

## Synthesis and Biological Evaluation of Some New Naphthyl Derivatives as Anti-microbial Activity

Amira M. El-Metwally

National Organization for Drug Control and Research,  
NODCAR, Cairo, Egypt.

**I**N CONNECTION with our previous interest in developing new approaches for synthesis of heterocyclic utilizing readily obtainable starting materials, we reported here synthesis of a new heterocyclic utilizing 1-acetyl naphthalene. Reaction of acetyl naphthalene with phenyl hydrazine, thiosemicarbazide and hydroxylamine was carried out to give compounds 1,2,5, respectively. Under claisen condensation acetyl naphthalene reacted with ethylacetoacetate to give acetophenone 3 which converted to pyrazoline derivative 4 by reaction with hydrazine hydrate. On the other hand when acetyl naphthalene reacted with 4-chloro benzaldehyde afforded the chalcone derivative 7, which reacted with hydroxylamine, bromine, hydrazine hydrate and hydrogen peroxide to give compounds 8, 9, 10, 11, respectively. The newly synthesized compounds were tested as anti-microbial activity.

In connection with our previous interest in developing new approaches for synthesis of heterocyclic utilizing readily obtainable starting materials, Naphthalene derivatives were reported to be used in stimulating the release of growth hormone from the pituitary of mammals and to treat medical disorders resulting from a deficiency in growth hormones<sup>(1-4)</sup>, other naphthalene derivatives were used as chiral precursor molecules for host guest interactions<sup>(5)</sup> and were useful as anti-inflammatory drugs for autoimmune disease, anticancer agents and pharmaceuticals for treatment of circulatory organ disease, anti-tumor, antibiotic and cell adhesion inhibitors<sup>(6)</sup>, some naphthalene derivatives were used as intermediates for heat-resistant polyesters, or for modification of other types of polymers<sup>(7,8)</sup>. Thus, it became of interest to collaborate between naphthalene and pyrazoline moiety in order to obtain new derivatives of potential biological activity.

### Results and Discussion

Reaction of 1-acetyl naphthalene with phenylhydrazine in boiling ethanol afforded the corresponding 1-methyl naphthylphenylhydrazide derivative 1. The structure of compound 1 was confirmed from its infrared spectrum which revealed the presence of absorption bands due to  $\nu_{\text{NH}}$  at  $3348\text{ cm}^{-1}$ ,  $\nu_{\text{C-H}}$  at  $2924\text{ cm}^{-1}$ ,  $\nu_{\text{C=N}}$  at  $1650\text{ cm}^{-1}$ ,  $\nu_{\text{C=C}}$  aromatic at  $1624\text{ cm}^{-1}$  and  $\nu_{\text{CH}_3}$  at  $1375\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of compound 1 showed signals at  $\delta$  2.31(3H, s,  $\text{CH}_3$ ),  $\delta$  7.2-8.13 (12H, m, Ar-H) and  $\delta$  10.71(1H, s, NH) ppm. The mass spectrum of compound 1 showed the molecular ion peak at  $m/z$  260(9.82%) and the base peak at  $m/z$  92 (100%). On the other hand the reaction of 1-acetyl

naphthalene with thiosemicarbazide in pyridine gave the corresponding 1-methylnaphthyl thiosemicarbazide derivative 2. The structure of compound 2 was derived from its infrared spectrum which revealed the presence of  $\nu\text{NH}_2$  at  $3390\text{ cm}^{-1}$ ,  $\nu\text{NH}$  at  $3223\text{ cm}^{-1}$ ,  $\nu\text{C=S}$  at  $2154\text{ cm}^{-1}$ ,  $\nu\text{C=N}$  at  $1643\text{ cm}^{-1}$ ,  $\nu\text{C=C}$  at  $1625\text{ cm}^{-1}$  and  $\nu\text{CH}_3$  at  $1373\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of compound 2 showed signals at  $\delta 2.10$  (3H,s, $\text{CH}_3$ ),  $\delta 6.88$ - $7.64$  (7H, m, Ar-H),  $\delta 9.43$  (2H, s,  $\text{NH}_2$ ) and  $\delta 11.1$  (1H, s, NH) ppm. The mass spectrum of compound 2 showed the molecular ion peak at  $m/z$  243(26.9%) and the base peak at  $m/z$  75(100 %).

Claisen condensation in the presence of Na metal 1-acetylnaphthalene with ethylacetate gave the  $\omega$ - acetonaphthoyl keton 3. The structure of compound 3 was derived from its infrared spectrum which revealed the presence of  $\nu\text{C=C}$  at  $1650\text{ cm}^{-1}$ ,  $\nu\text{C=O}$ (enolic  $\beta$  -diketone) which has broad and intense absorption at value of  $1645\text{ cm}^{-1}$ , with the absence of the band revealed to a higher frequencies at  $1720\text{ cm}^{-1}$  (doublet) where normal keto tautomer of  $\alpha$  - $\beta$  diketone,  $\nu\text{CH}_2$  at  $1418\text{ cm}^{-1}$  and  $\nu\text{CH}_3$  at  $1373\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of compound 3 showed signals at  $\delta 2.23$  (3H, s,  $\text{CH}_3$ ),  $\delta 4.51$  (2H, s,  $\text{CH}_2$ ) and  $\delta 6.23$ - $7.33$  (7H, m, Ar-H) ppm. The mass spectrum of compound 3 showed the molecular ion peak at  $m/z$  212(19%), and the base peak at  $m/z$  57(100%). The  $\omega$ -acetonaphthoyl ketone 3 was readily converted to 1-naphthyl pyrazoline derivative 4 by boiling in ethanol/acetic acid mixture with hydrazine hydrate, the reaction possibility takes place according to Scheme 2. The structure of compound 4 was derived from its infrared spectrum which revealed the presence of  $\nu\text{NH}$  of pyrazoline at  $3302\text{ cm}^{-1}$ ;  $\nu\text{CH}$  at  $2920\text{ cm}^{-1}$ ;  $\nu\text{C=N}$ - of cyclic pyrazoline at  $1630\text{ cm}^{-1}$ ;  $\nu\text{CH}_2$  at  $1420\text{ cm}^{-1}$  and  $\nu\text{CH}_3$  at  $1375\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of 4 showed signals at  $\delta 2.10$  (3H,s, $\text{CH}_3$ );  $\delta 3.41$  (2H,d, $\text{CH}_2$ );  $\delta 5.4$ - $5.6$  (1H,t,CH);  $\delta 6.11$ - $7.23$  (7H, m, Ar-H) and  $\delta 9.23$  (1H, s, NH) ppm. The mass spectrum of compound 4 showed the parent ion peak at  $m/z$  210 (45%) and the base peak at  $m/z$  142 (100%).

The reaction of 1-acetylnaphthalene with hydroxylamine in different media was also studied, thus 1-acetylnaphthalene was condensed with hydroxylamine hydrochloride in boiling ethanol and/or pyridine to give the same corresponding oxime derivative 5. The structure of compound 5 was supported by m.p. and mixed m.p. determination. The infrared spectrum of compound 5 showed  $\nu\text{OH}$  (oxime) at  $3231\text{ cm}^{-1}$ ;  $\nu\text{C=C}$  at  $1653\text{ cm}^{-1}$ ;  $\nu\text{C=N}$  at  $1610\text{ cm}^{-1}$  and  $\nu\text{CH}_3$  at  $1376\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of compound 5 showed signals at  $\delta 1.89$ (3H,s, $\text{CH}_3$ );  $\delta 6.21$ - $7.11$ (7H,m,Ar-H) and at  $\delta 11.02$ (1H,s,OH) ppm. The mass spectrum of compound 5 showed the parent ion peak at  $m/z$  185(15.5%) and the base peak at  $m/z$  126(100%). The structure of compound 5 was further established by its reaction with acetic anhydride to give the acetyl oxime derivative 6. The structure of 6 was derived from its infrared spectrum which showed  $\nu\text{C=O}$  at  $1708.8\text{ cm}^{-1}$ ;  $\nu\text{C=C}$  at  $1634\text{ cm}^{-1}$ ; and  $\nu\text{CH}_3$  at  $1370\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of compound 6 showed signals at  $\delta 2.9$ (3H,s, $\text{CH}_3$ );  $\delta 3.62$ (3H,s, $\text{COCH}_3$ ) and  $\delta 6.49$ - $7.35$ (7H,m,Ar-H) ppm. The mass spectrum of compound 6 showed the parent ion peak at  $m/z$  227(5.4%) and the base peak at  $m/z$  154(100%).

The reaction of 1-acetylnaphthalene with 4-chlorobenzaldehyde in boiling alcoholic sodium hydroxide solution afforded the chalcone derivative 7. The

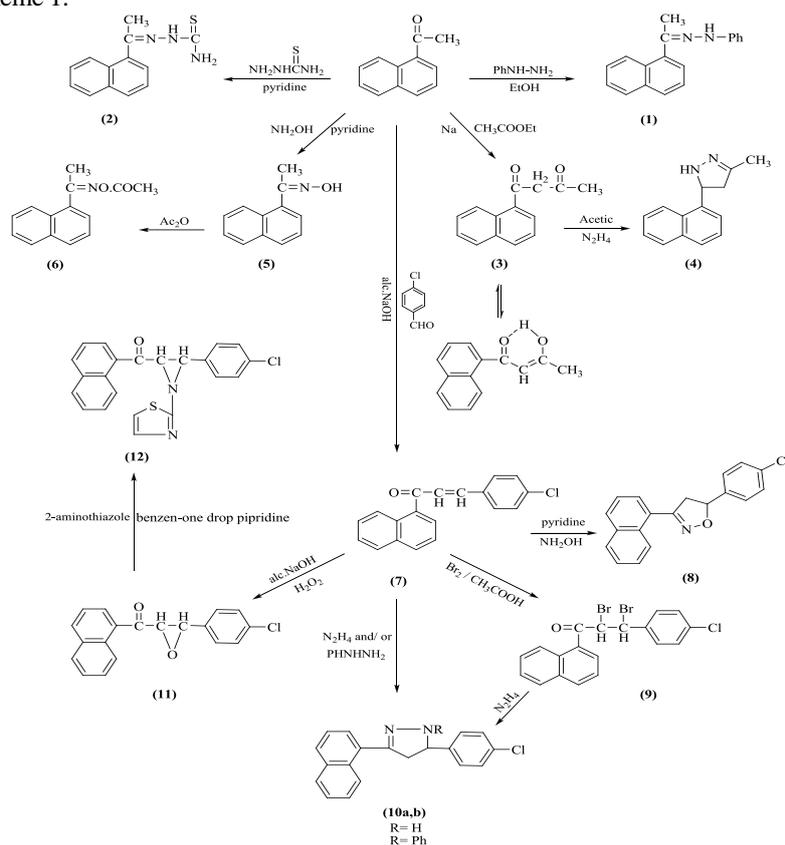
structure of compound 7 was derived from its infrared spectrum which revealed the presence of  $\nu$  C-H at  $3051.2\text{ cm}^{-1}$ ;  $\nu$  C=O at  $1716.5\text{ cm}^{-1}$ ; and  $\nu$  C=C at  $1658.7\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of compound 7 showed signals at  $\delta$  1.91-2.11(1H,d,CH);  $\delta$  2.51-2.65(1H,d,CH) and  $\delta$  6.59-7.85(11H,m,Ar-H) ppm. The mass spectrum of compound 7 showed the molecular ion peak at  $m/z$  292(21.91%) and the base peak at  $m/z$  76(100%).

$\alpha$ - $\beta$ -unsaturated carbonyl compounds are bi-functional intermediates in the synthesis number of different types organic heterocyclic compounds of expected biological activity as pyrazoline, oxazoline and epoxide derivatives. Thus, reaction of the chalcone derivative 7 with hydroxylamine hydrochloride in boiling pyridine afforded 3-naphthyl-5-(4-chlorophenyl) oxazoline 8, the structure of compound 8 was established from its infrared spectrum which revealed the presence of  $\nu$  C-H at  $3057$ - $2900\text{ cm}^{-1}$ ;  $\nu$  C=N at  $1629\text{ cm}^{-1}$ ;  $\nu$  C=C at  $1612\text{ cm}^{-1}$ ;  $\nu$  CH<sub>2</sub> at  $1446\text{ cm}^{-1}$ ;  $\nu$  C-O at  $1130\text{ cm}^{-1}$ ; and  $\nu$  C-Cl aromatic at  $831\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of compound 8 showed signals at  $\delta$  2.01 (1H, t, CH isoxazoline);  $\delta$  3.51(2H,d,CH<sub>2</sub> isoxazoline) and  $\delta$  6.63-7.95(11H,m,Ar-H). The mass spectrum of compound 8 showed the parent ion peak at  $m/z$  307 (42.3%) and the base peak at  $m/z$  77 (100%).

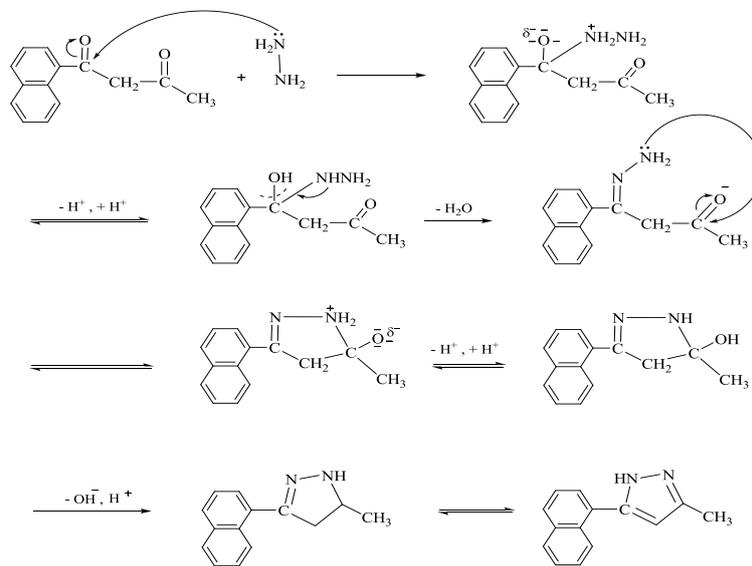
Bromination of chalcone in different media has been studied<sup>(9)</sup>, thus addition of bromine/acetic acid mixture to the chalcone derivative 7 afforded the naphthyl dibromo chalcone derivative 9. The structure of compound 9 was confirmed by its infrared spectrum which revealed the presence of absorption bands at  $\nu$  OH (enol form weak) at  $3519\text{ cm}^{-1}$ ;  $\nu$  CH at  $3053.1$ - $2802.4\text{ cm}^{-1}$ ;  $\nu$  C=O (aroyl) at  $1683.7\text{ cm}^{-1}$ ;  $\nu$  C-Cl at  $825.5\text{ cm}^{-1}$  and  $\nu$  C-Br at  $671.2\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of compound 9 showed signals at  $\delta$  4.4-4.9 (2H, d, CH-CH) and  $\delta$  6.32-7.95 (11H, m, Ar-H). The mass spectrum of compound 9 showed the parent ion peak at  $m/z$  452.5(18.83%) and the base peak at  $m/z$  111(100%). The structure of compound 9 was further established by its reaction with hydrazine hydrate in boiling butanol to give 10 a, the similarity of these compounds was obtained by the infrared spectra and mixed melting points determination with the sample which was prepared by the reaction of chalcone 7 with hydrazine hydrate.

Substituted 2- pyrazolines have received considerable attention in recent years and their applications as fluorescent brightening agents for fibers<sup>(10)</sup> and detergents<sup>(11)</sup> have been reported, 2-pyrazolines also exhibited local anesthetic<sup>(12)</sup>, hypoglycemic<sup>(13)</sup>, diuretic<sup>(14)</sup>, fungicidal<sup>(15)</sup>, antibacterial<sup>(16,17)</sup>, antimicrobial and insecticidal<sup>(18,19)</sup>, these interesting pharmacological properties of 2- pyrazolines led us to synthesis compounds collaborate between naphthalene and pyrazoline moiety in order to obtain new derivatives of potential biological activity via reaction of chalcone derivative 7 with hydrazine hydrate and/or phenyl hydrazine in boiling butanol to give compounds 10 a, b respectively. The infrared spectra of compounds 10 a, b, revealed the presence of absorption bands at  $\nu$  C=N (cyclic pyrazoline) at  $1630\text{ cm}^{-1}$ ;  $\nu$  C-H at  $2920$ - $3050\text{ cm}^{-1}$ ;  $\nu$  NH at  $3240$ ,  $3249\text{ cm}^{-1}$  and  $\nu$  C-Cl at  $823.5\text{ cm}^{-1}$ . The  $^1\text{H-NMR}$  (DMSO- $d_6$ ) spectrum of compounds 10 a,b showed signals at  $\delta$  2.6,2.7 (1H, t, CH pyrazoline);  $\delta$  2.9, 3.2 (2H, d, CH<sub>2</sub> pyrazoline);  $\delta$  6.31-7.83 (11H, m, Ar-H); 6.26 - 7.71 (16 H, m, Ar-H) and at  $\delta$  11.12 ,11.31(1H, s, NH pyrazoline). The mass spectrum of compound 10 b showed the parent ion peak at  $m/z$  382 (30.58%) and the

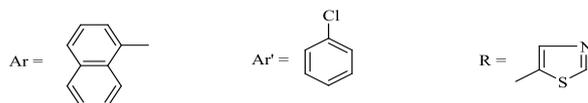
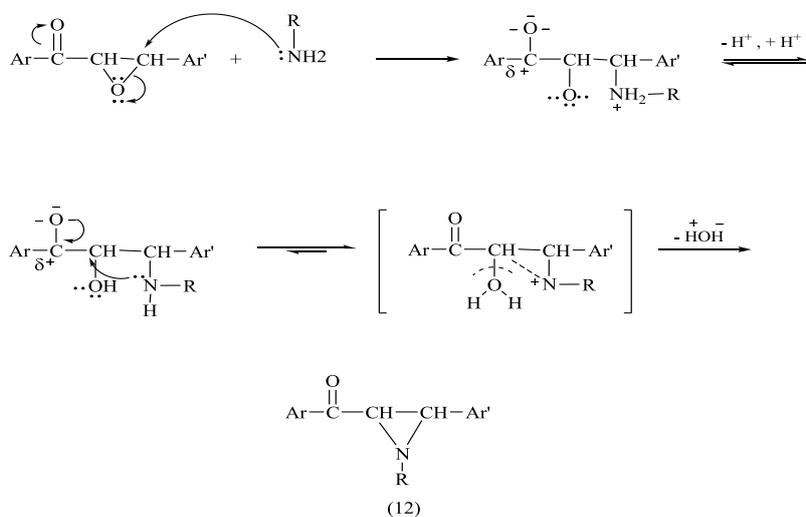
base peak at  $m/z$  223 (100%). On the other hand, the reaction of chalcone derivative 7 with hydrogen peroxide in boiling alcoholic sodium hydroxide solution gave the epoxide derivative 11. The infrared spectrum of compound 11 revealed the presence of the bands of  $\nu$  CH at 3053.1, 2839.2  $\text{cm}^{-1}$ ;  $\nu$  C=O (aroyl) at 1681.8  $\text{cm}^{-1}$ ;  $\nu$  C=C at 1633  $\text{cm}^{-1}$ ;  $\nu$  cyclic ether (epoxide) at 1128.3  $\text{cm}^{-1}$  and  $\nu$  C-Cl at 825.6  $\text{cm}^{-1}$ . The  $^1\text{H-NMR}$  (DMSO- $d_6$ ) of compound 11 showed signals at  $\delta$  4.14 (1H, d, CH);  $\delta$  4.45 (1H, d, CH) and at  $\delta$  6.32-7.91 (11H, m, Ar-H). The mass spectrum of compound 11 showed the parent ion peak at  $m/z$  308 (21.35%) and the base peak at  $m/z$  77 (100%). The structure of compound 11 was further established by its reaction with 2-aminothiazole which afforded N-thiazolo-2-naphthoyl-3-(4-chlorophenyl) aziridine (12). The infrared spectrum of compound 12 revealed the presence of absorption bands  $\nu$  C-H at 3084.2  $\text{cm}^{-1}$ ;  $\nu$  C=O (aroyl) at 1714.6  $\text{cm}^{-1}$ ;  $\nu$  C=C at 1627.8  $\text{cm}^{-1}$ ;  $\nu$  C=N at 1595.9  $\text{cm}^{-1}$ ;  $\nu$  C-S-C at 1402.2  $\text{cm}^{-1}$  and  $\nu$  C-Cl at 883.3  $\text{cm}^{-1}$ . The  $^1\text{H-NMR}$  (DMSO- $d_6$ ) of compound 12 showed signals at  $\delta$  3.82 (1H, d, CH);  $\delta$  4.11 (1H, d, CH) and  $\delta$  6.63-7.82 (13H, m, Ar-H). The mass spectrum of compound 12 showed the parent ion peak at  $m/z$  390 (9.21%) and the base peak at  $m/z$  169 (100%). The reaction possibility takes place according to Scheme 3. All compounds are listed in Scheme 1.



Scheme 1



Scheme 2



Scheme 3

### Screening for antimicrobial activity

In this study, the activity of the prepared compounds (1, 2, 3, 5, 7, 8, 10 and 12) was tested by the disk diffusion method<sup>(4)</sup>. The results were listed in Table 1. From Table 1 it is clear that compounds (1, 2, 3, 5, 8 and 10a) possessed moderate activity against Gram positive, while compounds (7, 11 and 12) possessed high activity. The compounds (1, 3 and 5) possessed moderate activity against Gram negative while compounds (2, 7, 8, 10, 11 and 12) possessed high activity. The compounds (1 and 2) possessed resistant activity against fungi, compounds (3, 5, 7, 10 and 11) possessed less activity, while compounds (7 and 12) possessed moderate activity.

**TABLE 1. Antimicrobial activity of some compounds at different concentration (PPM).**

No	(A): Gram +ve								(B): Gram -ve								(C): Antifungal activity							
	<i>Staphylococcus</i>				<i>Bacillus cereus</i>				<i>Serratia marcescense</i>				<i>Proteus mirabilis</i>				<i>Aspergillus fumigatus</i>				<i>Penicillium chrysogenum thom</i>			
	(ATCC-6538-p)				(NRRL:B659)				(NTC-989)								(PP-29)							
	75	125	175	250	75	125	175	250	75	125	175	250	75	125	175	250	75	125	175	250	75	125	175	250
1	+	+	+	++	+	+	+	++	+	+	++	++	+	+	+	++	R	R	R	R	R	R	R	R
2	+	+	+	+	+	+	++	++	+	+	++	+++	+	+	++	+++	R	R	R	R	R	R	R	R
3	+	+	++	++	+	++	++	++	+	+	+	++	+	+	++	++	+	+	+	+	R	R	R	R
5	+	+	+	+	+	+	++	++	+	+	+	+	+	+	+	++	R	R	+	+	+	+	+	+
7	+	++	++	+++	+	++	+++	+++	+	++	++	+++	+	++	++	+++	R	+	+	+	+	+	+	+
8	+	+	++	++	+	+	++	++	+	+	++	++	+	+	++	+++	+	+	++	++	+	+	+	++
10a	+	+	++	++	+	+	++	++	+	++	+++	+++	+	+	++	++	+	+	+	+	R	R	R	R
11	+	++	++	+++	+	+	++	+++	+	++	+++	+++	+	+	+	++	+	+	+	+	+	+	+	+
12	+	++	+++	+++	+	+	++	+++	+	++	++	+++	+	++	++	+++	+	++	++	++	+	+	++	++

R = Resistant

+ = Less activity (0.2-0.5 cm)

++ = Moderate activity (0.6-1.4 cm)

+++ = High activity (1.5-2.0)

### Experimental

All melting points are uncorrected and determined by the open capillary method using Gallen Kamp melting point apparatus. Microanalyses were carried out by the Micro- Analytical Unit at Cairo University. IR spectra (KBr disk) were recorded on FT/IR-300E Jasco spectrophotometer. <sup>1</sup>HNMR spectra were recorded in DMSO-d<sub>6</sub> solution on a Varian EM 390-90 MHz. Mass spectrometry was recorded Shimadzu, GC- MS (QP- 1000EX) .

*Reaction of acetyl naphthalene with phenyl hydrazine: Formation of 1- methyl naphthyl phenylhydrazide derivative 1*

A mixture of 1-acetyl naphthalene (0.01mol) and (0.01mol) of phenylhydrazine in 25 ml of ethanol was refluxed for 6 hr. After concentration and cooling the product that separated was recrystallized from ethanol to give 1 as yellow crystal m. p. 160°C; yield 60% calcd. for. C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>; C, 83.06; H, 6.15; N, 10.76% Found: C, 83.1; H, 6.2; N, 10.8% MS m/z 260(M<sup>+</sup>).

*Reaction of 1-acetyl naphthalene with thiosemicarbazide: Formation of 1-methyl naphthyl thiosemicarbazide derivative 2*

A mixture of 1-acetyl naphthalene (0.01mol) and (0.01mol) of thiosemicarbazide in 20 ml of pyridine was refluxed for 6hr. After cooling the product was poured in to cold dilute HCl and the solid obtained was recrystallized from benzene to give 2 as yellow crystals m.p. 160°C; yield 70% called. for. C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>S; C, 64.19; H, 5.34; N, 17.28; S, 13.16%. Found: C, 64.2; H, 5.3; N, 17.3; S, 13.2% MS m/z 243 (M<sup>+</sup>).

*Reaction of 1-acetyl naphthalene with ethylacetate: Formation of ω-aceto naphthoyl ketone 3*

A mixture of 1-acetyl naphthalene (0.01mol) and (10ml) of ethylacetate in the presence of (1gm) of sodium metal was heated on a steam-bath for 6 hr. The solid obtained after cooling was treated with water then recrystallized from ethanol to give 3 as buff crystals m.p.200°C; yield 60% calcd.for. C<sub>14</sub>H<sub>12</sub>O<sub>2</sub> ; C, 79.24; H, 5.66% Found C, 79.3; H, 5.7% MS m/z 212 (M<sup>+</sup>).

*Reaction of ω-acetonaphthoyl ketone 3 with hydrazine hydrate: Formation of 5-(1-naphthyl) 3-(methyl) pyrazoline derivative 4*

To a solution of 3 (0.01 mol) in ethanol/acetic acid mixture (30 ml 1:1), hydrazine hydrate (0.01 mol) was added and the reaction mixture was refluxed for 6hr. After concentration and cooling the solid that separated was recrystallized from ethanol to give 4 m.p. 210 °C; yield 52% calcd. for. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>; C, 80; H, 6.66; N, 13.33%, Found: C, 80.2; H, 6.54; N, 13.41% MS m/z 210 (M<sup>+</sup>).

*Reaction of 1-acetyl naphthalene with hydroxylamine hydrochloride: Formation of 1- naphthyl oxime derivative 5*

A mixture of 1- acetyl naphthalene (0.01mol) and hydroxyl amine hydrochloride (0.01mol) in 20 ml of pyridine was refluxed for 6hr. The reaction mixture was poured into ice-HCl and the solid that separated was collected, washed well with water and recrystallized from benzene to give 5 as white crystals m.p. 100°C; yield 80 % calcd. for. C<sub>12</sub> H<sub>11</sub>NO, C, 77.83; H, 5.94; N, 7.56 % Found: C, 77.8; H, 5.9; N, 7.7 % MS m/z 185(M<sup>+</sup>).

*Reaction of the oxime derivative 5 with acetic anhydride: Formation of the acetyl oxime derivative 6*

A solution of 5 (0.01mol) in acetic anhydride (20 ml) was refluxed on a water bath for 6hr. The solid that obtained after cooling was recrystallized from

benzene to give 6 as brown crystals m. p. 120 °C; Yield 10 % calcd. for. C<sub>14</sub>H<sub>13</sub>NO<sub>2</sub> C, 74; H, 5.72; N, 6.16 % Found: C, 74.1; H, 5.7; N, 6.2 % MS m / z 227 (M<sup>+</sup>).

*Reaction of acetyl naphthalene with 4-chlorobenzaldehyde: Formation of the chalcone derivative 7*

To a mixture of 1-acetyl naphthalene (0.01 mol) in (20 ml) of ethanol and aqueous sodium hydroxide solution (0.032 mol in 4 ml water) was added 4-chlorobenzaldehyde (0.01 mol dissolved in 5 ml ethanol) dropwise with continuous stirring for 2 hr. The reaction mixture was left to stand for overnight and then poured onto 50 ml H<sub>2</sub>O. The solid that separated was recrystallized from ethanol to give 7 as yellow crystals m. p. 120 °C; yield 50 % calcd. for. C<sub>19</sub>H<sub>13</sub>OCl, C, 77.94; H, 4.44; Cl, 12.13 % Found: C, 78.1; H, 4.4; Cl, 12.1 % MS m / z 292.5 (M<sup>+</sup>).

*Reaction of the chalcone derivative 7 with hydroxyl amine hydrochloride: Formation of 1-naphthyl oxazoline derivative 8*

A mixture of 7 (0.01 mol) and hydroxyl amine hydrochloride (0.01 mol) in (20ml) pyridine was refluxed for 6hr. After concentration and cooling the reaction mixture was poured onto ice- HCl the solid that separated was recrystallized from benzene to give 8 m.p. 190 °C; yield, 30 % calcd. for. C<sub>19</sub>H<sub>14</sub>NOCl; C, 74.14; H, 4.55; N, 4.55; Cl, 11.54 % Found: C, 74.1; H, 4.6; N, 4.4; Cl, 11.6 % MS m / z 307.5 (M<sup>+</sup>).

*Reaction of the chalcone derivative 7 with bromine / acetic acid mixture: Formation of the dibromo derivative 9*

A solution of 7 (0.01 mol) in glacial acetic acid (20 ml) was stirred and treated portionwise with bromine dissolved in (10 ml) of acetic acid at 60-70 °C, the solution was further stirred for 2hr. The reaction mixture was cooled in an ice – bath and the precipitated product was filtered then triturated with petroleum ether (b. p. 40-60) and stirred with conc. Ammonium hydroxide for 15 min. The reaction mixture was poured onto ice and the solid that separated was recrystallized from benzene-petroleum ether (b. p. 80-100) mixture (50-50) to give 9 as white crystals m. p. 140 °C; yield 60 % calcd. for. C<sub>19</sub>H<sub>13</sub>OBr<sub>2</sub>Cl: C, 50.38; H, 2.87; Br, 35.35; Cl, 7.84 % Found: C, 50.3; H, 2.9; Br, 35.4; Cl, 7.8 % MS m / z 452.5 (M<sup>+</sup>).

*Reactions of the chalcone derivative 7 and/or its dibromide derivative 9 with hydrazine hydrate and/or phenyl hydrazine: Formation of pyrazoline derivatives 10, a, b*

A mixture of 7 (0.01 mol) and /or 9 (0.01 mol); hydrazine hydrate and /or phenyl hydrazine (0.01 mol) in (30 ml) of n- butanol was refluxed for 6hr. The excess solvent was removed and the solid that separated was recrystallized from benzene-petroleum ether (b. p. 80-100) mixture to give 10 a, b, respectively. 10,a m. p. 200 °C, yield 30 % calcd, for. C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>Cl; C, 74.38; H, 4.89; N, 9.13; Cl, 11.58 % Found: C, 74.4; H, 4.9; N, 9.2; Cl, 11.5 % MS m / z 306.5 (M<sup>+</sup>). 10,b m. p. 100 °C, yield 60 % calcd. for. C, 78.4; H, 4.9; N, 7.3; Cl, 9.3 % MS m / z 382.5 (M<sup>+</sup>).

*Reaction of the chalcone derivative 7 with hydrogen peroxide: Formation of the epoxide derivative 11*

To a solution of 7 (0.01 mol) in a mixture of (50 ml) ethanol and aqueous NaOH solution (0.032 mol dissolved in 4 ml H<sub>2</sub>O) was added H<sub>2</sub>O<sub>2</sub> dropwise and the reaction mixture was refluxed for 6hr. After cooling, the reaction mixture was acidified with dilute hydrochloric acid. The solid that obtained was recrystallized from ethanol to give 11.

*Reaction of the epoxide derivative 11 with 2- aminothiazol: Formation of (N-2-thiazolyl) -2-naphthoyl-3(4-chlorophenyl) aziridine 12*

To a solution of 11(0.01mol) in dry benzene (50 ml) 2-aminothiazole (0.01 mol) was added and few drops of piperidine. The reaction mixture was stirred well for 3hr then left to stand for 2hr. after concentration and cooling the solid that obtained was recrystallized from petroleum ether (b.p. 80-100°C) to give 12 as yellow crystals m.p. 90 °C; yield 20% calcd. for. C<sub>22</sub>H<sub>15</sub>N<sub>2</sub>SOCl; C, 67.60; H, 3.6; N, 7.3; S, 8.1; Cl, 9.2% MS m/z 390.5 (M<sup>+</sup>).

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## التحضير والتأثير البيولوجي لبعض مشتقات النفتالين كمضادات للميكروبات

أميرة محمد المتولي

الهيئة القومية للرقابة والبحوث الدوائية - القاهرة - مصر .

1- أستيل نفتالين يتفاعل مع الفنيل هيدرازين ،الثايوسيمي كاربازيد ليعطي مشتق هيدرازيد (١) ومشتق الكاربازيد (٢) ويتكثف مركب ١- أستيل نفتالين مع هيدروكسيل امين هيدروكلوريد في ايثانول او بيريدين يعطي مشتق اوكسيم (٥) وايضا مركب ١- أستيل نفتالين يتفاعل مع ايثيل اسيتو اسيتات تحت ظروف كلازين لى يعطي اسيتونفتويل كيتون (٣) الذى يتحول الى مشتق البيرازولين بعد تفاعله مع الهيدرازين هيدرات (٤) . ١- أستيل نفتالين يتفاعل مع الالدهيد مثل ٤- كلوروبينزالدهيد ليعطي شالكون (٧) التى تتفاعل مع هيدروكسيل امين هيدروكلوريد ،برومين ، الهيدرازين هيدرات ،هيدروجين بيروكسيد. وهذه المركبات اختبرت كمضادات للميكروبات ووجد ان بعض من هذه المركبات لها تأثير على البكتريا والفطريات.