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UTILITY OF B-DIKETONES IN HETEROCYCLIC SYNTHESIS: SYNTHESIS OF NEW TETRAHYDROPYRIMIDINETHIONE, PYRAZOLE, THIOPHENE, DIHYDROPYRIDINE, DIHYDROPYRANE AND PYRIDAZINE DERIVATIVES

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ABSTRACT

The chemical reactivity of diketone 1 toward some nucleophilic and electrophilic reagents was investigated. diketone 1 was used as a key precursor for the synthesis of many important heterocyclic compounds. The synthesized compounds were characterized by IR, 1H-NMR, MS spectral and elemental analysis.

Key words: 2-naphthol, ethylbenzoylacetate, β-Diketone 1, aryl aldehyde, thiourea, hydrazine, phenylhydrazine, malononitrile, elemental sulphur, ethylcyanoacetate and arylidenemalononitrile.

INTRODUCTION

Among a wide variety of heterocyclic that have been explored for developing pharmaceutical important molecules such as pyrazoles, cyanopyridines, pyrimidinethiones and pyranes have played an important role in medicinal chemistry. Various biological applications have been reported for pyrazoles such as anticancer, antiviral, anti-inflammatory, antifungal, antimicrobial, antihistaminic, antiplatelet, analgesic, antihyperglycemic, antipyretic, anti-tumor, sedative, hypnoticativity (**Ramaiyan, 2010; Sherif *et al.,* 2010; Alka and Sharma, 2011; Chauhan *et al.,* 2011; Vishnuvardan *et al.,* 2011; Mistry *et al*, 2012**), antidepressant (**Rajendra *et al.,* 2005**), anticonvulsant (**Ozdemir *et al.,* 2007**). Cyanopyridine derivatives have attracted considerable attention as they appeared interest to possess anticonvulasnt (**Masereel *et al.,* 1998**), antibacterial (**Joachim *et al.,* 1963; Ghoneim *et al.,* 1988**), antitumor (**Ghorab, 1996**), antihypertensive (**Baldwin *et al.,* 1980**), cardiovascular (**Krauze *et al.,* 1985**) and antisoriasis (**Van *et al.,* 1980**) activities. Pyrimidinethiones have been found to possess antitubercular (**Paghdar *et al.,* 2007**), antitumor (**Ozaki, 1984**) and hypoglycemic (**Baucer *et al.,* 1968**) activities. Pyrane and fused 4H-pyrane derivatives have attracted a great interest owing to their antimicrobial activity (**El-Agrody *et al.,* 2001; Bedair *et al.,* 2000; El-Agrody *et al.,* 2000**), inhibition of influenza, virus sialidases (**Taylor *et al.,* 1998**), mutagenic activity (**Hirmoto *et al.,* 1997**), antiviral (**Martinez and Marco, 1997**), antiprol feraction agents (**Dell and Smith, 1993**), sex-pheromones (**Bianchi and Tava 1987**), antitumor (**Eiden and Denk, 1991**) and anti-inflammatory agents (**Shishoo *et al.,* 1981**). Moreover, pyrane derivatives are well known for their antihistaminic activity (**Noda *et al.,* 1978**). Also, naphthalene is important aryl ring in many active compounds such as anti-inflammatory, anti-bacterial, anti-microbial and anti-cancer (**Joan and Jimenez, 2001; Kunal and Bioorg, 2011**).

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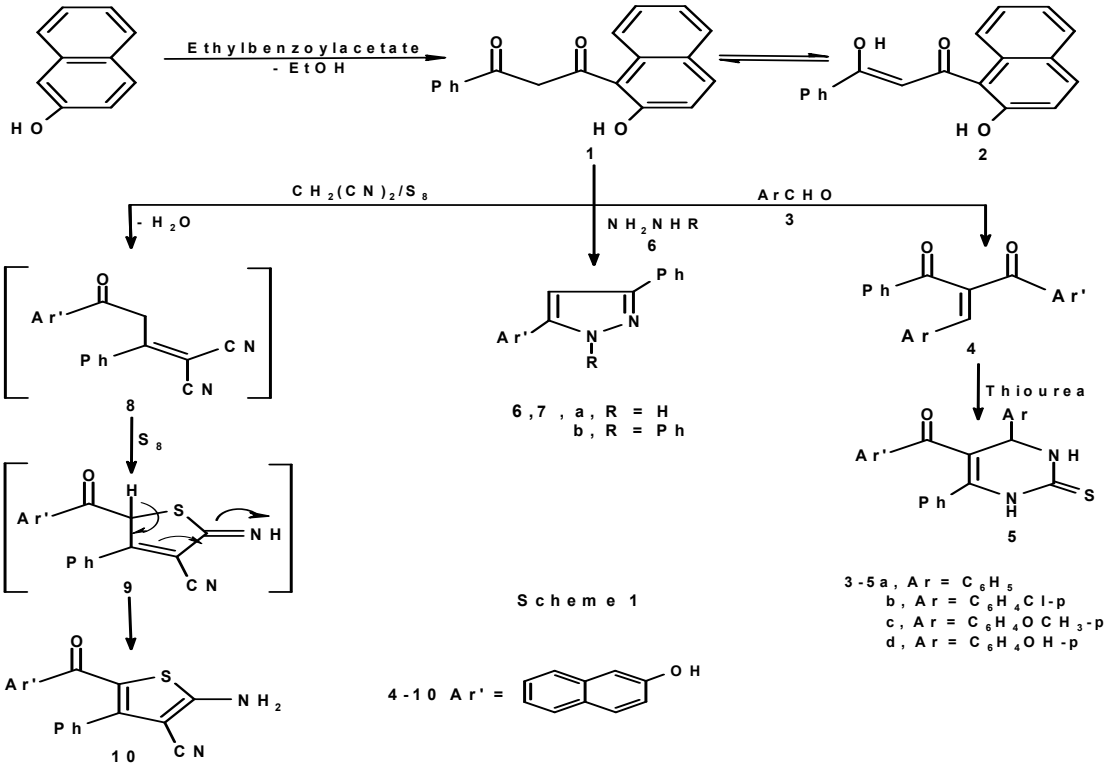
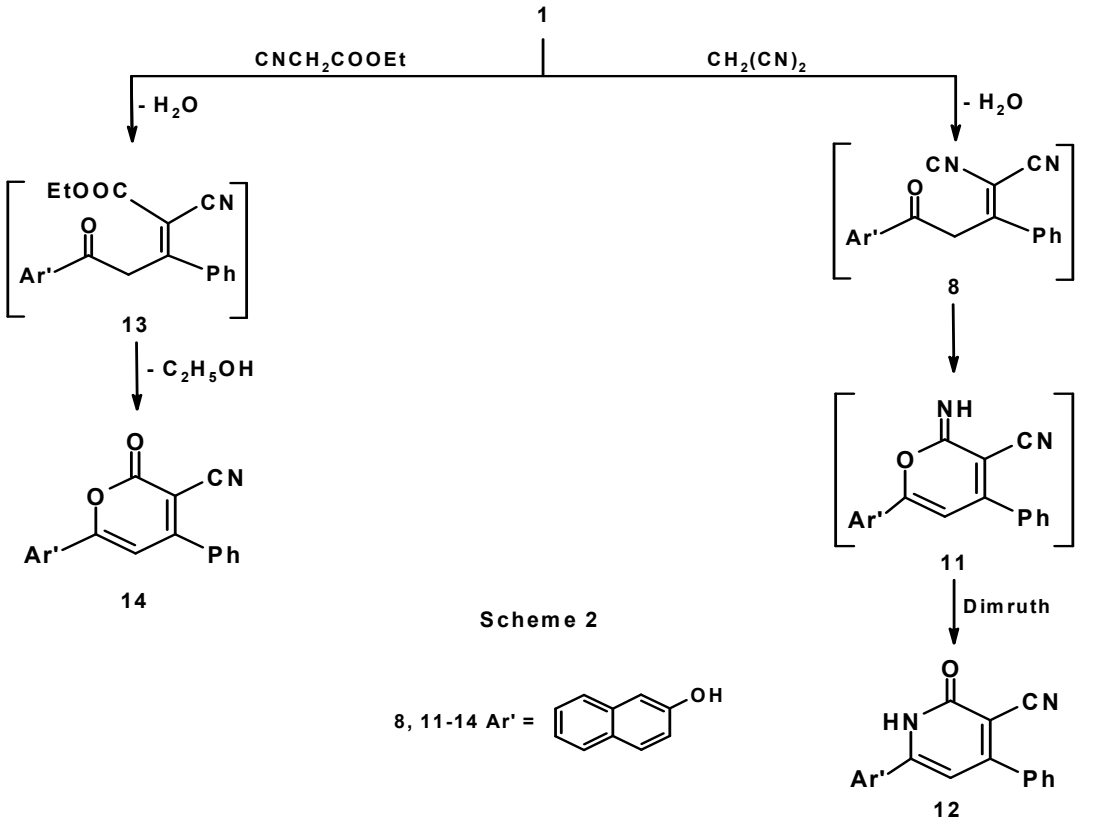
RESULTS AND DISCUSSION

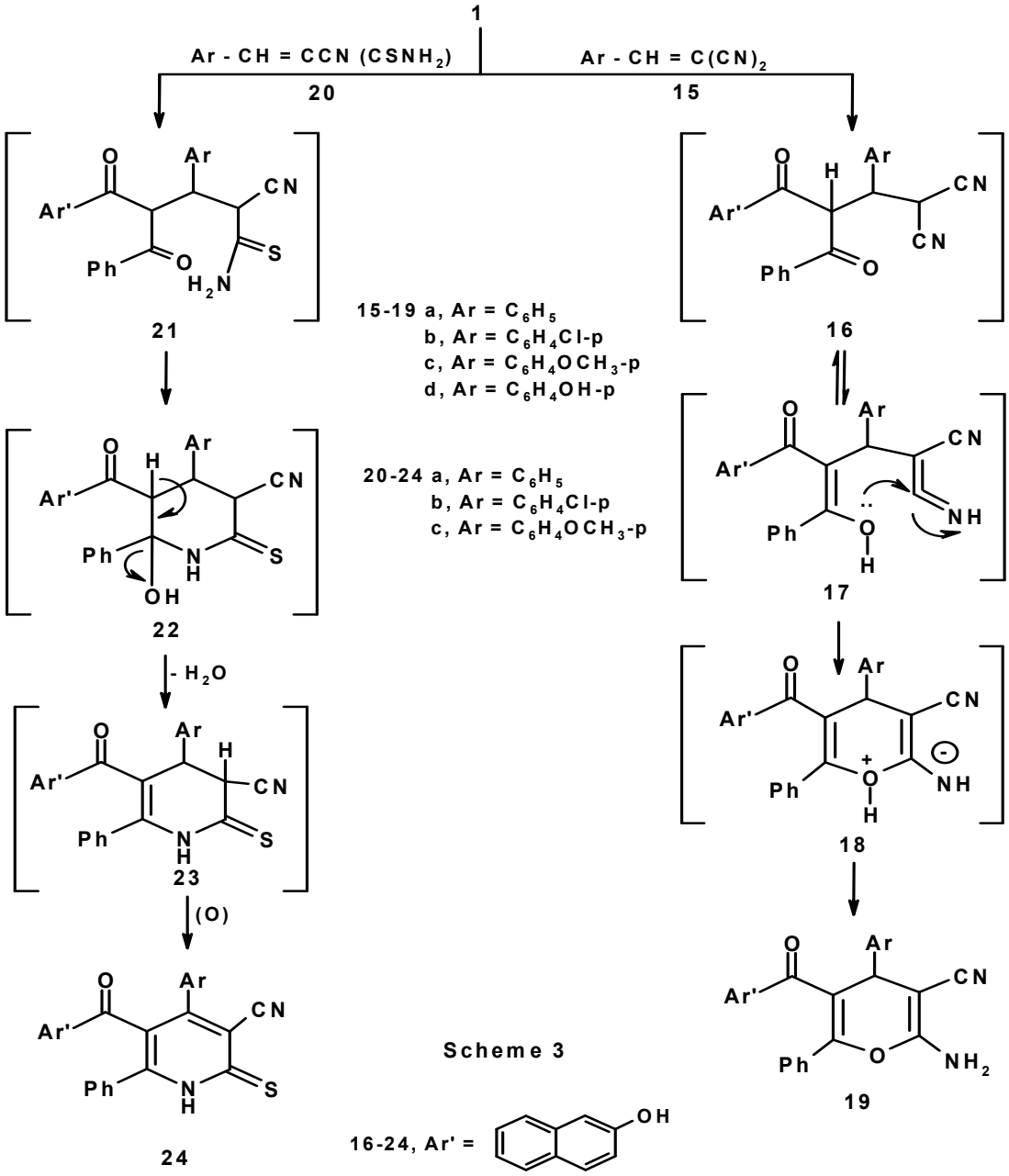
The diketone 1 is prepared in a quantitative yield in a demostic microwave oven from the reaction of 2-naphthol and ethylbenzoylacetate. Thus, β-diketone 1 reacted with aryl aldehyde 3a-d to afford the benzylidene derivatives 4a-d. (scheme 1). Structures of compounds 4a-d were established by elemental analysis and spectral data. Compounds 4a-d are allowed to react with thiourea to afford tetrahydropyrimidinethions 5a-d (scheme 1). Structures of tetrahydropyrimidinethions 5a-d were established by elemental analysis and spectral data. For example, The IR spectrum of 5a revealed an absorption band at 3447 cm^{-1} corresponding to OH group and a band at 3400 cm^{-1} corresponding to NH group and a band at 1637 corresponding to carbonyl group. The ^{1}H-NMR (DMSO-d_6) of the same product revealed to the presence of a signal at δ 4.35 ppm corresponding to C4 proton at pyrimidine ring, a multiplet signal at δ 7.11-8.37 ppm corresponding to aromatic protons and amino function and a signal at δ 9.79 ppm corresponding to OH function. The mass spectrum of the same product is in accordance with the proposed structure MS (m/z): 436 (M^+). Furthermore, the behavior of β-Diketone 1 toward nitrogen nucleophile was also investigated. Thus, β-diketone 1 reacted with hydrazine and phenylhydrazine to afford substituted pyrazoles 7a,b. Establishing structure pyrazoles 7a,b was based on their elemental and spectral data (scheme 1). In addition β-diketone 1 reacted with malononitrile and elemental sulphur to afford the thiophene derivative 10 (scheme 1). The formation of thiophene 10 from the reaction of diketone 1 and malononitrile is beleived to be formed *via* initial addition of malononitrile on the double bond system of carbonyl group of diketone 1 and subsequent elimination of water to afford the non-isolable intermediate 8. The intermediate 8 reacted with elemental sulphur to afford thiophene 10 *via* intermediacy of 9 (scheme 1). Establishing structure thiophene 10 was based on its elemental analysis and spectral data. The IR spectrum of 10 revealed an absorption band at 3440 cm^{-1} corresponding to OH group, 3331, 3202 cm^{-1} corresponding to NH_2 group, and a band at 2212 cm^{-1} corresponding to CN group and a band at 1638 corresponding to carbonyl group. The mass spectrum of the same product is in accordance with the proposed structure MS (m/z): 372 (M^++2).

The β-diketone 1 reacted with malononitrile to afford the dihydropyridine derivative 12 (scheme 2). The formation of dihydropyridine derivative 12 from the reaction of diketone 1 and malononitrile is beleived to be formed *via* initial addition of malononitrile to carbonyl group of diketone 1 and subsequent elimination of water to afford the non-isolable intermediate 8. The intermediate 8 tautomerizes and intramolecular cyclizes under the same reaction condition to afford the non-isolable intermediate 11 which underwent Dimruth rearrangement to afford 12 (scheme 2). Establishing structure 12 was based on its elemental analysis and spectral data. The IR spectrum of 12 revealed an absorption band at 2192 cm^{-1} corresponding to CN group and a band at 1636 corresponding to carbonyl group. The mass spectrum of the same product is in accordance with the proposed structure MS (m/z): 338 (M+). The β-diketone 1 is allowed to react with ethylcyanoacetate afforded the pyranone derivative 14 whose structure was based on its spectral analysis. The formation of pyranone derivative 14 is beleived to be formed *via* initial addition of ethylcyanoacetate on the double bond system of 1 and subsequent elimination of water to afford the non-isolable intermediate 13. The intermediate 13 tautomerizes and cyclizes under the same reaction condition to afford the pyranone derivative 14 (scheme 2).


Ethylbenzoylacetate
- EtOH
1
2
CH2(CN)2/S8
- H2O
NH2NHR
6
ArCHO
3
8
S8
9
10
6,7 , a, R = H
b, R = Ph
4
Thiourea
5
3-5a, Ar = C6H5
b, Ar = C6H4Cl-p
c, Ar = C6H4OCH3-p
d, Ar = C6H4OH-p
Scheme 1
4-10 Ar' =


1
CNCH2COOEt
CH2(CN)2
- H2O
- H2O
13
- C2H5OH
14
8
11
Dimruth
12
Scheme 2
8, 11-14 Ar' =

On the other hand the behaviour β-diketone 1 toward some electrophilic reagents was also investigated. Thus, β-diketone 1 reacted with arylidenemalononitrile 15a-d under reflux to afford the pyrane derivatives 19a-d (scheme 3). The formation of pyrane derivatives is beleived to be formed *via* intial addition of active methylene of 1 on the double bond system of arylidenemalononitrile to afford the acyclic intermediate 16 which tautomerizes into 17 that cyclizes under the same reaction condition to afford 18 that tautomerizes into pyrane derivative 19 (scheme 3). Establishing structure 19a-d. Were based on their elemental and spectral analyses. Similarly, β-diketone 1 reacted with arylidenes 20a-c to afford the dihydropyridinethione derivatives 24a-c (scheme 3). Establishing structure 24a-c were based on their elemental analyses and spectral data.



Scheme 3

Experimetal

All melting points were measured using Akofler Block instrument and are uncorrected. IR spectra (KBr) were recorded on a FTIR 5300 spectrometer (υ, cm^{-1}). The ^{1}H-NMR spectra were recorded in DMSO-d6 and $CDCl_3$ at 300 MHz and 400 MHz on a Varian Gemini NMR. 1000 EX mass spectrometer at 70 ev. The purity of synthesized compounds was checked by thin layer chromatography TLC (aluminum sheets) using n-hexane, ethyl acetate (9:1, V/V) eluent. Elemental analyses were carried out by the Microanalytical Research Center, Faculty of Science, and Microanalytical Unit, Faculty of Pharmacy, Cairo University, Egypt.

Preparation of 1-(2-hydroxynaphthalen -1-yl)-3-phenylpropane-1,3-dione (1)

A mixture of ethyl benzoylacetate (0.01 mol), β-naphthol (0.01 mol) was exposed to microwave irradiation for 4-6 mins, the reaction mixture was allowed to reach room temperature, then diluted with ethanol with stirring and the solid product that formed, was filtrated and crystallized from ethanol to give brown crystals; yield (85%); M.p.136-138^{o}C; IR (KBr) ν cm^{-1} = 3434 (OH), 3056 (CH-arom), 2967 (CH-aliph), 1727, 1637 (2CO) cm-1; ^{1}H-NMR (DMSO-d6) δ = 4.38 (s, 2H, CH_2), 7.13-8.29 (m, 11H, aromatic H), 9.92 (s, 1H, OH) ; MS: m/z (%) 290 (M^+), Anal.calcd for $C_{19}H_{14}O_3$ (290): C,78.61; H,4.86; O, 16.53; Found: C, 78.62; H,4.86;O, 16.54%.

Synthesis of phenylpropane-1, 3-dione (4a-d)

General procedure: A mixture of compound 1 (0.01 mol), appropriate aryl aldehydes (0.01 mol) in ethanol (30 ml) with catalytic amount of piperidine was heated under reflux for 3 hr. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give 4a-d.

2-Benzylidene-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (4a).

It was obtained as pale green crystals from ethanol; Yield: 61%; m.p.:145–147^{o}C; IR (KBr, cm^{-1}): 3453 (OH), 3057 (C-H arom), 1726, 1637 (2C=O); ^{1}H-NMR (DMSO-d6) δ = 5.24 (s, 1H,CH-olifinic), 7.06-8.34 (m, 16H, aromatic protons), 9.95 (s, 1H, OH); MS (m/z): 378 (M+), Anal. calcd fo $C_{26}H_{18}O_3$ (378): C, 82.52; H, 4.79; O, 12.68; Found: C, 82.51; H, 4.78; O, 12.69%.

2-(4-Chlorobenzylidene)-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (4b)

It was obtained as pale yellow crystals from ethanol; Yield: 69 %; m.p.: 170–172 oC; IR (KBr, cm-1): 3437 (OH), 3057 (C-H aromatic), 1725, 1637 (2C=O); 1H-NMR (DMSO-d6) δ = 6.68 (s, 1H, CH-olifinic), 7.20-8.94 (m, 15H, aromatic protons), 9.96 (s, 1H, OH); MS (m/z): 414 (M^++2), Anal.calcd for $C_{26}H_{17}ClO_3$ (412): C, 75.64; H, 4.15; O, 11.63; Found: C, 75.63; H, 4.14; O, 11.64%.

1-(2-Hydroxynaphthalen-1-yl)-2-(4-methoxybenzylidene)-3-phenylpropane-1,3-dione (4c)

It was obtained as green crystals from ethanol; Yield: 69 %; m.p.: 160–162 oC; IR (KBr, cm-1): 3453 (OH), 3056 (C-H aromatic), 2922 (C-H aliphatic), 1720, 1637 (2C=O); 1H-NMR (DMSO-d6) δ = 3.84 (s, 3H, OCH3), 5.20 (s, 1H, CH-olifinic), 7.54-8.30 (m, 15H, aromatic protons), 9.94 (s, 1H, OH); MS (m/z): 408 (M^+), Anal.calcd for C27H20O4 (408)**:**C, 79.40; H, 4.94; O, 15.67; Found:C, 79.39; H, 4.93; O, 15.68%.

2-(4-hydroxybenzylidene)-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (4d)

It was obtained as pale yellow crystals from ethanol; Yield: 70 %; m.p.: 176–177 oC; IR (KBr, cm-1): 3453 (OH), 3046 (C-H

aromatic), 1730, 1636 (2C=O); 1H-NMR (DMSO-d6) δ = 5.48 (s, 1H, CH-olifinic), 7.59-8.38 (m, 15H, aromatic protons), 9.95 (s, 1H, OH), 9.97 (s, 1H, OH); MS (m/z): 394 (M+), Anal.calcd for $C_{26}H_{18}O_4$ (394),C, 79.17; H, 4.60; O, 16.23 Found: C, 79.16; H, 4.59; O, 16.24%.

Synthesis of compounds (5a-d)

General procedure: To boiling solution of compound 4a-d (0.01 mol) and thiourea (0.01 mol) in ethanolic potassium hydroxide (30 ml, 10%), was added. The reaction mixture was refluxed for 20 hr, then allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent *(4,6-Diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(2-hydroxynaphthalen- 1-yl)methanone (5a)*. It was obtained as yellow crystals from ethanol; Yield: 77 %; m.p.: 150–152 ^oC; IR (KBr, cm^{-1}): 3447, 3400 (OH/NH), 3058 (C–H aromatic), 2964 (C–H aliphatic), 1637 (C=O); ^{1}H-NMR (DMSO-d6) δ=4.35 (s, 1H, CH-pyrimidine), 7.11-8.37 (m, 18H, aromatic protons+2NH), 9.79 (s,1H, OH); MS (m/z): 436 (M^+), Anal. calcd for $C_{27}H_{20}N_2O_2S$ (436)*:*C,74.29; H, 4.62; N, 6.42; Found: C, 74.30; H, 4.63; N, 6.41%.

(4-(4-Chlorophenyl)-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(2-hydroxynaphthalen-1-yl)methanone (5b).

It was obtained as yellow crystals from ethanol; Yield: 77%; m.p.: 177–179 oC; IR (KBr, cm-1): 3400/3374 (OH/NH), 3061 (C–H aromatic), 2934 (CH aliphatic), 1685 (C=O). 1H-NMR (DMSO-d6) δ = 4.35 (s, 1H, CH-pyrimidine), 7.21-8.38 (m, 17H, aromatic protons+2NH), 9.97 (s, 1H, OH); MS (m/z): 470 (M+), Anal.calcd for $C_{27}H_{19}ClN_2O_2S$ (470)*:* C, 68.86; H, 4.07; N, 5.95; Found: C, 68.85; H, 4.06; N, 5.96%.

(2-Hydroxynaphthalen-1-yl)(4-(4-methoxyphenyl)-6-phenyl-2-thioxo-1,2,3, 4-tetrahydropyrimidin-5-yl) methanone (5c)

It was obtained as pale yellow crystals from ethanol; Yield: 77 %; m.p.: 157–159 oC; IR (KBr, cm-1): 3444,3400 (OH/NH), 3057 (C–H aromatic), 2965 (C–H aliphatic), 1637 (C=O); ^{1}H-NMR (DMSO-d6) δ =3.80 (s, 3H, OCH_3), 4.40 (s, 1H, CH-pyrimidine), 7.11-8.35 (m, 17H, aromatic protons+2NH), 9.96 (s, 1H, OH); MS (m/z): 466 (M^+), Anal.calcd for $C_{28}H_{22}N_2O_3S$ (466): C, 72.08; H, 4.75; N, 6.00; Found: C, 72.09; H, 4.74; N, 6.01%.

(2-hydroxynaphthalen-1-yl)(4-(4-hydroxyphenyl)-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methanone (5d)

It was obtained as yellow crystals from hexan; Yield: 80 %; m.p.: 170–172^oC; IR (KBr, cm^{-1}): 3443,3400 (OH/NH), 3057 (C–H aromatic), 2965 (C–H aliphatic), 1637 (C=O); ^{1}H-NMR (DMSO-d6) δ = 4.36 (s, 1H, CH-pyrimidine), 7.21-8.38 (m, 17H, aromatic protons+2NH), 9.95 (s, 1H, OH), 9.97 (s, 1H, OH); MS (m/z): 452 (M^+), Anal.calcd for $C_{27}H_{20}N_2O_3S$ (452)*:* C, 71.66; H, 4.45; N, 6.19; Found: C, 71.65; H, 4.44; N, 6.20%.

Synthesis of compounds (7a,b)

General procedure: A mixture of 1 (0.01 mol) and hydrazine hydrate or phenyl hydrazine in ethanol (30 mL) was heated under reflux for 12 hrs. The reaction mixture was allowed to cool and poured into crushed ice. The separated solid was filtered, washed with water and crystallized from the proper solvent to give 7a,b.

1-(3-Phenyl-1H-pyrazol-5-yl)naphthalen-2-ol (7a)

It was obtained as pale brown crystals from ethanol; Yield: 55%; m.p.: 182–184^oC; IR (KBr, cm^{-1}): 3417 (OH), 3202 (NH), 3050 (C–H aromatic); ^{1}H-NMR

(DMSO-d6) δ = 6.85 (s, 1H, CH-pyrazole), 6.96-8.10 (m, 11H, aromatic protons), 10.10 (s, 1H, OH),12.95 (s, 1H, NH); MS (m/z): 286 (M^+), Anal.calcd for $C_{19}H_{14}N_2O$ (286): C, 79.70; H, 4.93; N, 9.78; Found: C, 79.71; H, 4.92; N, 9.79%.

1-(3-Diphenyl-1H-pyrazol-5-yl) naphthalen-2-ol (7b)

It was obtained as brown crystals from ethanol; Yield: 62%; m.p.: 202–204°C; IR (KBr, cm^{-1}): 3417 (OH), 3065 (C–H aromatic); ^{1}H-NMR (DMSO-d6) δ = 7.11 (s, 1H, CH-pyrazole), 7.21-8.38 (m, 16H, aromatic protons), 9.97 (s, 1H, OH); MS (m/z): 362 (M^+), Anal. calcd for $C_{25}H_{18}N_2O$ (362): C, 82.85; H, 5.01; N, 7.73; Found: C, 82.86; H, 5.00; N, 7.74%.

Preparationof 2-amino-5-(2-hydroxy-1-naphthoyl)-4-phenylthiophene-3-carbonitrile (10)

Equimolar amounts of 1 (0.01 mol), malononitrile and elemental sulfur (0.01 mol) in ethanol (30 mL) containing piperidine (1.2 mL) were refluxed for 15 hrs, poured onto cold water (30 mL) and acidified with HCl (pH= 3). The solid product thus formed was filtered and crystallized from dioxane. It was obtained as yellow crystals; Yield: 86%; m.p.: 178-180 °C; IR (KBr, cm-1): 3440 (OH), 3331, 3202 (NH_2), 3058 (C–H aromatic), 2212 (C≡N), 1638 (C=O); ^{1}H-NMR (DMSO-d6) δ = 7.20-8.38 (m, 11H, aromatic protons), 9.97 (s, 1H, OH),12.02 (s, 2H, NH2); MS (m/z): 372 (M^++2), Anal. calcd for: $C_{22}H_{14}N_2O_2S$ (370): C, 71.33; H, 3.81; N, 7.56; Found: C, 71.34; H, 3.82; N, 7.55%.

Preparation 6-(2-hydroxynaphthalen-1-yl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile (12)

A mixture of 1 (0.01 mol), malononitrile (0.01 mol) in ethanol (30 ml) containing catalytic amount of piperidine was heated under reflux for 24 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent. It was obtained as pale yellow crystals from ethanol; Yield: 76 %; m.p.: 146–148°C; IR (KBr, cm^{-1}): 3408 (OH), 3400 (NH), 3060 (C–H aromatic), 2192 (C≡N), 1636 (C=O);^{1}H-NMR (DMSO-d6) δ = 7.09 (s, 1H,=CH), 7.20-8.39 (m, 11H, aromatic protons), 9.70 (s, 1H, NH), 9.98 (s, 1H, OH); MS (m/z): 338 (M^+), Anal.calcd for $C_{22}H_{14}N_2O_2$ (338) C, 78.09; H, 4.17; N, 8.28; found: C, 78.08; H, 4.16; N, 8.29%.

Preparation of 6-(2-hydroxynaphthalen-1-yl)-2-oxo-4-phenyl-2H-pyran-3-carbonitrile (14)

A mixture of 1 (0.01 mol), ethylcyanoacetate in ethanol (30 ml) containing catalytic amount of piperidine was heated under reflux for 24 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent. It was obtained as pale yellow crystals from ethanol; Yield: 83 %; m.p.: 160–162°C; IR (KBr, cm^{-1}): 3450 (OH), 3062 (C–H aromatic), 2196 (C≡N), 1658 (C=O);^{1}H-NMR (DMSO-d6) δ = 6.92-8.38 (m, 12H, aromatic), 9.20 (s, 1H, OH); MS (m/z): 339 (M+), Anal.calcd for C22H13NO3 (339)**:**C, 77.87; H, 3.86; N, 4.13; found: C, 77.86; H, 3.85; N, 4.14%.

Synthesis of compounds (19a-d)

General procedure: A mixture of 1 (0.01 mol) and arylidine malononitrile 15a–d (0.01 mol) in ethanol (40 ml) containing catalytic amount of piperidine (1.2 ml) was refluxed for 6 hrs and poured onto cold water (30 ml) and acidified with HCl (pH= 3). The solid product was collected and crystallized from ethanol to afford 19a-d.

2-Amino-5-(2-hydroxy-1-naphthoyl)-4,6-diphenyl-4H-pyran-3-carbonitrile (19a)

It was obtained as brown crystals from ethanol; Yield: 81 %; m.p.: 168–170 oC; IR (KBr, cm-1): 3448 (OH), 3420, 3400 (NH_2), 3064 (C–H aromatic), 2932 (CH

aliph), 2197 (C≡N), 1640 (C=O).), 1H-NMR (DMSO-d6) δ = 4.35 (s, 1H, 4H-pyrane), 7.20-8.37 (m, 18H, aromatic protons + NH2), 9.97 (s, 1H, OH), Anal.calcd for C29H20N2O3 (444): C, 78.36; H, 4.54; N, 6.30; Found: C, 78.37; H, 4.53; N, 6.31%.

2-Amino-4-(4-chlorophenyl)-5-(2-hydroxy-1-naphthoyl)-6-phenyl-4H-pyran-3-carbonitril (19b)

It was obtained as pale yellow crystals from ethanol; Yield: 81%; m.p.:160–162^{o}C; IR (KBr, cm^{-1}): 3447 (OH), 3420, 3400 (NH2), 3058 (C–H aromatic), 2191(C≡N), 1639 (C=O), ^{1}H-NMR (DMSO-d6) δ= 4.36 (s, 1H, 4H-pyrane), 7.17-8.34 (m, 17H, aromatic protons+ NH2), 9.95 (s, 1H, OH); MS (m/z): 480 (M^{+}+2), Anal.calcd for $C_{29}H_{19}ClN_2O_3$ (478): C, 72.73; H, 4.00; N, 5.85; found: C, 72.72; H, 4.01; N, 5.86%.

2-Amino-5-(2-hydroxy-1-naphthoyl)-4-(4-methoxyphenyl)-6-phenyl-4H-pyran-3-carbonitrile (19c)

It was obtained as pale yellow crystals from ethanol; Yield: 85%; m.p.:216–218^{o}C; IR (KBr, cm^{-1}): 3450 (OH), 3345, 3210 (NH_2), 2924 (C–H aliph), 2193 (C≡N), 1624 (C=O); ^{1}H-NMR (DMSO-d6) δ = 3.83 (s, 3H, OCH_3), 4.40 (hump, 1H, 4H-pyrane), 7.07-8.29 (m, 17H, aromatic protons + NH_2), 9.93 (s, 1H, OH); MS (m/z): 474 (M^{+}), Anal.calcd for $C_{30}H_{22}N_2O_4$ (474): C, 75.94; H, 4.67; N, 5.90; found: C, 75.93; H, 4.66; N, 5.91%.

2-Amino-5-(2-hydroxy-1-naphthoyl)-4-(4-hydroxyphenyl)-6-phenyl-4H-pyran-3-carbonitrile (19d)

It was obtained as brown crystals from ethanol; Yield: 79 %; m.p.: 163–165^{o}C; IR (KBr, cm-1): 3347 (OH), 3300, 3222 (NH_2), 3063 (CH arom), 2934 (C–H aliph), 2199 (C≡N), 1624 (C=O).); ^{1}H-NMR (DMSO-d6) δ = 4.50 (s, 1H, 4H-pyrane), 6.92 (s, 2H, NH_2), 6.94-8.38 (m, 15H, aromatic protons), 9.98 (s, 1H, OH), 10.02 (s, 1H, OH); Anal.calcd for C29H20N2O4 (460): C, 75.15; H, 4.38; N, 6.08; Found: C, 75.14; H, 4.37; N, 6.09%.

Synthesis of compounds (24a-d)

General procedure: A mixture of compound 1 (0.01 mol) and arylidine cyanothioacetamide derivatives 20a-c (0.01 mol) in ethanol with catalytic amount of piperidine was heated under reflux for 10 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent give 24a-c.

5-(2-Hydroxy-1-naphthoyl)-4,6-diphenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (24a)

It was obtained as yellow crystals from ethanol; Yield: 76%; m.p.: 173–175 ^{o}C; IR (KBr, cm^{-1}): 3434 (OH), 3400 (NH), 3071 (C–H aromatic), 2189 (C≡N), 1634 (C=O); 1H-NMR (DMSO-d6) δ=7.58-8.36 (m, 17H, aromatic and NH protons), 9.96 (s, 1H, OH); MS (m/z): 459 (M^{+} +1), Anal.calcd for $C_{29}H_{18}N_2O_2S$ (458):C, 75.96; H, 3.96; N, 6.11; found: C, 75.97; H, 3.95; N, 6.12%.

4-(4-Chlorophenyl)-5-(2-hydroxy-1-naphthoyl)-6-phenyl-2-thioxo-1,2-dihydropyridine-3carbonitrile (24b)

It was obtained as yellow crystals from ethanol; Yield: 76 %; m.p.: 173–175 ^{o}C; IR (KBr, cm^{-1}): 3464 (OH), 3433 (NH), 3070 (C–H aromatic), 2193(C≡N), 1634 (C=O);^{1}H-NMR (DMSO-d6) δ = 7.15-8.32 (m, 16H, aromatic and NH protons), 9.94 (s, 1H, OH); MS (m/z): 494 (M^{+}+2), Anal.calcd for $C_{29}H_{17}ClN_2O_2S$ (492)***:*** C, 70.65; H, 3.48; N, 5.68; found: C, 70.65; H, 3.48; N, 5.68%.

5-(2-Hydroxy-1-naphthoyl)-4,6-diphenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile(24c)

It was obtained as yellow crystals from ethanol; Yield: 76 %; m.p.: 178–180 oC; IR (KBr, cm-1): 3408 (OH), 3400 (NH), 3072

(C–H aromatic), 2924 (CH aliph), 2190 (C≡N), 1634 (C=O); ^{1}H-NMR (DMSO-d6) δ = 3.90 (s, 3H, OCH_3),7.16-8.33 (m, 16H, aromatic and NH protons), 9.95 (s, 1H, OH); MS (m/z): 488 (M^+), Anal.calcd for $C_{30}H_{20}N_2O_3S$(488):C,73.75; H, 4.13; N, 5.73;Found: C, 73.74; H, 4.12; N, 5.74%.

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استخدام مركبات البيتا ثنائي الكيتون في تحضير مركبات غير متجانسة الحلقة: تحضير مشتقات جديدة من المركبات رباعي هيدروبيرميدين ثيون، بيرازول، ثيوفين، ثنائي هيدرو بيريدين، ثنائي هيدروبيران ومشتقات البيريدازين

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نلاحظ نشاط المركبات البيتا ثنائي الكيتون تجاه الكواشف النيكليوفيلية والالكتروفيلية ودورها في تحضير مركبات مهمة في تحضيرالعديد من المركبات غير المتجانسة الحلقة والتي قمنا باثبات تركيبها من خلال التحاليل الطيفية المختلفة، لقد قمنا بتفاعل المركب البيتا ثنائي الكيتون ١، الذي تم تحضيره بتفاعل البيتا نافثول مع ايثيل بنزويل استات في الميكروويف، مع الالدهيدات الاروماتية 3a-d واعطت المركبات 4a-d والتي بدورها تفاعلت مع الثيويوريا واعطت المركبات المركبات رباعي هيدروبيرميدين ثيون 5a-d، كما قمنا بتفاعل المركب البيتا ثنائي الكيتون ١ مع الهيدرازين والفينيل هيدرازين واعطي التفاعل المركبان 7a,b، وقمنا بتحضير مشتق الثيوفين ١٠ بتفاعل المركب ١ مع المالونونيتريل في وجود الكبريت. كذلك تم تفاعل المركب ١ مع المالونونيتريل فقط واعطي المشتق ثنائي هيدروبيريدين ١٢, بينما حصلنا علي المشتق ثنائي هيدروبيران ١٤ بتفاعل المركب١ مع ايثيل سيانواستات، أيضا تم تحضير مشتقات البيران 19a-d ومشتقات رباعي هيدروبيريدين ثيون 24a-c من خلال تفاعل المركب ١ مع كلا من مشتقات اريلادين مالونونيتريل 15a-d ومشتقات اريلادين سيانو ثيواستاميد20a-c علي التوالي.

الكلمات الاسترشادية: ٢-النفثول، إيثيل بنزويل اتات، ب-كيتون ثنائي، آريل الدهيد، ثيوريا، الهيدرازين، فينيل الهيدرازين، مالونونيترايل، الكبريت العنصري، إيثيل سيانو اتات، اريلدين مالونيتريل.

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