One-Pot Synthesis of 13-Acetyl-9-methyl-11-oxo(or thioxo)-8-oxa-10,12-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trienes under Microwave Irradiation

Qingfang Cheng,[a,b]* Qifa Wang,[a] Tin Tan,[b] Na Chen,[b] and Mei Shuai[b]

[a]Jiangsu Key Laboratory of Marine Biotechnology, Huaihai Institute of Technology, Lianyungang 222005, China
[b]Department of Chemical Technology, Huaihai Institute of Technology, Lianyungang, Jiangsu 222005, China
*E-mail: spring817191@sina.com

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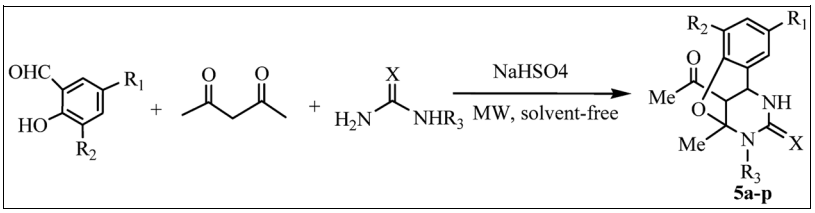

Oxygen-bridged monastrol analogs, 13-acetyl-9-methyl-11-oxo(or thioxo)-8-oxa-10,12-diazatricyclo[7.3. $1.0^{2,7}$] trideca-2,4,6-trienes, were synthesized by one-pot three component condensation reaction of substituted salicylaldehyde, acetylacetone and urea or thiourea with nontoxic, inexpensive, and easily available $NaHSO_4$ as catalyst under microwave irradiation and solvent-free conditions in short time with good yields. The structures of the products were characterized by IR, ^{1}H NMR, ^{13}C NMR spectra, and elemental analyses.

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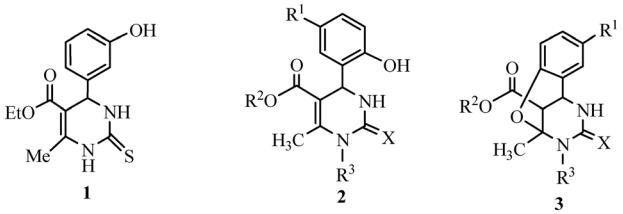
INTRODUCTION

3,4-Dihydropyrimidin-2-(1*H*)-ones(DHPMs) and their derivatives are an important class of heterocyclic compounds having important biological and pharmacological activities [1–4]. Monastrol, one of DHPMs, ethyl 6-methyl-4-(3-hydroxyphenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate(**1**), is a recently highlighted compound [5,6], which showed promise in a new strategic approach to cancer research and has been found to affect the function of mitotic kinesin Eg5, a motor protein responsible for spindle bipolarity [7,8]. Thus, kinesin spindle protein represents an attractive target for biochemical studies because human Eg5 inhibitors induce cell death via apoptosis [9]. One of the simple and direct method for the synthesis of monastrol analogs known as Biginelli reaction involves the one-pot condensation of an aldehyde with a hydroxyl, a β-ketoester and urea or thiourea. Lewis acids and transition metal salts such as $Sr(OTf)_2$ [10], *p*-TsOH [11], HPA [12], $NiCl_2{\cdot}6H_2O$ [13], $LaCl_3$ [14], $InBr_3$ [15], Bakers' yeast [16] have been used to catalyze this Biginelli reaction. Obviously, most of these catalysts and solvents are not acceptable in the context of green synthesis and the procedure involved harsh condition, long reaction time and low yield etc. We reported [17,18] the three-component heterocyclization of salicylaldehyde or substitued salicylaldehyde, β-ketoester and urea or thiourea catalyzed by nontoxic, inexpensive $NaHSO_4$ under solvent-free conditions, the reaction formed two different products, 4-(2-hydroxyphenyl) pyrimidines(**2**) and oxygen-bridged pyrimidine derivatives, 9-methyl-11-oxo(or thioxo)-8-oxa-10,12-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene (**3**) depending on the ester alkyl group (Scheme 1).

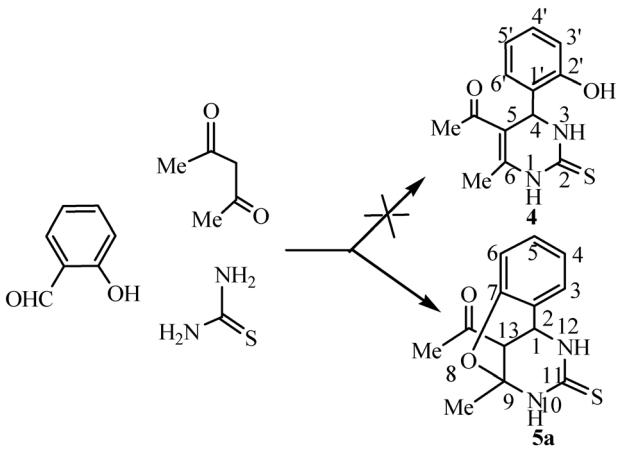
This oxygen-bridged pyrimidine structures were not discussed in several recent reports [12–14], but were supported by others [15,16,19]. Microwave-assisted reactions have received a great deal of attention since 1986 [20], because microwave-assisted reactions are efficient, higher yields, clean, safe, and greater selectivity for the targeted product under milder reaction conditions [21,22]. We have reported one-pot, three-component reaction of aromatic aldehydes, malononitrile, and barbituric acid under microwave irradiation successfully [23]. Thus, as a part of our program towards environment-friendly multicomponent reactions(MCRs) [24,25], we would like to report herein, a simple one-pot, three-component reaction of substitued salicylaldehydes with urea(or thiourea, phenylurea) and acetylacetone, as active methylene component for the synthesis of some new monastrol analogs under microwave irradiation and solvent-free conditions using $NaHSO_4$ as a nontoxic, inexpensive, and easily available catalyst. However, the obtained products will be oxygen-bridged monastrol analogs, 13-acetyl-9-methyl-11-thioxo-8-oxa(or thioxo)-10,12- diazatricyclo[7.3.1.$0^{2,7}$] trideca-2,4, 6-triene derivatives rather than free hydroxyl compounds.

The three-component cyclocondensation reaction of salicylaldehyde, acetylacetone and thiourea was first performed to examine the effectiveness of $NaHSO_4$ (Scheme 2). This three-component cyclocondensation reaction may be performed under relatively simple reaction conditions by heating together the three components,

Scheme 1



Scheme 2



salicylaldehyde, acetylacetone and thiourea, in the ratio of 1:1:1.5 and NaHSO4 (20 mol %), to 85°C under microwave irradiation. After the completion of the reaction, the reaction mixture was poured onto crushed ice. From which the monastrol derivative were isolated by filtration and recrystallized from ethanol.

The product showed a NMR spectra inconsistent with the expected free hydroxyl dihydropyrimidinone **4** when the structure of the product was characterized by ^{1}H, ^{13}C NMR. Both of ^{1}H NMR and ^{13}C NMR spectra showed the Biginelli product will be an oxygen-bridged compound, 13-acetyl-9-methyl-11-thioxo-8-oxa-10,12-diaza-tri-cyclo [7.3.1.0^{2,7}]trideca- 2,4,6-triene **5a** (Scheme 2). Structure **5a** is assigned to this oxygen-bridged product on the basis of comparisons of its ^{1}H and ^{13}C NMR spectra with those of a similar structural dihydropyrilnidinone **4**, reported in the previous article [26]. The presence of a new proton signal at 3.37–3.44 ppm in the ^{1}H NMR spectrum of compound **5a** was assigned to H-13, implying the proton was connected to a *sp* carbon and the lack of a double bond between C-9 and C-13, or the presence of all oxygen-bridge. This conclusion was supported by the presence of a proton signal at 4.31 ppm, assigned to H-1. In the case of **4**, The corresponding signal appeared at about 5.25 ppm for the proton at C-4. These facts indicate that there is no double bond between C-9 and C-13 in the molecule of **5a**. The above conclusion from ^{1}H NM R was supported by ^{13}C NMR, there are three carbon signals at 46.0, 81.5, and 52.2 ppm in the ^{13}C NMR spectrum of **5a**, assigned to C-1, C-9, and C-13, respectively. This oxygen-bridged pyrimidine structures were not discussed in previous article [27], but were supported by the other [26].

To evaluate the effectiveness of the catalyst in inducing this Biginelli three component condensation reaction and confirm the structures of oxygen-bridged products, we initiated a series of exploratory experiments involving substituted salicylaldehyde, acetylacetone and urea(or thiourea, phenylurea) with $NaHSO_4$ as catalyst under microwave irradiation and solvent-free conditions (Scheme 3). The results presented in the Table 1 indicate the scope and generality of the method, which is efficient, not only for urea or thiourea, phenylurea, but also for salicylaldehyde as well as substituted salicylaldehydes. In most cases, the reactions proceeded smoothly to produce the corresponding monastrol analogs in short time (10–15 min) with good yields. The products will be oxygen-bridged compounds, 13-acetyl-9-methyl-11-thioxo-8-oxa(or thioxo)-10,12-diazatricyclo[7.3.1.0^{2,7}] trideca-2,4,6-trienes **5b-p** (Scheme 3).

Selected ^{1}H and ^{13}C NMR spectral datas of **5a-p** are summarized in Table 2. It was found that in the ^{1}H NMR spectrum of compounds **5a-p**, the signals of H-13 appeared at range of 3.31–3.54 ppm and the signals of H-1 appeared at range of 4.21–4.62 ppm; in the ^{13}C NMR spectrum of compounds **5a-p**, the carbon signal of C-1 appeared at range of 41.2–45.6 ppm, the carbon signal of C-9 appeared at range of 81.5–84.9 ppm and the carbon signal of C-13 appeared at range of 45.3–56.5 ppm. This oxygen-bridged structures are supported by both of ^{1}H and ^{13}C NMR.

In conclusion, we have described a high-yield one-pot three-component cyclocondensation reaction method for the preparation of some new oxygen-bridged monastrol derivatives by the Biginelli of substituted salicylaldehyde, acetylacetone with thiourea(or urea, phenylurea) using nontoxic, cheap, and easily available $NaHSO_4$ catalyst under microwave irradiation and solvent-free conditions. Compared to other methods, this new method has the advantage of good yields, mild reaction conditions, inexpensive reagents, short reaction time, and environmentally friendly reaction conditions. Additionally, the products are oxygen-bridged monastrol analogs, 13-acetyl-9-methyl-11-thioxo-8- oxa(or thioxo)-10, 12-diazatricyclo[7.3.1.0^{2,7}] trideca-2,4,6-trienes rather than free hydroxyl compounds.

Scheme 3

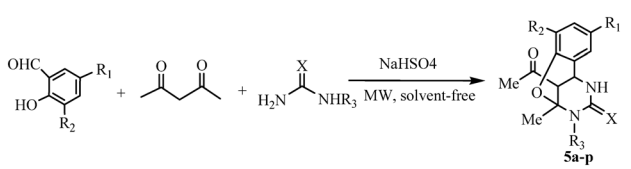


Table 1

The results on the reaction of substituted salicylaldehyde, acetylacetone and urea (or thiourea, phenylurea).

Products[a]	R^1	R^2	R^3	X	Time (min)	Yield[b] (%)	Mp (°C)
5a	H	H	H	S	10	91	202–204
5b	H	H	H	O	10	93	250–252
5c	H	H	Ph	O	12	86	168–170
5d	Cl	H	H	S	12	90	>300
5e	Cl	H	H	O	12	92	220–222
5f	Cl	H	Ph	O	15	84	145–147
5g	Br	H	H	S	12	89	255–257
5h	Br	H	H	O	12	91	287–289
5i	Br	H	Ph	O	15	82	155–157
5j	NO_2	H	H	S	15	87	210–212
5k	NO_2	H	H	O	15	88	235–237
5l	NO_2	H	Ph	O	15	82	165–167
5m	H	NO_2	H	S	15	86	260–262
5n	H	NO_2	H	O	15	89	240–242
5o	$C(CH_3)_3$	$C(CH_3)_3$	H	S	10	90	123–125
5p	$C(CH_3)_3$	$C(CH_3)_3$	H	O	10	92	181–183

[a]Products were characterized by ^1H, ^{13}C NMR, IR, and elemental analyses.
[b]Isolated yield.

EXPERIMENTAL

IR spectra were recorded on a Nicolet FT IR-500 spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE 400 MHz spectrometer at 400 MHz and 75 MHz. Elemental analysis was performed on an Elementar Vario EL III analyzer. Melting points were determined on a XT-5A digital melting-points apparatus and are uncorrected.

General procedure for the synthesis of oxygen-bridged Monastrol derivatives 5a-p. A mixture of the appropriate salicylaldehyde (2 mmol), acetylacetone(2 mmol), urea or thiourea (3 mmol), and $NaHSO_4$ (0.4 mmol) was refluxed in a sealed Discover reaction vessel under microwave irradiation (the temperature was set at 85°C) for the time period as indicated in Table 1. After cooled, ice water was added to the mixture, and the crude products collected by filtration were recrystallised from EtOH, to give the products **5a-p** (Table 1). All products were characterized by ^1H, ^{13}C NMR, IR, and by elemental analyses.

13-Aacetyl-9-methyl-11-thioxo-8-oxa-10,12-diazatricyclo [7.3.1.0^{2,7}]trideca-2,4,6-triene (5a). Yellow powder, yield 91%, mp 202–204°C, IR(KBr), (ν_{max}/cm^{-1}): 3351, 3229, 1706. ^1H NMR (DMSO-*d*6) δ_H: 9.17(s, 1H, NH), 6.78–7.16 (m, 5H, ArH, NH), 4.27(dd, *J* = 3.5, 2.9 Hz, 1H, H-1), 3.37–3.44 (m, 1H, H-13), 2.27 (s, 3H, CH_3), 1.66 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.4, 31.3, 41.2, 46.0, 81.5, 117.3, 121.4, 124.7, 129.9, 130.1, 152.1,

Table 2

Selected ^1H and ^{13}C NMR spectral datas of **5a-p.**

					δ (ppm)				
Products	R^1	R^2	R^3	X	H-1	H-13	C-1	C-9	C-13
5a	H	H	H	S	4.27	3.37–3.44	41.2	81.5	46.0
5b	H	H	H	O	4.23	3.36–3.42	41.2	83.1	45.3
5c	H	H	Ph	O	4.21	3.32–3.51	43.2	83.6	53.8
5d	Cl	H	H	S	4.54	3.37–3.44	45.6	82.6	53.9
5e	Cl	H	H	O	4.52	3.33–3.45	44.0	84.1	55.2
5f	Cl	H	Ph	O	4.47	3.31–3.52	44.7	84.5	55.8
5g	Br	H	H	S	4.42	3.39–3.45	44.9	83.6	53.1
5h	Br	H	H	O	4.36	3.35–3.46	44.7	83.3	56.5
5i	Br	H	Ph	O	4.32	3.32–3.54	44.3	83.9	56.5
5j	NO_2	H	H	S	4.62	3.35–3.40	43.8	83.5	54.7
5k	NO_2	H	H	O	4.53	3.32–3.43	43.1	84.7	55.6
5l	NO_2	H	Ph	O	4.53	3.43–3.52	44.1	84.3	55.9
5m	H	NO_2	H	S	4.62	3.35–3.40	44.3	83.6	55.2
5n	H	NO_2	H	O	4.39	3.39–3.46	45.6	84.9	56.4
5o	$C(CH_3)_3$	$C(CH_3)_3$	H	S	4.43	3.41–3.47	43.7	82.3	52.3
5p	$C(CH_3)_3$	$C(CH_3)_3$	H	O	4.46	3.43–3.48	44.1	82.7	52.9

176.9, 205.3. *Anal*. Calcd. for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68. Found: C, 59.59; H, 5.41; N, 10.64.

13-Aacetyl-9-methyl-11-oxo-8-oxa-10,12-diazatricyclo [7.3.1.0^{2,7}]trideca-2,4,6-triene (5b). Yellow powder, yield 93%, mp 250–252°C, IR(KBr), (ν_{max}/cm^{-1}): 3372, 3232, 1713. ^{1}H NMR (DMSO-*d*6) δ_H: 7.45(s, 1H, NH), 6.72–7.16 (m, 5H, ArH, NH), 4.23(dd, *J* = 3.6, 3.1 Hz, 1H, H-1), 3.36–;3.42 (m, 1H, H-13), 2.13 (s, 3H, CH_3), 1.59 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 27.3, 33.1, 41.2, 45.3, 83.1, 117.3, 121.0, 126.6, 129.6, 129.8, 152.3, 156.0, 204.9. *Anal*. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.39; H, 5.73; N, 11.38. Found: C 63.32; H, 5.71; N, 11.31.

13-Aacetyl-9-methyl-10-phenyl-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5c). Green powder, yield 86%, mp 168–170°C, IR(KBr), (ν_{max}/cm^{-1}): 3211, 3098, 1709, 1679. ^{1}H NMR (DMSO-*d*6) δ_H: 7.53 (s, 1H, NH), 6.79∼7.32 (m, 9H, arom), 4.21(dd, *J* = 2.2, 2.9 Hz, 1H, H-1), 3.32–3.51 (m, 1H, H-13), 2.29 (s, 3H, CH_3), 1.66 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 25.9, 30.8, 43.2, 53.8, 83.6, 113.1, 116.9, 118.2, 121.3, 123.3, 128.7, 129.9, 131.2, 150.9, 151.3, 155.7, 205.1. *Anal*. Calcd. for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.72; H, 5.56; N, 8.61.

13-Aacetyl-9-methyl-4-chlor-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5d). Yellow powder, yield 90%, mp > 300°C, IR(KBr), (ν_{max}/cm^{-1}): 3316, 3239, 3089, 1719. ^{1}H NMR (DMSO-*d*6) δ_H: 9.04(s, 1H, NH), 7.63(s, 1H, NH), 7.16(t, *J* = 7.1 Hz, 1H, ArH), 6.91(s, 1H, ArH), 6.64(t, *J* = 7.1 Hz, 1H, ArH), 4.54(dd, *J* = 3.0, 2.6 Hz, 1H, H-1), 3.37–3.44(m, 1H, H-13), 2.19(s, 3H, CH_3), 1.67 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 25.9, 32.1, 45.6, 53.9, 82.6 114.8, 120.3, 126.8, 130.4, 131.5, 150.8, 178.2, 206.2. *Anal*. Calcd. for $C_{13}H_{13}N_2O_2ClS$: C, 52.61; H, 4.42; N, 9.44. Found: C, 52.54; H, 4.50; N, 9.36.

13-Aacetyl-9-methyl-4-chlor-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5e). Gray powder, yield 92%, mp 220–222°C, IR(KBr), (ν_{max}/cm^{-1}): 3241, 3098, 1721, 1692. ^{1}H NMR (DMSO-*d*6) δ_H: 7.51(s, 1H, NH), 7.41(s, 1H, NH), 7.30(t, *J* = 7.0 Hz, 1H, ArH), 7.06(s, 1H, ArH), 6.76 (t, *J* = 7.0 Hz, 1H, ArH), 4.52(dd, *J* = 3.4, 2.9 Hz, 1H, H-1), 3.33–3.45(m, 1H, H-13), 2.23 (s, 3H, CH_3), 1.65(s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.2, 31.8, 44.0, 55.2, 84.1, 113.6, 120.7, 128.9, 130.9, 131.5, 150.8, 156.8, 205.8. *Anal*. Calcd. for $C_{13}H_{13}N_2O_3Cl$: C, 55.62; H, 4.67; N, 9.98. Found: C, 55.55; H, 4.62; N, 9.91.

13-Aacetyl-9-methyl-4-chlor-10-phenyl-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5f). Green powder, yield 84%, mp 145–147°C, IR(KBr), (ν_{max}/cm^{-1}): 3202, 3071, 1701, 1669. ^{1}H NMR (DMSO-*d*6) δ_H: 7.58 (s, 1H, NH), 6.79–8.38 (m, 8H, arom), 4.47(dd, *J*=3.0, 2.8 Hz, 1H, H-1), 3.31–3.52(m, 1H, H-13), 2.22(s, 3H, CH_3), 1.66(s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.7, 32.3, 44.7, 55.8, 84.5, 113.8, 117.2, 118.4, 121.5, 123.7, 128.9, 130.9, 131.8, 150.8, 151.5, 156.8, 205.4. *Anal*. Calcd. for $C_{19}H_{17}N_2O_3Cl$: C, 63.96; H, 4.80; N, 7.85. Found: C, 63.91; H, 4.86; N, 7.79.

13-Aacetyl-9-methyl-4-bromo-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5g). Yellow powder, yield 89%, mp 255–257°C, IR(KBr), (ν_{max}/cm^{-1}): 3323, 3229, 3078, 1709. ^{1}H NMR (DMSO-*d*6) δ_H: 9.11(s, 1H, NH), 7.28 (s, 1H, NH), 7.26 (d, *J* = 7.0 Hz, 1H, ArH), 7.14(s, 1H, ArH), 6.74 (d, *J* = 7.0 Hz, 1H, ArH), 4.42(dd, *J* = 3.1, 2.8 Hz, 1H, H-1), 3.39–3.45(m, 1H, H-13), 2.28 (s, 3H, CH_3), 1.67 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.1, 31.2, 44.9, 53.1, 83.6, 112.9, 119.4, 127.9, 130.8, 131.7, 150.5, 177.5, 205.9. *Anal*. Calcd. for $C_{13}H_{13}N_2O_2BrS$: C, 45.76; H, 3.84; N, 8.21. Found: C, 45.71; H, 3.88; N, 8.28.

13-Aacetyl-9-methyl-4-bromo-11-oxo-8-oxa-10,12-diazatricyclo [7.3.1.0^{2,7}]trideca-2,4,6-triene (5h). Yellow powder, yield 91%, mp 287–289°C, IR(KBr), (ν_{max}/cm^{-1}): 3236, 3084, 1715, 1688. ^{1}H NMR (DMSO-*d*6) δ_H: 7.56(s, 1H, NH), 7.32(s, 1H, NH), 7.22 (d, *J* = 7.0 Hz, 1H, ArH), 7.16(s, 1H, ArH), 6.74(d, *J* = 7.0 Hz, 1H, ArH), 4.36 (dd, *J* = 3.5, 3.1Hz, 1H, H-1), 3.35–3.46(m, 1H, H-13), 2.16 (s, 3H, CH_3), 1.64 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.7, 32.3, 44.7, 56.5, 83.3, 111.6, 119.4, 128.7, 131.8, 131.9, 151.3, 155.5, 205.2. *Anal*. Calcd. for $C_{13}H_{13}N_2O_3Br$: C, 48.02; H, 4.03; N, 8.62. Found: C, 48.07; H, 3.98; N, 8.66.

13-Aacetyl-9-methyl-4-bromo-10-phenyl-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5i). Green powder, yield 82%, mp 155–157°C, IR(KBr), (ν_{max}/cm^{-1}): 3209, 3081, 1708, 1672. ^{1}H NMR (DMSO-*d*6) δ_H: 7.55 (s, 1H, NH), 6.89–8.21 (m, 8H, arom), 4.32(dd, *J* = 3.0, 2.7 Hz, 1H, H-1), 3.32–3.54 (m, 1H, H-13), 2.16(s, 3H, CH_3), 1.63(s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.1, 31.9, 44.3, 56.5, 83.9, 112.6, 117.9, 119.4, 121.2, 122.6, 128.5, 130.8, 131.2, 150.5, 151.3, 155.5, 204.8. *Anal*. Calcd. for $C_{19}H_{17}N_2O_3Br$: C, 56.87; H, 4.27; N, 6.98. Found: C, 56.80; H, 4.21; N, 6.91.

13-Aacetyl-9-methyl-4-nitro-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5j). Yellow powder, yield 87%, mp 210–212°C, IR(KBr), (ν_{max}/cm^{-1}): 3341, 3247, 3109, 1726. ^{1}H NMR (DMSO-*d*6) δ_H: 9.32(s, 1H, NH), 8.13(s, 1H, NH), 8.10(s, 1H, ArH), 7.08 (d, *J* = 7.0 Hz, 1H, ArH), 7.05 (d, *J* = 7.0 Hz, 1H, ArH), 4.62(dd, *J* = 3.6, 2.9 Hz, 1H, H-1), 3.35–3.40 (m, 1H, H-13), 2.33 (s, 3H, CH_3), 1.73 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.9, 32.7, 43.8, 54.7, 83.5, 115.4, 123.8, 124.7, 124.9, 140.8, 165.9, 179.6, 206.7. *Anal*. Calcd. for $C_{13}H_{13}N_3O_4S$: C, 50.80; H, 4.26; N, 13.68. Found: C, 50.89; H, 4.2 1; N, 13.62.

13-Aacetyl-9-methyl-4-nitro-11-oxo-8-oxa-10,12-diazatricyclo [7.3.1.0^{2,7}]trideca-2,4,6-triene (5k). Yellow powder, yield 88%, mp 235–237°C, IR(KBr), (ν_{max}/cm^{-1}): 3259, 3121, 1735, 1699. ^{1}H NMR (DMSO-*d*6) δ_H: 8.32(s, 1H, NH), 7.69(s, 1H, NH), 8.21 (s, 1H, ArH), 7.35 (d, *J* = 7.0 Hz, 1H, ArH), 7.13 (d, *J* = 7.0 Hz, 1H, ArH), 4.53(dd, *J* = 3.3, 2.7 Hz, 1H, H-1), 3.32–3.43 (m, 1H, H-13), 2.31 (s, 3H, CH_3), 1.71 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 27.1, 32.3, 43.1, 55.6, 84.7, 114.8, 123.4, 124.1, 124.8, 140.7, 157.9, 166.3, 206.4. *Anal*. Calcd. for $C_{13}H_{13}N_3O_5$: C, 53.60; H, 4.50; N, 14.43. Found: C, 53.53; H, 4.59; N, 14.48.

13-Aacetyl-9-methyl-4-nitro-10-phenyl-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5l). Green powder, yield 82%, mp 165–167°C, IR(KBr), (ν_{max}/cm^{-1}): 3189, 3059, 1691, 1663. ^{1}H NMR (DMSO-*d*6) δ_H: 8.39 (s, 1H, NH), 7.01–8.31 (m, 8H, arom), 4.53(dd, *J* = 3.1, 2.6 Hz, 1H, H-1), 3.43–3.52(m, 1H, H-13), 2.30 (s, 3H, CH_3), 1.70 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.8, 32.5, 44.1, 55.9, 84.3, 113.8, 115.1, 117.6, 123.5, 124.3, 124.7, 129.3, 141.1, 151.4, 158.2, 166.9. *Anal*. Calcd. for $C_{19}H_{17}N_3O_5$: C, 62.12; H, 4.66; N, 11.44. Found: C, 62.07; H, 4.61; N, 11.38.

13-Aacetyl-9-methyl-6-nitro-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5m). Yellow powder, yield 86%, mp 260–262°C, IR(KBr), (ν_{max}/cm^{-1}): 3322, 3251, 3114, 1728. ^{1}H NMR (DMSO-*d*6) δ_H: 9.32(s, 1H, NH), 8.13 (s, 1H, NH), 8.10(d, 1H, ArH), 7.41–7.53(m, 1H, ArH), 7.01 (d, 1H, ArH), 4.62(dd, *J* = 3.3, 2.7 Hz, 1H, H-1), 3.35–3.40 (m, 1H, H-13), 2.27(s, 3H, CH_3), 1.73 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.5, 32.4, 44.3, 55.2, 83.6, 114.5, 121.5, 125.3, 134.3, 135.5, 155.6, 178.7, 206.9. *Anal*. Calcd. for $C_{13}H_{13}N_3O_4S$: C,50.80; H, 4.26; N, 13.68. Found: C, 50.86; H, 4.22; N, 13.61.

13-Aacetyl-9-methyl-6-nitro-11-oxo-8-oxa-10,12-diazatricyclo [7.3.1.0^{2,7}]trideca-2,4,6-triene (5n). Yellow powder, yield 89%, mp 240–242°C, IR(KBr), (ν_{max}/cm^{-1}): 3265, 3125, 1739, 1698. ^{1}H NMR (DMSO-*d*6) δ_H: 8.15 (s, 1H, NH), 7.52 (s, 1H, NH), 8.26 (d, 1H, ArH), 7.51–7.62(m, 1H, ArH), 7.16(d, 1H, ArH), 4.39(dd, *J* = 3.5, 2.9 Hz, 1H, H-1), 3.39–3.46 (m, 1H, H-13), 2.29(s, 3H, CH_3), 1.69 (s, 3H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 26.8, 31.3, 45.6, 56.4, 84.9, 115.1, 121.7, 125.8, 134.8, 135.7, 155.8, 156.8, 206.1. *Anal*. Calcd. for $C_{13}H_{13}N_3O_5$: C, 53.60; H, 4.50; N, 14.43. Found: C, 53.55; H, 4.57; N, 14.51.

13-Aacetyl-9-methyl-4,6-dit-butyl-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5o). Yellow powder, yield 90%, mp 123–125°C, IR(KBr), (ν_{max}/cm^{-1}): 3327, 3209, 3054, 1697. ^{1}H NMR (DMSO-*d*6) δ_H: 11.71(s, 1H, NH), 9.98 (s, 1H, NH), 7.64(s, 1H, ArH), 7.56 (s, 1H, ArH), 4.43(dd, *J* = 2.5, 2.1 Hz, 1H, H-1), 3.41–3.47(m, 1H, H-13), 2.21 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.38(s, 9H, CH_3), 1.29(s, 9H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 24.7, 29.6, 31.5, 32.3, 34.5, 35.0, 43.7, 52.3, 82.3, 120.7, 128.9, 131.6, 137.0, 141.9, 158.3, 199.4, 204.7. *Anal*. Calcd. for $C_{21}H_{30}N_2O_2S$: C, 67.34; H, 8.07; N, 7.48. Found: C, 67.41; H, 8.01; N, 7.42.

13-Aacetyl-9-methyl-4,6-dit-butyl-11-oxo-8-oxa-10,12-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene (5p). Yellow powder, yield 92%, mp 181–183°C, IR(KBr), (ν_{max}/cm^{-1}): 3221, 3069, 1703, 1682. ^{1}H NMR (DMSO-*d*6) δ_H: 9.78(s, 1H, NH), 9.64(s, 1H, NH), 7.65(s, 1H, ArH), 7.57 (s, 1H, ArH), 4.46(dd, *J* = 2.7, 2.4 Hz, 1H, H-1), 3.43–3.48 (m, 1H, H-13), 2.33 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.39(s, 9H, CH_3), 1.30(s, 9H, CH_3). ^{13}C NMR (DMSO-*d*6) δ_C: 25.3, 29.36, 31.9, 32.7, 34.7, 35.2, 44.1, 52.9, 82.7, 120.6, 127.6, 131.8, 136.7, 140.6, 157.2, 158.6, 204.3. *Anal*. Calcd. for $C_{21}H_{30}N_2O_3$: C, 70.36; H, 8.44; N, 7.82. Found: C, 70.30; H, 8.41; N, 7.89.

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