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REGIOSELECTIVE NITROSO DIELS-ALDER CYCLOADDITION REACTIONS OF 5-DIENYL PYRIMIDINONES AND TRANSFORMATION TO NOVEL 4-AMINO-ALCOHOL TETHERED PYRIMIDINONES

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Abstract – A highly regioselective nitroso Diels-Alder (NDA) cycloaddditon of nitroso benzene with variedly substituted 5-dienyl pyrimidinones with and the transformation of adducts to novel, unnatural, biologically important 4-amino alcohols is reported.

INTRODUCTION

In the last few years, a number of pyrimidinone and pyrimidindione derivatives have emerged in the field of chemotherapy. In this context, C-5 or C-6 substituted pyrimidinone and pyrimidindione derivatives showed selective antitumor, antiviral, antitubercular and antifungal activities.[1] Recently, pyrimidinone derivatives *viz.* 2-methylthio-6-[(2-alkylamino)ethyl]-4(*3H*)-pyrimidinones have been shown to possess activity against positive strand (rubella virus and sindbis virus) and negative strand (vesicular stomatitis virus) RNA virus.[2] A series of 1-(biphenylmethylamidoalkyl)pyrimidinones has also been designed as nanomolar inhibitors of recombinant lipoprotein-associated phospholipase A_2 with high potency in whole human plasma.[3] Also, thienopyrimidine derivatives have been reported to possess useful molluscidal and larvacidal activities against *Biomphalaria alexendra* and *Schistosoma mansoni,* snails.[4]

The Hetero Diels-Alder reaction (HDA) has emerged as the method of choice for the stereocontrolled synthesis of six-membered heterocycles. Many biologically imperative molecules such as dihydropyrones and dihydropyridones, building blocks to a wide range of natural products of interest, have been synthesized using this methodology.[5] The HDA cyloadditions with various nitroso dienophiles *viz.* nitrosobenzene, α-nitrosoalkenes, acylnitroso, α-acetoxynitroso compounds *etc.* have become an

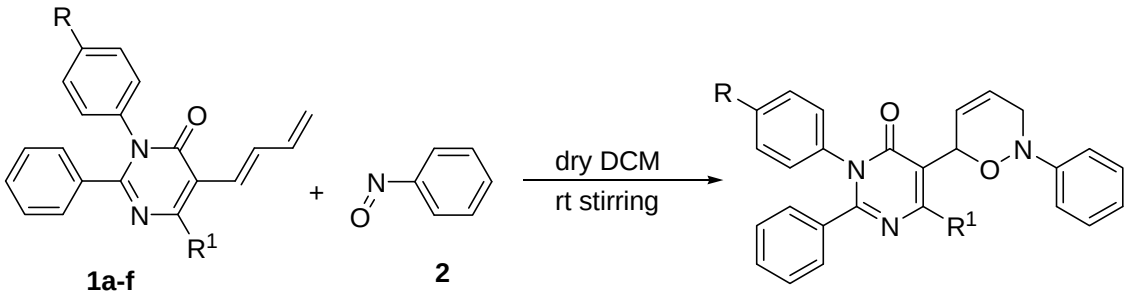
This paper is dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday

integral part of the modern armamentarium for the total synthesis of a number of novel compounds and natural products.[6] The nitroso Diels-Alder (NDA) reactions is also remarkable synthetic transformation because it produces a 1,4-amino-oxo group in a single synthetic opeartion. In most instances, the NDA cycloaddition reactions are reported to be concerted and occur with complete stereoselection. Moreover, if the diene is dissymmetric enough in terms of π-electron density, the HDA cycloaddition reactions occur with high enantio- and regioselectivity.[7]

As a part of our enduring interest in building heterocyclic systems of biological enormity, we have reported the synthesis of variedly substituted 5-dienyl pyrimidinones[8,9] and have also employed the dienyl moiety as $2\pi/4\pi$ component in various thermal,[9] Lewis acid catalysed Diels-Alder and imino Diels-Alder cycloadditions.[10] In continuation of these studies we report herein the cycloaddition reactions of 5-dienyl pyrimidinones with nitrosobenzene[11] and subsequent transformation of adducts to previously unknown 5-(4-amino alcohol) tethered pyrimidinones.

RESULTS AND DISCUSSION

Thus, the treatment of **1a-f** with 1.1 *eq* of nitrosobenzene **2** in dry dichloromethane for 5-6 h resulted in the regioselective formation of HDA adducts **3a-f** in excellent yields (75-85%) (**Scheme 1**).



1a-f

1a R=H R^1=Me
1b R=Me, R^1=Me
1c R=H, R^1= H
1d R=Me, R^1=H
1e R=H, R^1=morpholine
1f R=H, R^1=pyrollidine

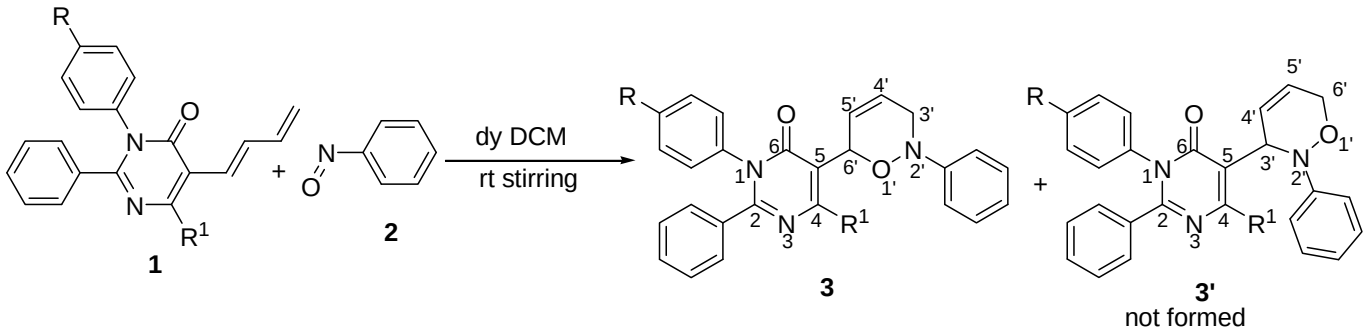
2

3a-f

3a R=H R^1=Me
3b R=Me, R^1=Me
3c R=H, R^1= H
3d R=Me, R^1=H
3e R=H, R^1=morpholine
3f R=H, R^1=pyrollidine

Scheme 1

The adducts **3a-f** were characterized as 2,3,6-trisubstituted-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3*H*-pyrimidin-4-ones on the basis of analytical data and spectral evidences. The ^{1}H NMR spectrum of the crude adduct revealed the exclusive formation of one regioisomer **3** and did not indicate the presence of alternative regioisomer **3'**even in traces. (**Scheme 2**)



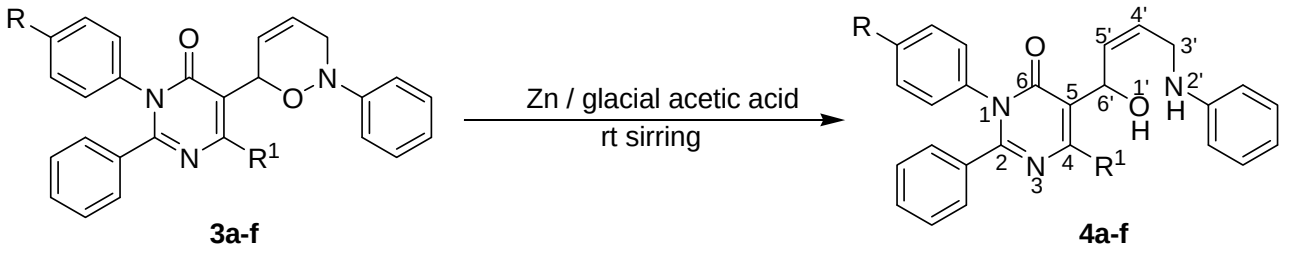
Scheme 2

The observed cycloadducts were configured as *meta*-regiomers on the basis of literature reports on the cycloaddition between 1-substituted dienes and nitroso dienophiles.[12] The observed *meta*-regioselectivity in these hetero Diels-Alder cycloadditions is probably due to the favourable electronic factors and unfavorable steric interaction between the phenyl groups of the nitrosobenzene and pyrimidinone ring during cycloaddition reactions.

The compound **3a**, for example, 6-Methyl-2,3-diphenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3*H*-pyrimidin-4-one was analyzed for $C_{27}H_{23}N_3O_2$ and showed the molecular ion peak at 421. Its IR spectrum exhibited a sharp absorption at 1488 and 1521 cm^{-1} corresponding to cyclic nitroso compound and a sharp absorption at 1662 cm^{-1} due to the carbonyl of the pyrimidinone ring. The salient feature of the ^1H spectrum include a singlet at δ 2.56 corresponding to three protons of the methyl group, a fine splitted doublet of an AB quartet δ 4.00 (J = 2.7 Hz and 14.4 Hz) assinged to two methylene protons, a multiplet at δ 6.08 for the two olefenic protons at $C_{4'}$ and $C_{5'}$ and a doublet at δ 6.33 (J = 1.5Hz) corresponding to the methine at $C_{6'}$. Its ^{13}C spectra also attest the presence of the required carbons along with a characteristic carbonyl peak at δ 162.6.

Amino alcohols are attractive compounds, either as ligands for asymmetric stereoselective catalysis[13] or as building blocks for the preparation of biologically active molecules.[14] Some of the chiral amino alcohols are natural products, such as cinchonine, cinchonidine, quinine, quinidine, ephedrine and norephedrine.[15] Consequently, the construction of this structural motif attracts extensive efforts by organic chemists. Developing novel methods to prepare amino alcohols with efficiency remains one of the major challenges. Many inroads have been made in this regard which include hydrogenation of pthalimido ketone,[16] reductive cross-coupling of chiral *N*-tert-butanesulfinyl imines with aldehydes,[17] Indium trichloride catalyzed Mukaiyama aldol reaction of keto ester,[18] amino ketones reduction.[19] and the reductive cleavage of 3,6-dihydro-1,2-oxazines.[20] Keeping in view of the importance of amino alcohols, it was considered appropriate to explore the cleavage of the N-O bond of the above synthesized 5-dihydrooxazine substituted pyrimidinones.

Thus the treatment of a solution of **3a-f** in glacial acetic acid with zinc powder resulted in the good yields (70-75%) of previously unknown amino alcohols **4a-f**. (**Scheme 3**)



3a-f **4a-f**

3a R=H R^1=Me
3b R=Me R^1=Me
3c R=H, R^1= H
3d R=Me R^1=H
3e R=H, R^1=morpholine
3f R=H, R^1=pyrollidine

4a R=H R^1=Me
4b R=Me R^1=Me
4c R=H, R^1= H
4d R=Me R^1=H
4e R=H, R^1=morpholine
4f R=H, R^1=pyrollidine

Scheme 3

These aminoalcohols were characterized as 5-(1-hydroxy-4-phenylamino-but-2-enyl)-3*H*-pyrimidin-4-ones **4** through their analytical data and spectral evidences. The compound **4a**, for example, was analyzed for $C_{27}H_{25}N_3O_2$ showed the molecular ion peak at 423. Its IR spectrum exhibited a sharp absorption at 1647 cm^{-1} due to the carbonyl of the pyrimidinone ring, a broad absorption at 3357cm^{-1} assigned to intramolecularly hydrogen bonded OH group. Its ^1H spectrum showed a singlet at δ 2.47 corresponding to three methyl protons of the pyrimidinone ring, a doublet of a doublet of an AB quatret at δ 3.99 (J = 1.5 Hz, 6.6Hz and 14.1Hz) assigned to the methylene protons at $C_{3'}$. The 1.5 Hz coupling with NH proton disappears in the presence of D_2O. A doublet of a doublet at δ 5.62 (J = 2.7 and 8.7 Hz) corresponding to a proton for $C_{6'}$. The small splitting of 2.7 Hz was assigned to the coupling with OH proton due to its disappearance in the presence of D_2O. A doublet of a triplet of a doublet (dtd) at δ 5.76 (J = 0.9Hz, 6.6 Hz, 10.8 Hz) corresponding to the $C_{4'}$ proton, a triplet of a doublet of a doublet (tdd) at δ 6.12 (J = 1.5Hz, 8.7 Hz, 10.8 Hz) assigned to a proton at $C_{5'}$. Its ^{13}C spectra showed the expected number of carbons and a characteristic carbonyl peak at δ 163.6. The absence of the IR absorptions at 1488 and 1521 cm^{-1} corresponding to the characteristic N-O stretching for cyclic nitroso compounds further supports the structure of amino alcohols. In conclusion, a facile, high yielding route for the synthesis of functionalized 3,6-dihydro-1,2-oxazines substituted pyrimidinones and their corresponding reductive ring cleavage to yield novel, unnatural, multicomponent 1,4-amino alcohol tethered pyrimidinones is devised.

EXPERIMENTAL

GENERAL REMARKS

Melting points were determined by open capillary using Veego Precision Digital Melting Point apparatus (MP-D) and are uncorrected. IR spectra were recorded on a Shimadzu D-8001 spectrophotometer. ^{1}H NMR spectra were recorded in deuterochloroform with Joel (300 MHz) spectrometers using TMS as internal standard. Chemical shift values are expressed as ppm downfield from TMS and *J* values are in Hz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, m: multiplet, q: quartet, br: broad peak and brs: broad singlet. ^{13}C NMR spectra were also recorded on Joel 300 (75.0 MHz) spectrometers in deuterochloroform using TMS as internal standard. Mass spectra were recorded on Shimadzu GCMS-QP-2000 mass spectrometer. Elemental analyses were performed on Heraus CHN-O-Rapid Elemental Analyzer. Column chromatography was performed on a silica gel (60–120) mesh.

STARTING MATERIALS:

All starting materials *viz* 5-dienylpyrimidinones[8] and nitroso benzene[11] were prepared by reported procedures. Dichloromethane was dried over *di*-phosphorous pentoxide and stored over molecular sieve (4Å).

GENERAL PROCEDURE:

A) 5-(2-PHENYL-3,6-DIHYDRO-2*H*-[1,2]OXAZIN-6-YL)-3*H*-PYRIMIDIN-4-ONE

A solution of 5-dienylpyrimidinone **1** (1.0 *eq*) and nitrosobenzene **2** (1.1 *eq*) in dry CH_2Cl_2 was stirred at rt for 4-5 h. The progress of the reaction was monitored with the help of tlc. After the completion of the reaction, the mixture was concentrated under *vacuo* and the crude reaction mixture thus obtained was chromatographed on 60-120-mesh silica gel to yield 5-dihydroxaxinyl pyrimidinones **3** [eluent: 1 : 5: EtOAc : hexane]. The products were recrystallized from 1 : 2: CH_2Cl_2 : hexane.

B) 5-(1-HYDROXY-4-PHENYLAMINO-BUT-2-ENYL)-3*H*-PYRIMIDIN-4-ONES

To the solution of 5-dihydroxazinylpyrimidinones **3** (1.0 mmol) in glacial acetic acid, zinc powder (2.0 m mol) was added in small lots and the reaction mixture was stirred at rt for 0.5-1.0 h. The progress of the reaction was checked with the help of tlc monitoring. After the completion of the reaction, the reaction mixture was vigorously washed with ice cold saturated aqueous $NaHCO_3$ and extracted in CH_2Cl_2. The mixture was concentrated under *vacuo* and the crude reaction mixture thus obtained was chromatographed on 60-120-mesh silica gel to yield 5-(4-amino alcohol) substituted pyrimidinones **4** [eluent: 1 : 5: EtOAc : hexane]. The products were recrystallized from 1 : 3: EtOAc : hexane.

6-Methyl-2,3-diphenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3*H*-pyrimidin-4-one (3a):
Pale Yellow solid (85%) mp 116–118 °C. IR (KBr): ν_{max} = 1488, 1521, 1662.5, 3041.5, 3056.9 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 2.56 (s, 3H, CH_3), 3.92 -4.04 (dABq, J = 2.7Hz, 14.4Hz, 2H, CH_2), 6.08 (m, 2H, $H_{4'}$, $H_{5'}$), 6.33-6.34 (d, J = 1.5 Hz, 1 H, $H_{6'}$), 6.97-7.38 (m, 15 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 22.9, 47.5, 51.1 ($C_{3'}$), 73.0, 116.1, 119.1, 122.4, 123.3, 128.0, 128.7, 128.8, 128.9, 129.7, 134.6, 151.2, 162.6 (C=O) ppm. MS *m*/*z* 421 $[M]^+$. Anal. Calcd for $C_{27}H_{23}N_3O_2$: C 76.94, H 5.50, N 9.97. Found C 77.05, H 5.65, N 9.75.

6-Methyl-2-phenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3-*p*-tolyl-3*H*-pyrimidin-4-one (3b):
Pale Yellow solid (82%) mp 121–123 °C. IR (KBr): ν_{max} = 1495, 1533, 1663.4, 3052.2, 3062.6 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 2.31 (s, 3H, CH_3), 2.55 (s, 3H, -$CH_3C_6H_4$), 3.99-4.08 (dABq, J = 2.7Hz, 14.4Hz, 2H, CH_2), 6.05 (m, 2H, $H_{4'}$, $H_{5'}$), 6.31-6.33 (d, J = 1.5 Hz, 1 H, $H_{6'}$), 6.97-7.38 (m, 14 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 22.7, 23.3 46.8, 51.8 ($C_{3'}$), 72.8, 115.9, 118.8, 122.2, 123.1, 127.9, 128.6, 128.8, 129.0, 129.6, 134.5, 150.8, 162.4 (C=O) ppm. MS *m*/*z* 436 $[M]^+$. Anal. Calcd for $C_{28}H_{25}N_3O_2$: C 77.22, H 5.79, N 9.65. Found C 77.36, H 5.85, N 9.58.

2,3-Diphenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3*H*-pyrimidin-4-one (3c):
Pale Yellow solid (79%) mp 112-114 °C. IR (KBr): ν_{max} = 1488, 1518, 1658.2, 3046.2, 3058.6 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 3.93-3.97 (dABq, J = 3.0Hz, 14.7Hz, 2H, CH_2), 5.85-5.87 (d, J = 1.8 Hz, 1 H, $H_{6'}$), 6.16-622 (m, 2H, $H_{4'}$, $H_{5'}$), 6.90-7.33 (m, 15 H, ArH), 8.19 (s, 1H, H_4) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 52.3 ($C_{3'}$), 72.5, 115.9, 118.8, 122.2, 123.1, 127.9, 128.6, 128.8, 129.0, 129.6, 134.5, 151.8, 162.4 (C=O) ppm. MS *m*/*z* 407 $[M]^+$. Anal. Calcd for $C_{26}H_{21}N_3O_2$: C 76.64, H 5.19, N 10.31. Found C 76.85, H 5.25, N 10.35.

2-Phenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3-*p*-tolyl-3*H*-pyrimidin-4-one (3d):
Pale Yellow solid (78%) mp 114-115 °C. IR (KBr): ν_{max} = 1492, 1522, 1660.5, 3048.2, 3060.6cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 2.29 (s, 3H, CH_3), 3.95-4.00 (dABq, J = 2.7Hz, 14.7Hz, 2H, CH_2), 5.93-5.96 (d, J = 1.8 Hz, 1 H, $H_{6'}$), 6.14-620 (m, 2H, $H_{4'}$, $H_{5'}$), 6.92-7.36 (m, 14 H, ArH), 8.20 (s, 1H, H_4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 23.4, 52.4 ($C_{3'}$), 72.6, 115.7, 118.5, 121.6, 122.8, 126.9, 128.3, 128.4, 128.7, 129.2, 134.7, 150.6, 162.2 (C=O) ppm. MS *m*/*z* 421 $[M]^+$. Anal. Calcd for $C_{27}H_{23}N_3O_2$: C 76.94, H 5.50, N 9.97. Found C 77.06, H 5.62, N 9.85.

6-Morpholin-4-yl-2,3-diphenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-3*H*-pyrimidin-4-one (3e):

Pale Yellow solid (80%) mp 128–130 °C. IR (KBr): ν_{max} = 1527.5, 1584.2, 1647.15, 2331.8, 2360.7, 2852.3, 3004.9cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 3.71-3.87 (m, 8H, H, morpholine), 4.00-4.07 (dABq, J = 2.7Hz, 14.7Hz, 2H, CH_2), 5.98-5.99 (d, J = 1.8Hz, 1H, $H_{6'}$), 6.02-6.10 (m, 2H, $H_{4'}$, $H_{5'}$), 6.96-7.29 (m, 15 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 50.3, 50.9 ($C_{3'}$), 67.1, 96.1, 98.1, 116.0, 122.1, 122.5, 127.8, 128.2, 128.7, 128.8, 129.1, 129.2, 129.7, 130.1, 134.9, 137.65, 150.3, 162.7 (C=O) ppm. MS m/z 492 $[M]^+$. Anal. Calcd for $C_{30}H_{28}N_4O_3$: C 73.15, H 5.73, N 11.37. Found C 73.25, H 5.85, N 11.18.

2,3-Diphenyl-5-(2-phenyl-3,6-dihydro-2*H*-[1,2]oxazin-6-yl)-6-pyrrolidin-1-yl-3*H*-pyrimidin-4-one (3f):

Pale Yellow solid (80%) mp 122–124 °C. IR (KBr): ν_{max} = 1510.6, 1548.5, 1652.6, 2255.8, 2258.7, 3008.9 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 2.01-2.07 (m, 4H, -CH_2-CH_2-), 3.73-3.79 (m, 4H, -CH_2-N-CH_2-), 3.98-4.04 (dABq, J = 2.4Hz, 15.0Hz, 2H, CH_2), 5.96-5.98 (d, J = 1.8Hz, 1H, $H_{6'}$), 6.01-6.08 (m, 2H, $H_{4'}$, $H_{5'}$), 6.96-7.29 (m, 15 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 23.8, 45.4, 51.6 ($C_{3'}$), 70.2, 98.6, 116.2, 122.4, 126.5, 127.8, 127.9, 128.8, 129.7, 129.9, 130.3, 135.6, 137.8, 151.4, 162.6 (C=O) ppm. MS m/z 476 $[M]^+$. Anal. Calcd for $C_{30}H_{28}N_4O_2$: C 75.61, H 5.92, N 11.76. Found C 75.75, H 5.98, N 11.55.

5-(1-Hydroxy-4-phenylamino-but-2-enyl)-6-methyl-2,3-diphenyl-3*H*-pyrimidin-4-one (4a):

White solid (72%) mp 108-110 °C. IR (KBr): ν_{max} = 1514, 1647.1, 2848.6, 2918.1, 3357.6, 3388.7 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 2.48 (s, 3H, CH_3), 3.92-4.06 (ddABq, J = 1.5Hz, 6.6Hz, 14.1Hz, 2H, CH_2), 5.60-5.63 (dd, J = 2.7Hz, 8.7Hz, 1H, $H_{6'}$), 5.72-5.80 (dtd, J = 0.9Hz, 6.6 Hz, 10.8 Hz, 1H, $H_{4'}$), 6.07-6.14 (tdd, J = 1.5Hz, 8.7 Hz, 10.8 Hz,1H, $H_{5'}$), 6.62-7.36 (m, 15 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 23.2, 48.2, 52.0 ($C_{3'}$), 72.6, 116.3, 119.4, 122.6, 123.8, 128.2, 128.6, 128.9, 130.2, 130.6, 134.8, 150.8, 162.4 (C=O) ppm. MS m/z 423 $[M]^+$. Anal. Calcd for $C_{27}H_{25}N_3O_2$: C 76.57, H 5.95, N 9.92. Found C 76.76, H 6.02, N 9.81.

5-(1-Hydroxy-4-phenylamino-but-2-enyl)-6-methyl-2-phenyl-3-*p*-tolyl-3*H*-pyrimidin-4-one (4b):

White solid (75%) mp 110-112 °C. IR (KBr): ν_{max} = 1512, 1655.1, 2845.6, 2925.1, 3366.6, 3392.7 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 2.32 (s, 3H, CH_3), 2.56 (s, 3H, -$CH_3C_6H_4$) 3.94-4.07 (ddABq, J = 1.5Hz, 6.6Hz, 14.7Hz, 2H, CH_2), 5.62-5.64 (dd, J = 2.7Hz, 8.7Hz, 1H, $H_{6'}$), 5.74-5.80 (dtd, J = 0.9Hz, 6.6 Hz, 10.5 Hz, 1H, $H_{4'}$), 6.06-6.15 (tdd, J = 1.5Hz, 8.7 Hz, 10.5 Hz,1H, $H_{5'}$), 6.62-7.36 (m, 14 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 22.9, 24.2, 46.9, 52.0 ($C_{3'}$), 72.6, 116.3, 119.4, 122.6, 123.8, 128.2, 128.6, 128.9, 130.2, 130.6, 134.8, 150.8, 162.5 (C=O). MS m/z 437 $[M]^+$. Anal. Calcd for $C_{28}H_{27}N_3O_2$: C 76.86,

H 6.22, N 9.60. Found C 76.98, H 6.45, N 9.51.

5-(1-Hydroxy-4-phenylamino-but-2-enyl)-2,3-diphenyl-3*H*-pyrimidin-4-one (4c):

White solid (70%) mp 104-106 °C. IR (KBr): ν_{max} = 1516, 1648.1, 2852.6, 2924.1, 3348.6, 3395.5 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 3.88-4.04 (ddABq, *J* = 1.5Hz, 6.6Hz, 14.4Hz, 2H, CH_2), 5.62-5.68 (dd, *J* = 2.7Hz, 8.7Hz, 1H, $H_{6'}$), 5.74-5.82 (dtd, *J* = 0.9Hz, 6.6 Hz, 10.2 Hz, 1H, $H_{4'}$), 6.06-6.12 (tdd, *J* = 1.5Hz, 8.7 Hz, 10.2 Hz,1H, $H_{5'}$), 6.64-7.34 (m, 15 H, ArH), 8.19 (s, 1H, H_4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 52.0 ($C_{3'}$), 72.8, 116.3, 118.5, 122.6, 124.2, 128.3, 128.8, 128.6, 130.4, 130.8, 134.6, 150.6, 162.2 (C=O). MS *m*/*z* 409 $[M]^+$. Anal. Calcd for $C_{26}H_{23}N_3O_2$: C 76.26, H 5.66, N 10.26. Found C 76.36, H 5.92, N 10.04.

5-(1-Hydroxy-4-phenylamino-but-2-enyl)-2-phenyl-3-*p*-tolyl-3*H*-pyrimidin-4-one (4d):

White solid (72%) mp 106-108 °C. IR (KBr): ν_{max} = 1506, 1650.3, 2848.6, 2933.7, 3344.5, 3388.6 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 2.30 (s, 3H, CH_3), 3.90-4.05 (ddABq, *J* =1.5Hz, 6.6Hz, 14.7Hz, 2H, CH_2), 5.60-5.64 (dd, *J* =2.7Hz, 8.7Hz, 1H, $H_{6'}$), 5.75-5.83 (dtd, *J* = 0.9Hz, 6.6 Hz, 10.5 Hz, 1H, $H_{4'}$), 6.05-6.10 (tdd, *J* = 1.5Hz, 8.7 Hz, 10.5 Hz,1H, $H_{5'}$), 6.65-7.38 (m, 15 H, ArH), 8.20 (s, 1H, H_4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 23.2, 52.2 ($C_{3'}$), 72.6, 116.2, 119.0, 121.8, 123.6, 127.8, 128.2, 128.9, 130.1, 130.3, 134.7, 150.5, 162.5 (C=O). MS *m*/*z* 409 $[M]^+$. Anal. Calcd for $C_{27}H_{25}N_3O_2$: C 76.57, H 5.95, N 9.92. Found C 76.65, H 5.99, N 9.81.

5-(1-Hydroxy-4-phenylamino-but-2-enyl)-6-morpholin-4-yl-2,3-diphenyl-3*H*-pyrimidin-4-one (4e):

White solid (73%) mp 112–114 °C. IR (KBr): ν_{max} = 1508, 1652.5, 2850.2, 2933.9, 3334.6, 3399.5cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 3.72-3.97 (m, 8H, H, mopholine), 3.92-4.06 (ddABq, *J* = 1.5Hz, 6.6Hz, 14.4Hz, 2H, CH_2), 5.65-5.69 (dd, *J* = 2.7Hz, 8.4Hz, 1H, $H_{6'}$), 5.78-5.85 (dtd, *J* = 0.9Hz, 6.6 Hz, 10.2 Hz, 1H, $H_{4'}$), 6.06-6.10 (tdd, *J* = 1.5Hz, 8.4 Hz, 10.2 Hz,1H, $H_{5'}$), 6.78-7.40 (m, 15 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 50.6, 51.1 ($C_{3'}$), 67.2, 95.8, 98.6, 116.2, 122.6, 122.8, 127.9, 128.5, 129.0, 129.3, 129.5, 129.6, 129.9, 130.2, 134.9, 137.9, 150.2, 162.5 (C=O) ppm. MS *m*/*z* 492 $[M]^+$. Anal. Calcd for $C_{30}H_{28}N_4O_3$: C 72.85, H 6.11, N 11.33. Found C 72.95, H 6.21, N 11.12.

5-(1-Hydroxy-4-phenylamino-but-2-enyl)-2,3-diphenyl-6-pyrrolidin-1-yl-3*H*-pyrimidin-4-one (4f):

White solid (71%) mp 110-112 °C. IR (KBr): ν_{max} = 1512, 1648.5, 2845.2, 2932.9, 3335.6, 3392.5cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ_H = 2.02-2.08 (m, 4H, -CH_2-CH_2-), 3.72-3.79 (m, 4H, -CH_2-N-CH_2-), 3.90-4.05 (ddAbq, *J* = 1.5Hz, 6.6Hz, 14.4Hz, 2H, CH_2), 5.66-5.70 (dd, *J* =2.7Hz, 8.7Hz, 1H, $H_{6'}$), 5.78-5.85 (dtd, *J* = 0.9Hz, 6.6 Hz, 10.5 Hz, 1H, $H_{4'}$), 6.07-6.11 (tdd, *J* = 1.5Hz, 8.7 Hz, 10.5 Hz,1H, $H_{5'}$),

6.69-7.35 (m, 15 H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 23.8, 45.8, 51.1 ($C_{3'}$), 67.6, 95.7, 98.8, 116.3, 122.2, 122.5, 126.9, 128.2, 129.4, 129.5, 129.6, 129.8, 129.9, 130.5, 134.9, 138.1, 150.1, 162.2 (C=O) ppm. MS *m*/*z* 478$^+$. Anal. Calcd for $C_{30}H_{30}N_4O_2$: C 75.29, H 6.32, N 11.71. Found C 72.36, H 6.42, N 11.55.

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