 3-(2-methoxy-4-propylphnoxymethylen)- (1H)-1,2,4-triazole-5-thion moiety

H3	H5	H6	H7a	H7b	Ha	Hb	Hc	NH
6.71-6.82	6.63-6.67	6.90-6.97	5.02-5.16	3.64-3.68	2.38-2.45	1.48-1.56	0.82-0.88	13.92-14.19

Table 2: IR bands of studied compounds

Compd.	IR, cm^{-1}				
	ν_{NH}	ν_{CH} (aromatic)	ν_{CH} (saturated)	$\nu_{C=C}$ $\nu_{C=N}$	ν_{C-O}
K	3332; 3206	3030	2950	1601; 1600; 1517	1222
1	3098	3055	2926; 2862	1584; 1506	1161
2	3105	3055	2933; 2869	1597;1518;1497	1140
3	3098	3041	2926	1604; 1578; 1496	1154
4	3098	3062	2926; 2862	1601; 1499	1141
5	3270	3055	2955; 2933; 2869	1611; 1586; 1506	1136
6	3248	3062	2941; 2869	1589; 1509	1141
7	3084	3026	2969; 2933; 2840	1602; 1571; 1502	1166

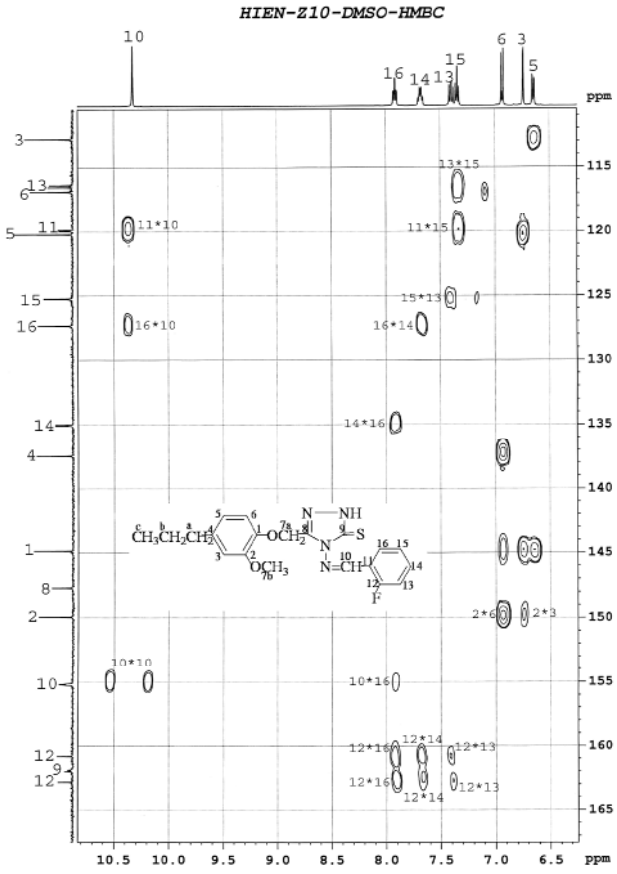


Figure 2: HMBC spectrum of **1**

In contrast, the chemical shifts and the splitting patterns of the aldehyde moiety were much more complex (table 3). In many cases, the assignment of proton signals must base on 2D NMR spectra such as HMQC, HMBC and NOESY.

Table 3: ^{1}H NMR signals of H10 - H17

Compd.	H10	H12	H13	H14	H15	H16	Others
1	9.87, s	7.83, m	7.52, t, (7.0)	7.61, m	7.52, t, (7.0)	7.83, m	-
2	10.25, s	-	7.34, d, (7,5)	7.47, dd, (7.5; 1.0)	7.31, t, (7.5)	7.83, d, (7.0)	H17: 2.50, s
3	9.84, s	7.62, m	-	7.41, m	7.41, m	7.62, m	H17: 2.36, s
4	9.77, s	7.72, m	7.34, d, (8.0)	-	7.34, d, (8.0)	7.72, m	H17: 2.39, s
5	10.33, s	-	7.39, t, (9.0)	7.68, m	7.34, t, (8.0)	7.91, m	-
6	10.69, s	-	7.62, m	7.62, m	7.45, m	7.97	-
7	9.94, s	7.85, d, (8.5)	7.60, d, (8.5)	-	7.60, d, (8.5)	7.85, d, (8.5)	-

The proton in imine group (H10) appears as a singlet at 9.7 - 10.7 ppm. The chemical shift of these imine protons varies from compound to compound, depending on the electron property and the position of the substitutents in the second benzene ring. For example, groups that are electron-donating at *meta* or para position compared to the imine group cause up-field shifts, but when these groups are at *ortho* position, they cause down-field shifts. When these groups are at *ortho* position, the Van der Vaals repulsions between them and the triazole ring diminish the coplanar of the conjugated system. Whereas electron-withdrawing substituents always cause down-field shifts (table 3).

The assignment of the ^{13}C NMR signals in many cases bases on both their chemical shifts and their *2D* spectrum data. For example, the ^{13}C NMR signals of compound **1** are assigned as in figure 2. The chemical shifts of C1-C9 in eugenol and triazole moieties of **1** - **7** small change from one to another, so they are briefly listed as in table 4.

Table 4: ^{13}C NMR signals of C1 - C9 of examined compounds, ppm

C1	C2	C3	C4	C5
144.6-145.7	149.7-150.2	112.6-113.2	136.7-137.6	119.9-120.5
C6	**C7a**	**C7b**	**C8**	**C9**
115.5-116.9	60.8-61.5	55.3-55.9	146.9-148.1	160.6-164.4

The chemical shifts of C10 - C16 in aldehyde moiety of **1** - **7** are listed in table 5. Under the influent of F, in compound 5, the δ_C of C11, C12, C13, C14 are split into 2 components (table 5).

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Table 5: ^{13}C NMR data of C10 - C16 of examined compounds, ppm

Compd.	C10	C11	C12	C13	C14	C15	C16
1	162.0	131.9	128.6	128.9	132.6	128.9	128.6
2	161.9	139.2	131.1	127.1	126.3	130.2	132.8
3	162.0	131.9	138.4	125.9	128.9	128.8	133.3
4	162.0	143.0	129.6	128.6	129.3	128.6	129.6
5	162.0	119.87, 119.95	160.85, 162.87	116.36, 116.53	135.03, 135.10	125.25	127.34
6	162.8	133.9	135.1	127.7	129.8	127.6	130.1
7	162.1	130.9	130.1	129.1	137.2	129.1	130.1