A Facile Synthesis of 2-Alkyl-3-α-carboxy-α-styryl/Heterylvinyl Quinazolin-4(3*H*)-ones and 3-Arylidene/Heterylmethylidene-4-aroyl-1*h*-[1,4]benzodiazepine-2,5(3*H*,4*H*)-diones and Their Transformation into Novel Heterocyclyl and Heterocyclo Analogues

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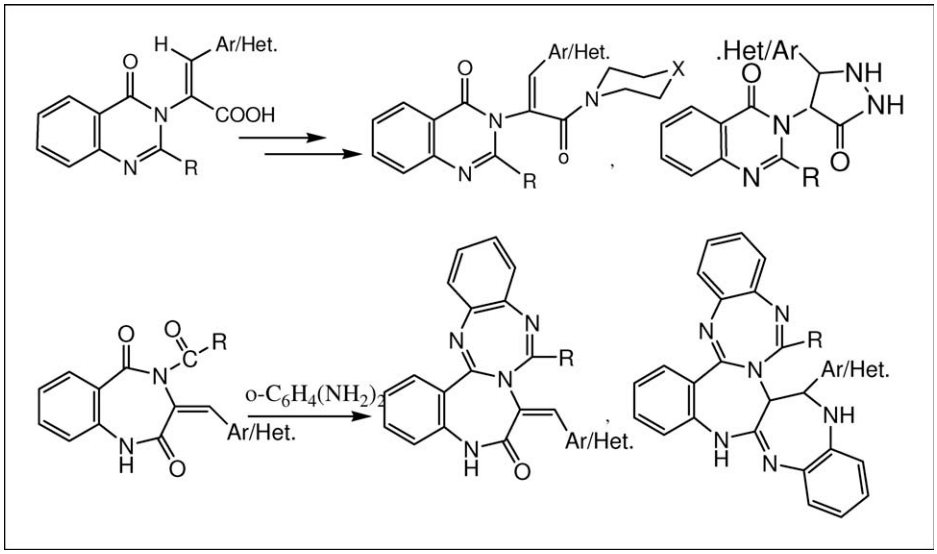
Received July 10, 2010
DOI 10.1002/jhet.756
Published online 25 October 2011 in Wiley Online Library (wileyonlinelibrary.com).



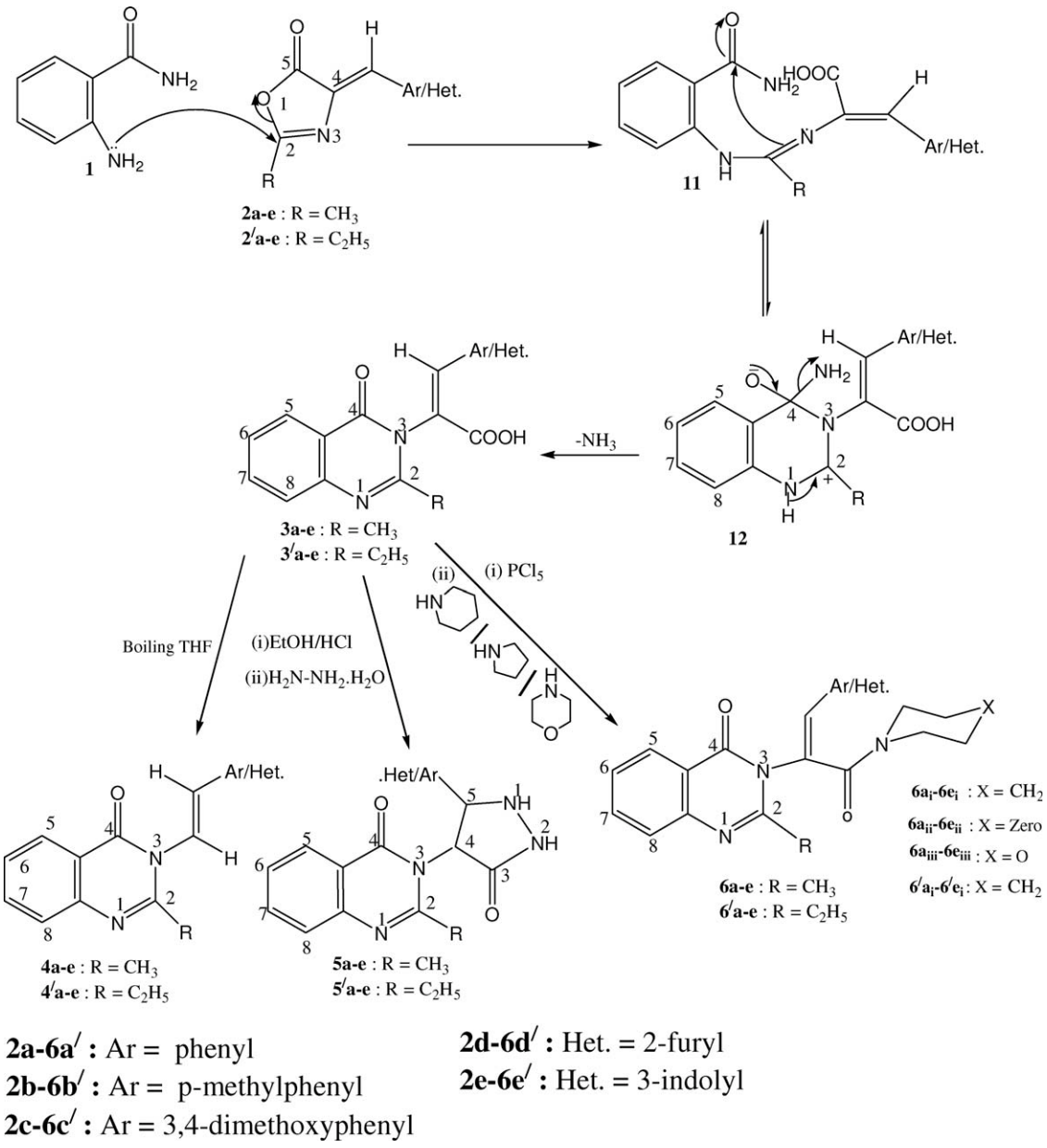
Condensation of 2-methyl-/2-ethyl- and 2-phenyl-/p-tolyl-4-arylidene-/heterylmethylidene-2-oxazolin-5-ones (γ-azlactones) **2** with o-aminobenzamide **1** in acetic acid resulted in the formation of two entirely different heterocyclic systems, differently substituted quinazoline compounds, 2-methyl-/2-ethyl-3-α-carboxy-α-styryl-/β-heteryl-α-carboxyvinyl-quinazolin-4(3*H*)-ones **3a–3e** and **3′a–3′e** and differently substituted 1,4-benzodiazepine compounds, 3-arylidene-/heteryl methylidene-4-aroyl-1*H*-[1,4]benzodiazepine-2,5(3*H*,4*H*)-diones **7a–7e** and **7′a–7′e**. Compounds **3a–3e** and **3′a–3′e** have been converted into compounds, **4a–4e** and **4′a–4′e; 5a–5e,** and **5′a–5′e;** and **6a–6e** and **6′a–6′e** through different transformations. Benzodiazepines, **7a–7e** and **7′a–7′e**, on condensation with *o*-phenylenediamine have generated three novel heterocyclic systems **8a–8e** and **8′a–8′e; 9a–9e** and **9′a–9′e;** and **10a–10e** and **10′a–10′e**.

J. Heterocyclic Chem., **49**, 173 (2012).

INTRODUCTION

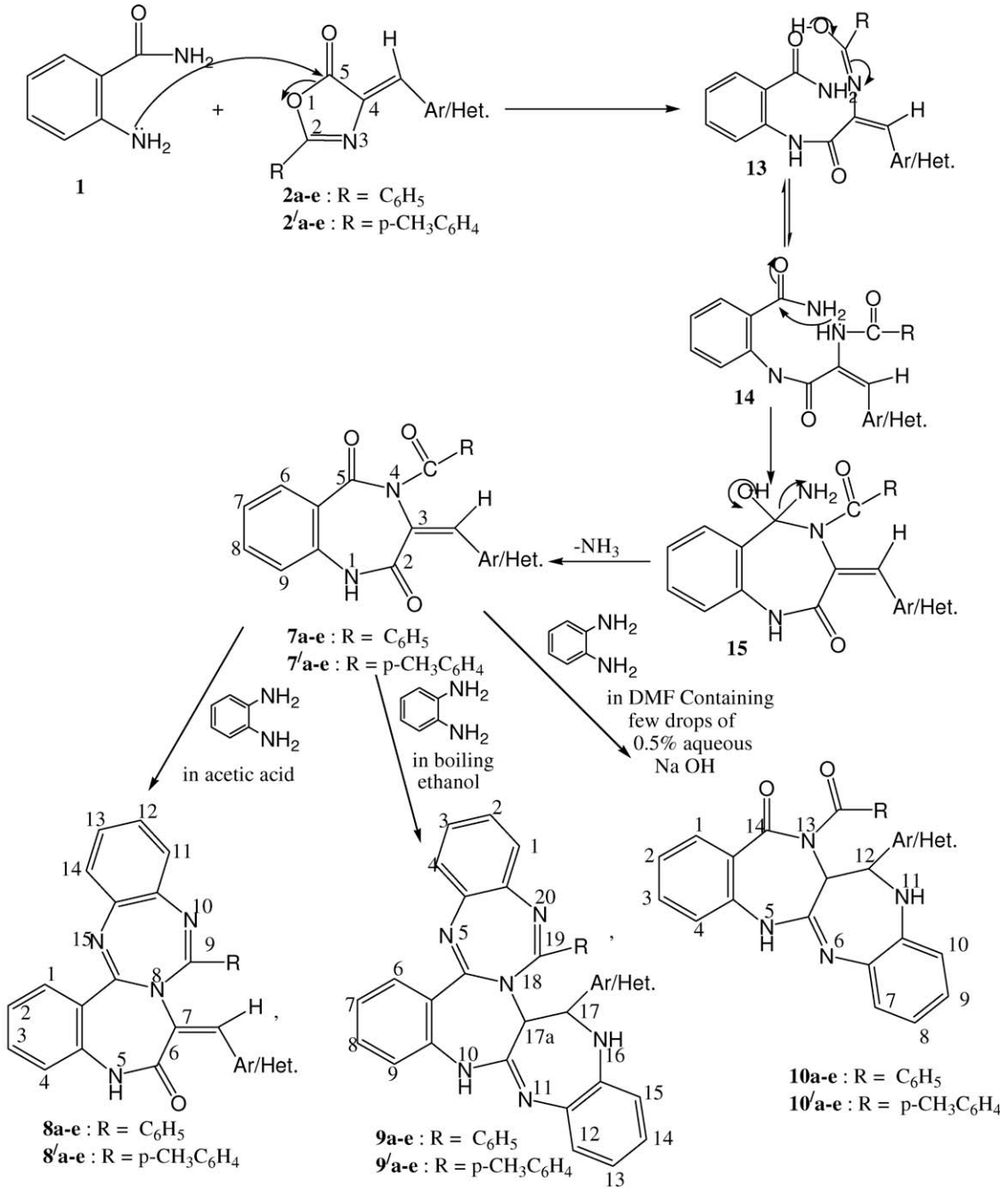
4-Benzylidene-2-substituted-2-oxazolin-5-ones (γ-azlactones) are the compounds with a significant synthetic potential and several biological and technological applications [1–7]. These compounds can be, for example, used as inhibitors of the enzyme activity or as fluorescent sensors [3,6]. In addition, the oxazolone molecule serves as a general template for the stereoselective synthesis of amino acids and heterocyclic scaffolds [2]. It is evident from the literature that azlactones substituted unsaturatedly [8] at C_4 have proved to be versatile intermediates in the synthesis of amino acids [9], cycloaliphatic [10], and cyclopropyl amino acids [11]. These compounds are easily transformed into *N*-acyl-α, β-didehydroamino acid derivatives, which are powerful synthetic tools [12]. Some of the azlactone derivatives particularly 4-(*p-N*,*N*-dimethylaminophenyl methylene)-2-phenyl-2-oxazolin-5-one, is embedded in a plasticized PVC polymer film. On the other hand, compounds possessing quinazolinone nucleus show potent biological activities including anticonvulsant [13], antihypertensive [14], antidiabetic [15], anticoagulant [16], antidiuretic [17], antibacterial [18], antiviral [19], anticancer [20], and anti-HIV [21] activities. The benzodiazepines are a class of drugs with hypnotic [22], anxiolytic, anticonvulsant, amnestic, and muscle relaxant properties. They

Scheme 1



serve as cholecystokinin A and B antagonists [23], opioid receptor ligands [24], platelet-activating factor antagonists [25], HIV inhibitors [26], and farnesyltransferase inhibitors [27]. Benzodiazepines can be used in anxiety disorders, insomnia, involuntary movement disorders, and in detoxification from alcohol and other substances. Pyrazole derivatives have been found to possess varied biological activities. Pyrazole itself and several *N*-subsituted pyrazoles are inhibitor and deactivators of liver alcohol dehydrogenase [28–30]. A large number of pyrazole derivatives were synthesized, which have exhibited potent analgesic [31], antibacterial [32], antifungal [33], AIDS [34], and hypoglycemic [35] activities. Triazepine [36,37] derivatives have a wide range of biological activities including anti-angiogenesis, herbicidal effects, antimetastatic effects, and antibacterial and fungicidal properties. Keeping this in view, it was thought of interest to synthesize certain azlactones capable of attending the reactions, which could exploit them in their transformation into various other heterocyclic systems containing the aforementioned vital moieties with the expectation of their activities supplemented or at least comparable to those of quinozolinone, 1,5- and 1,4-benzodiazepine, 1,3,5-benzotriazepine and pyrazolidine derivatives. These heterocyclic systems have been prepared as per (Schemes 1 and 2), respectively.

Scheme 2



7a-10a/ : Ar = phenyl
7b-10b/ : Ar = p-methylphenyl
7c-10c/ : Ar = 3,4-dimethoxyphenyl
7d-10d/ : Het. = 2-furyl
7e-10e/ : Het. = 3-indolyl

RESULTS AND DISCUSSION

The condensation reaction between *o*-aminobenzamide **1** and 2-methyl-4-benzylidene-2-oxazolin-5-one **2a** (R = CH_3, Ar = C_6H_5) in 1:1 molar proportion in acetic acid at room temperature yielded [7] a colorless crystalline compound, mp 235°C. Its mass spectrum revealed the molecular ion peak at *m*/*z* 258 suggesting the loss of elements of ammonia only from the starting materials.

Table 1

Physical and analytical data of compounds **3–10**.

Compounds	R	Ar	Mp (°C)	Yield (%)	Molecular formula	Analysis % calcd./found		
						C	H	N
3a	Methyl	Pheyl	235	93	$C_{18}H_{14}N_2O_3$	70.58	4.57	9.1
						70.52	4.56	9.03
3b	Methyl	4-Methylphenyl	240	85	$C_{19}H_{16}N_2O_3$	71.25	5	8.75
						71.19	4.8	8.71
3c	Methyl	3,4-Dimethoxy-phenyl	220	80	$C_{20}H_{18}N_2O_5$	65.57	4.91	7.65
						65.51	4.9	7.6
3d	Methyl	2-Furyl	212	81	$C_{16}H_{12}N_2O_4$	64.86	4.05	9.45
						64.8	4.03	9.42
3e	Methyl	3-Indolyl	240	79	$C_{20}H_{15}N_3O_3$	69.56	4.34	12.17
						69.51	4.33	12.13
3′a	Ethyl	Phenyl	247	90	$C_{19}H_{16}N_2O_3$	71.25	5	8.75
						71.18	4.9	8.71
3′b	Ethyl	4-Methylphenyl	242	87	$C_{20}H_{18}N_2O_3$	71.85	5.38	8.38
						71.8	5.37	8.33
3′c	Ethyl	3,4-Dimethoxy-phenyl	245	84	$C_{21}H_{20}N_2O_5$	66.31	5.26	7.36
						66.25	5.24	7.31
3′d	Ethyl	2-Furyl	248	80	$C_{17}H_{14}N_2O_4$	65.8	4.51	9.03
						65.73	4.5	8.98
3′e	Ethyl	3-Indolyl	218	85	$C_{21}H_{17}N_3O_3$	70.19	4.73	11.69
						70.14	4.71	11.62
4a	Methyl	Phenyl	140	86	$C_{17}H_{14}N_2O$	77.86	5.34	10.68
						77.77	5.33	10.65
4b	Methyl	4-Methylphenyl	148	82	$C_{18}H_{16}N_2O$	78.26	5.79	10.14
						78.17	5.77	10.09
4c	Methyl	3,4-Dimethoxy-phenyl	160	85	$C_{19}H_{18}N_2O_3$	70.8	5.59	8.69
						70.67	5.58	8.62
4d	Methyl	2-Furyl	146	88	$C_{15}H_{12}N_2O_2$	71.42	4.76	11.11
						71.35	4.74	11.04
4e	Methyl	3-Indolyl	153	79	$C_{19}H_{15}N_3O$	72.96	7.38	2.5
						72.88	7.37	2.46
4′a	Ethyl	Phenyl	146	88	$C_{18}H_{16}N_2O$	78.26	5.79	10.14
						78.13	5.77	10.06
4′b	Ethyl	4-Methylphenyl	142	85	$C_{19}H_{18}N_2O$	78.62	6.2	9.65
						78.54	6.19	9.58
4′c	Ethyl	3,4-Dimethoxy-phenyl	165	82	$C_{20}H_{20}N_2O_3$	71.42	5.95	8.33
						71.34	5.94	8.3
4′d	Ethyl	2-Furyl	148	86	$C_{16}H_{14}N_2O_2$	72.18	5.26	10.52
						71.97	5.25	10.49
4′e	Ethyl	3-Indolyl	154	87	$C_{20}H_{17}N_3O$	76.19	5.39	13.33
						76.08	5.38	13.29
5a	Methyl	Phenyl	202	76	$C_{18}H_{16}N_4O_2$	67.5	5	17.5
						67.38	4.9	17.44
5b	Methyl	4-Methylphenyl	213	79	$C_{19}H_{18}N_4O_2$	68.26	5.38	16.76
						68.18	5.36	16.71
5c	Methyl	3,4-Dimethoxy-phenyl	201	74	$C_{20}H_{20}N_4O_4$	63.15	5.26	14.73
						62.99	5.25	14.68
5d	Methyl	2-Furyl	208	77	$C_{16}H_{14}N_4O_3$	61.93	4.51	18.06
						61.86	4.5	18.01
5e	Methyl	3-Indolyl	215	71	$C_{20}H_{17}N_5O_2$	66.85	4.73	19.49
						66.76	4.72	19.43
5′a	Ethyl	Phenyl	205	76	$C_{19}H_{18}N_4O_2$	68.26	5.38	16.76
						68.17	5.37	16.71
5′b	Ethyl	4-Methylphenyl	224	72	$C_{20}H_{20}N_4O_2$	68.96	5.74	16.09
						68.85	5.73	16.03
5′c	Ethyl	3,4-Dimethoxy-phenyl	236	82	$C_{21}H_{22}N_4O_4$	63.95	5.58	14.21
						63.87	5.57	14.16
5′d	Ethyl	2-Furyl	225	71	$C_{17}H_{16}N_4O_3$	62.96	4.93	17.28
						62.87	4.92	17.23

(*Continued*)

Table 1
(*Continued*)

Compounds	R	Ar	Mp (°C)	Yield (%)	Molecular formula	Analysis % calcd./found		
						C	H	N
5′e	Ethyl	3-Indolyl	215	76	$C_{21}H_{19}N_5O_2$	67.56	5.09	18.76
						67.47	5.08	18.72
6a$_i$	Methyl	Phenyl	240	80	$C_{23}H_{23}N_3O_2$	73.99	6.16	11.26
						78.83	6.15	11.22
6b$_i$	Methyl	4-Methylphenyl	245	83	$C_{24}H_{25}N_3O_2$	74.41	6.45	10.85
						74.34	6.44	10.82
6c$_i$	Methyl	3,4-Dimethoxy-phenyl	225	79	$C_{25}H_{27}N_3O_4$	69.28	6.23	9.69
						69.19	6.21	9.62
6d$_i$	Methyl	2-Furyl	230	81	$C_{21}H_{21}N_3O_3$	69.42	5.78	11.57
						69.33	5.77	11.51
6d$_{ii}$	Methyl	2-Furyl	232	85	$C_{20}H_{19}N_3O_2$	72.07	5.7	12.61
						71.93	5.68	12.56
6e$_i$	Methyl	3-Indolyl	222	83	$C_{25}H_{25}N_4O_2$	72.63	6.05	13.55
						72.52	6.04	13.51
6e$_{iii}$	Methyl	3-Indolyl	220	80	$C_{24}H_{23}N_4O_3$	72.07	5.7	12.61
						71.96	5.68	12.57
6′a$_i$	Ethyl	Phenyl	242	78	$C_{24}H_{25}N_3O_2$	74.41	6.45	10.85
						74.36	6.44	10.81
6′b$_i$	Ethyl	4-Methylphenyl	228	84	$C_{25}H_{27}N_3O_2$	74.81	6.73	10.47
						74.73	6.71	10.41
6′c$_i$	Ethyl	3,4-Dimethoxy-phenyl	231	82	$C_{26}H_{29}N_3O_4$	69.79	6.48	9.39
						69.67	6.47	9.33
6′d$_i$	Ethyl	2-Furyl	224	78	$C_{22}H_{23}N_3O_3$	70.02	6.1	11.14
						69.89	6.09	11.08
6′e$_i$	Ethyl	3-Indolyl	243	85	$C_{26}H_{27}N_4O_2$	73.06	6.32	13.11
						73.01	6.3	13.07
7a	Phenyl	Phenyl	234	80	$C_{23}H_{16}N_2O_3$	75	4.34	7.6
						74.79	4.32	7.57
7b	Phenyl	4-Methylphenyl	220	78	$C_{24}H_{18}N_2O_3$	75.39	4.71	7.32
						75.28	4.7	7.25
7c	Phenyl	3,4-Dimethoxy-phenyl	260	85	$C_{25}H_{20}N_2O_5$	70.09	4.67	6.54
						69.98	4.66	6.5
7d	Phenyl	2-Furyl	228	87	$C_{21}H_{14}N_2O_4$	70.39	3.91	7.82
						70.32	3.9	7.78
7e	Phenyl	3-Indolyl	212	78	$C_{25}H_{17}N_3O_3$	73.71	4.17	10.31
						73.63	4.15	10.25
7′a	*p*-Tolyl	Phenyl	243	82	$C_{24}H_{18}N_2O_3$	75.39	4.71	7.32
						75.25	4.7	7.28
7′b	*p*-Tolyl	4-Methylphenyl	232	86	$C_{25}H_{20}N_2O_3$	75.75	5.05	7.07
						75.61	5.03	7.03
7′c	*p*-Tolyl	3,4-Dimethoxy-phenyl	250	90	$C_{26}H_{22}N_2O_5$	70.58	4.97	6.33
						70.51	4.96	6.28
7′d	*p*-Tolyl	2-Furyl	236	88	$C_{22}H_{16}N_2O_4$	70.96	4.3	7.52
						70.87	4.28	7.48
7′e	*p*-Tolyl	3-Indolyl	224	82	$C_{26}H_{19}N_3O_3$	74.1	4.51	9.97
						74.02	4.5	9.92
8a	Phenyl	Phenyl	222	68	$C_{29}H_{20}N_4O$	79.09	4.54	12.72
						78.81	4.53	12.65
8b	Phenyl	4-Methylphenyl	227	72	$C_{30}H_{22}N_4O$	79.29	4.84	12.33
						79.18	4.82	12.28
8c	Phenyl	3,4-Dimethoxy-phenyl	202	70	$C_{31}H_{24}N_4O_3$	74.4	4.8	11.2
						73.92	4.79	10.92
8d	Phenyl	2-Furyl	245	73	$C_{27}H_{18}N_4O_2$	75.34	4.18	13.02
						75.29	4.16	12.97
8e	Phenyl	3-Indolyl	260	69	$C_{31}H_{21}N_5O$	77.66	4.38	14.61
						77.62	4.37	14.56
8′a	*p*-Tolyl	Phenyl	241	72	$C_{30}H_{22}N_4O$	79.29	4.84	12.33
						79.21	4.83	12.29

(*Continued*)

Table 1
(*Continued*)

Compounds	R	Ar	Mp (°C)	Yield (%)	Molecular formula	Analysis % calcd./found		
						C	H	N
8′b	*p*-Tolyl	4-Methylphenyl	243	69	$C_{31}H_{24}N_4O$	79.48	5.12	11.96
						79.35	5.11	11.92
8′c	*p*-Tolyl	3,4-Dimethoxy-phenyl	252	71	$C_{32}H_{26}N_4O_3$	74.7	5.05	10.89
						74.62	5.04	10.84
8′d	*p*-Tolyl	2-Furyl	228	73	$C_{28}H_{20}N_4O_2$	75.67	4.5	12.61
						75.59	4.48	12.57
8′e	*p*-Tolyl	3-Indolyl	223	69	$C_{32}H_{23}N_5O$	77.89	4.66	14.19
						77.8	4.65	14.14
9a	Phenyl	Phenyl	238	75	$C_{35}H_{25}N_6$	79.39	4.72	15.87
						79.33	4.71	15.8
9b	Phenyl	4-Methylphenyl	244	69	$C_{36}H_{27}N_6$	79.55	4.97	15.46
						79.5	4.95	15.4
9c	Phenyl	3,4-Dimethoxy-phenyl	256	74	$C_{37}H_{29}N_6O_2$	75.38	4.92	14.26
						75.34	4.91	14.2
9d	Phenyl	2-Furyl	243	68	$C_{33}H_{23}N_6O$	76.3	4.43	16.18
						76.23	4.41	16.12
9e	Phenyl	3-Indolyl	247	71	$C_{37}H_{26}N_7$	78.16	4.57	17.25
						78.07	4.56	17.2
9′a	*p*-Tolyl	Phenyl	236	72	$C_{36}H_{27}N_6$	79.55	4.97	15.46
						79.51	4.95	15.4
9′b	*p*-Tolyl	4-Methylphenyl	240	75	$C_{37}H_{29}N_6$	79.71	5.2	15.08
						79.65	5.19	15.01
9′c	*p*-Tolyl	3,4-Dimethoxy-phenyl	238	68	$C_{38}H_{31}N_6O_2$	75.62	5.14	16.18
						75.57	5.12	16.13
9′d	*p*-Tolyl	2-Furyl	250	74	$C_{34}H_{25}N_6O$	76.54	4.69	15.75
						76.48	4.68	15.69
9′e	*p*-Tolyl	3-Indolyl	253	69	$C_{38}H_{28}N_7$	78.35	4.81	16.83
						78.3	4.8	16.76
10a	Phenyl	Phenyl	232	71	$C_{29}H_{22}N_4O_2$	75.98	4.8	12.22
						75.91	4.78	12.18
10b	Phenyl	4-Methylphenyl	238	74	$C_{30}H_{24}N_4O_2$	76.27	5.08	11.86
						76.22	5.07	11.81
10c	Phenyl	3,4-Dimethoxy-phenyl	202	75	$C_{31}H_{26}N_4O_4$	71.81	5.01	10.81
						71.75	4.99	10.77
10d	Phenyl	2-Furyl	245	66	$C_{27}H_{20}N_4O_3$	72.32	4.46	12.5
						72.27	4.44	12.46
10e	Phenyl	3-Indolyl	250	68	$C_{31}H_{23}N_5O_2$	74.84	4.62	14.08
						74.78	4.61	14.05
10′a	*p*-Tolyl	Phenyl	236	72	$C_{30}H_{24}N_4O_2$	76.27	5.08	11.86
						76.23	5.06	11.81
10′b	*p*-Tolyl	4-Methylphenyl	243	75	$C_{31}H_{26}N_4O_2$	76.54	5.34	11.52
						76.47	5.33	11.48
10′c	*p*-Tolyl	3,4-Dimethoxy-phenyl	264	69	$C_{32}H_{28}N_4O_4$	72.18	5.26	10.52
						72.11	5.24	10.47
10′d	*p*-Tolyl	2-Furyl	250	73	$C_{28}H_{22}N_4O_3$	72.72	4.76	12.12
						72.66	4.75	12.07
10′e	*p*-Tolyl	3-Indolyl	250	76	$C_{32}H_{25}N_5O_2$	75.14	4.89	13.69
						75.08	4.88	13.62

Based on the elemental analysis and spectral data, the structure of the compound was assigned as 3-(α-carboxy-α-styryl)-2-methylquinazolin-4(3*H*)-one **3a** (R = CH_3, Ar = C_6H_5). Structure assigned to the product **3a** was further supported by its decarboxylation on refluxing it in THF for 2 h, resulting in the formation of a colorless compound **4a,** mp 142°C. In the mass spectrum, the molecular ion peak of the product **4a** was observed at *m/z* 262 corresponding to the decarboxylated product of 3-(α-carboxy-α-styryl)-2-methyl quinazolin-

4(3*H*)-one **3a** (R = CH_3, Ar = C_6H_5). Based on the rest of spectral data and elemental analysis, the structure of the compound was assigned as 2-methyl-3-(α-styryl)quinazolin-4(3*H*)-one **4a**. Exactly identical products **3′a** and **4′a** were obtained when 2-ethyl-4-benzylidene-2-oxazolin-5-one **2′a** was reacted with *o*-aminobenzamide. Using other differently substituted benzylidine/heterylmethylidene-2-methyl/2-ethyl-2-oxazolin-5-ones **2b–2e** and **2′b–2′e**, analogously structured **3b–3e** and **3′b–3′e** quinazoline compounds were generated in total conformity with the expected results. Compounds **3** were converted into their acid chloride with $SOCl_2$ in benzene, and the latter compounds were treated with piperidine, pyrolidine, and morpholine to produce the corresponding piperidide, pyrolidide, and morpholide cyclic tertiary amides **6**. The ethyl esters of compounds **3** on treatment with hydrazine produced 3-(5-aryl/heteryl-3-oxo-pyrazolidin-4-yl)-2-methyl/ethyl-quinazolin-4(3*H*)-ones **5**.

Similar condensation of *o*-aminobenzamide **1** with 2-phenyl-4-(*p*-methylbenzylidene)-2-oxazolin-5-one **2b** (R = C_6H_5, Ar = *p*-$CH_3C_6H_4$) in 1:1 molar proportion was carried out by refluxing in dry benzene containing few drops of acetic acid yielding a colorless crystalline compound, mp 232°C. Its mass spectrum revealed the molecular ion at *m*/*z* 396 indicating again the loss of ammonia from uniequimolar proportion of the starting materials. Based on elemental analysis and spectral data, the structure of the compound was assigned as 3-(*p*-methylbenzylidene)-4-benzoyl-1*H*-[1,4]benzodiazepine-2,5(3*H*,4*H*)-dione **7b** (R = C_6H_5, Ar = *p*-$CH_3C_6H_4$). Again, the reaction was carried with *o*-aminobenzamide and 2-(*p*-tolyl)-4-(*p*-methyl benzylidene)-2-oxazolin-5-one **2′b** for the formation of **7′b** and expected results were obtained. Other benzodiazepine analogues **7a, 7c–7g** and **7′a, 7′c–7′g** have been synthesized with positive results.

Conclusively, the formation of the entirely two different kinds of products, a quinazolinone **3** or a 1,4-benzodiazepine **7** analog when an alkyl or aryl group receptively is present at 2-position of the 2-oxazolinone can be explained by the nucleophilic attack by the amino group of the *o*-aminobenzamide **1** on two different sites, either C-2 (R = CH_3/C_2H_5) or C-5 (R = C_6H_5/*p*-$CH_3C_6H_4$) of **2** forming intermediates **11** and **12** of Scheme 1 or **14** and **15** of Scheme 2, respectively. Nucleophilic attack of azomethine nitrogen of **11** or imide nitrogen of **14** on the amide carbonyl carbon and subsequent cyclization of these intermediates followed by elimination of ammonia from **12** or **15** lead to the formation of stable **3** or **7** (Schemes 1 and 2).

Further, condensation of 3-benzylidene-4-benzoyl-1*H*-[1,4]benzodiazepine-2,5(3*H*,4*H*)-dione **7a** (R = C_6H_5, Ar = C_6H_5) with *o*-phenylene diamine in 1:1 molar ratio in acetic acid yielded **8a** as the main product along with slight traces of **10a** (TLC) and vise versa when the reaction was carried out in same molar proportion in DMF containing few drops of dilute (0.5%) aqueous NaOH. When the reaction of compound **7a** was carried with double the quantity of *o*-phenylene diamine, that is, in 1:2 molar ratio and for prolonged time in boiling ethanol, it resulted in the formation of a doubly fused compound **9a** as the main product with slight traces of **8a** and **10a** (TLC). The products **8a**, **9a**, and **10a** were separated by fractional crystallization and purified by repeated crystallization. Based on spectral data and elemental analysis, these three novel condensed heterocyclic systems were characterized and assigned their structures. Condensation of other differently substituted **7b–7e** and **7′a–7′e** with *o*-phenylenediamine under different conditions have yielded differently substituted three novel condensed heterocyclic systems, **8b–8e** and **8′b–8′e**; **9b–9e** and **9′a–9′e**; and **10b–10e** and **10′a–10′e** in good yields.

EXPERIMENTAL

General. Melting points were measured in open capillaries on a perfit melting point apparatus and are uncorrected. IR spectra on KBr were recorded on Bruker–4800 infrared spectrometer. NMR and EIMS/HRMS spectra were recorded on Bruker AC-400 (400 and 100 MHz) and JEOL D-300 mass spectrometer, respectively. Elemental analysis was carried out on simple CHNS analyzer (CHNS-932, LECO Corporation). ^1H and ^{13}C chemical shifts are reported in parts per million (ppm) from tetramethylsilane as internal standard. All experiments were performed in oven-dried glass apparatus. SISCO silica was usedign as adsorbent for TLC (0.5-mm thick plates), and TLC plates were eluted with 1:9 ratios of ethyl acetate and *n*-hexane. The column chromatography was performed over silica gel (60–120 mesh) with graded solvent systems of ethyl acetate–petroleum ether (60–80).

General procedures. 2-Methyl-/2-ethyl- and 2-phenyl-/*p*-tolyl-4-arylidene/heterylmethylidene-oxazolin-5-ones **2** were prepared by the erlenmayer synthesis of azlactones [38].

Procedure for the synthesis of 3a–3e and 3′a–3′e. *o*-Aminobenzamide **1** (0.1 mol) was dissolved in acetic acid (5 mL) in a boiling tube and a solution of 2-methyl-4-benzylidene-2-oxazolin-5-one **2a** (R = CH_3, Ar = C_6H_5, 0.1 mol) was added to it. The reaction mixture was heated at about 95°C on a water bath for 1 h and then set aside for cooling. Colorless compound that separated out on cooling was filtered, washed with few drops of methanol, and recrystallized from a mixture of ethyl acetate and few drops of methanol. The pure 3-(α-carboxy-α-styryl)-2-methylquinazolin-4(3*H*)-one **3a** (R = CH_3, Ar = C_6H_5) was obtained. Similarly, **3′a** was obtained when *o*-aminobenzamide **1** was treated with 2-ethyl-4-benzylidene-2-oxazolin-5-ones **2′a** (R = C_2H_5, Ar = C_6H_5, 0.1 mol). The other arylidene and heterylmethylidene analogs, **3b–3e** and **3′b–3′e** were obtained similarly.

Procedure for the synthesis of 4a–4e and 4′a–4′e. A mixture of 3-(α-carboxy-α-styryl)-2-methylquinazolin-4(3*H*)-one

3a (R = CH_3, Ar = C_6H_5, 0.01 mol) and THF (10 mL) was taken in 50-mL round-bottom flask and refluxed for 3 h. THF was then removed by distillation at reduced pressure, and the colorless residue that remained in the flask was collected and crystallized from petroleum ether–chloroform mixture to give 2-methyl-3-(α-styryl)-quinazolin-4(3*H*)-one **4a**. The other substituted styryl and heterylvinyl analogs **4b–4e** were also obtained. Similarly, the exact identical product **4′a** was obtained from **3′a**. The other analogs **4b–4e** and **4′b–4′e** were obtained from corresponding compounds, **3b–3e** and **3′b–3′e**, respectively.

Procedure for the synthesis of 5a–5e and 5′a–5′e. 3-(α-Carboxy-α-styryl)-2-methylquinazolin-4(3*H*)-one **3a** (R = CH_3, Ar = C_6H_5, 0.025 mol) was converted into its ethyl ester with ethanol and HCl as usual. To this ester was added hydrazine hydrate in 1:1 molar ratio, and the reaction mixture was refluxed for 2 h and poured into water. The colorless compound that precipitated out in the flask was filtered and crystallized from petroleum ether chloroform mixture to give 3-(5-phenyl-3-oxopyrazolidin-4-yl)-2-methylquinazolin-4(3*H*)-one **5a.** The other analogs **5b–5e** and **5′a–5′e** were obtained from corresponding substrates in very good yield.

Procedure for the synthesis of 6a–6e and 6′a–6′e. 3-(α-Carboxy-α-styryl)-2-methylquinazolin-4(3*H*)-one **3a** (R = CH_3, Ar = C_6H_5, 0.025 mol) was converted into its acid chloride with $SOCl_2$ in benzene and worked up as usual. To this acid chloride was added piperidine (X = CH_2) and the reaction mixture in 1:1 molar ratio was refluxed for 2 h and poured into water. The colorless compound that precipitated out in the flask was filtered and crystallized from petroleum ether chloroform mixture to give the compound **6a$_i$** (X = CH_2). The other analogs **6b–6e** and **6′b–6′e** were also obtained in good yield. Starting from **3d** and using pyrrolidine (X = 0) and starting from **3e** and using morpholine (X = O), analogs **6d$_{ii}$** and **6e$_{iii}$** were also obtained.

Procedure for the synthesis of 7a–7e and 7′a–7′e. *o*-Aminobenzamide **1** (0.1 mol) and 2-phenyl-4-benzylidene-2-oxazolin-5-one **2a** (R = C_6H_5, Ar = C_6H_5, 0.1 mol) were taken in dry benzene (50 mL) and refluxed on a water bath initially for about 3–4 h. The refluxing was continued for a further period of 10–12 min after the addition of a few drops of acetic acid. The colorless compound that separated out was filtered and crystallized from acetic acid. The pure 3-benzylidene-4-benzoyl-1*H*-[1,4]benzodiazepine-2,5(3*H*, 5*H*)-dione **7a** was obtained in 80% yields, and the other arylidene/heterylmethylidene analogs **7b–7e** were obtained similarly in good yields. Similar procedure was adopted to generate **7′a** when *o*-aminobenzamide **1** (0.1 mol) was treated with 2-(*p*-tolyl)-4-benzylidene-2-oxazolin-5-one **2′a** (R = *p*-$CH_3C_6H_4$, Ar = C_6H_5) (0.1 mol) and its other analogues **7′b–7′e** were also generated similarly from corresponding substrates.

Procedure for the synthesis of 8a–8e and 8′a–8′e, 9a–9e and 9′a–9′e, and 10a–10e and 10′a–10′e. A well-grinded mixture of 3-benzylidene-4-benzoyl-1*H*-[1,4]benzodiazepine-2,5(3*H*,4*H*)-dione **7a** (0.1) and *o*-phenylenediamine (0.1 mol) (Thomas Baker Chm., Mumbai, India) was refluxed in acetic acid (10 mL) for about 2 h. The reaction product was monitored by TLC when a very prominent spot of the main product **8a** was detected along with trailing spot of the minor product **10a**. The reaction mixture was cooled when the main product solidified, could be separated by filtration and was washed with acetic acid. The filtrate along with combined washings contained only the minor product **10a** (TLC). The product **8a** was crystallized from boiling ethanol. When the same reaction was carried out in DMF containing few drops of 0.5% aqueous NaOH solution, the observed results were reversed. The main spot was due to **10a**, whereas **8a** was detected only as very minor product (TLC). The reaction mixture was poured into ice cold water when **10a** separated out as fluffy solid leaving at the bottom a sticky minor product **8a**. Compound **10a** was crystallized from hot methanol. When the reaction of **7a** with *o*-phenylenediamine was carried out in 1:2 molar ratio in boiling ethanol for a prolonged period (6 h), it resulted in the formation of a doubly condensed compound **9a** as the main product with very slight traces of **8a** and **10a.** On cooling for overnight, shining pale yellow crystals of **9a** separated, which were filtered, dried, and purified after two repeated crystallizations from hot ethanol. The other analogs **8b–8e** and **8′b–8′e, 9b–9e** and **9′b–9′e,** and **10b–10e** and **10′b–10′e** were also obtained from the corresponding substrates.

Spectral data of some constituent representatives from each kind. ***3-(α-Carboxy-α-styryl)-2-methylquinazolin-4(3H)-one (3a).*** IR (KBr, ν, cm^{-1}): 3334, 3224, 3156, 2640, 1720, 1642, 1515, 1238, 1215. ^{1}H NMR (DMSO-d_6) δ: 2.30 (s, 3H, CH_3), 7.21–7.90 (m, 9H, ArH), 7.98 (s, 1H, =C=CH-—Ar), 10.52 (s, 1H, COOH). ^{13}C NMR (DMSO-d_6) δ: 22.1, 120.3, 122.1, 124.2, 125.9, 126.2, 126.7, 127.3, 127.9, 128.2, 128.6, 129.1, 132.6, 135.8, 145.7, 162.6, 164.6, 165.8. MS *m*/*z*: 306 (M^+).

3-(α-Carboxy-α-styryl)-2-ethylquinazolin-4(3H)-one (3′a). IR (KBr, ν, cm^{-1}): 3410, 3225, 3060, 2832, 1685, 1624, 1235, 1210. ^{1}H NMR (DMSO-d_6) δ: 1.85 (t, 3H, CH_3), 2.71 (q, 2H, CH_2), 7.10–7.80 (m, 9H, ArH), 7.92 (s, 1H, =C=CH—Ar), 10.82 (s, 1H, COOH). ^{13}C NMR (DMSO-d_6) δ: 5.7, 24.2, 120.1, 122.7, 124.4, 125.8, 126.1, 126.9, 127.5, 128.6, 129.3, 129.7, 130.0, 132.0, 133.8, 145.3, 162.1, 164.5, 165.8. MS *m*/*z*: 320 (M^+).

2-Methyl-3-α-styryl-quinazolin-4(3H)-one (4a). IR (KBr, ν, cm^{-1}): 3233, 3114, 2976, 2940, 1660, 1632, 1525, 1548, 1215. ^{1}H NMR (DMSO-d_6) δ: 2.21 (s, 3H, CH_3), 7.10–7.62 (m, 9H, ArH), 7.82 (d, *J* = 14.5 Hz, 1H, =C=CH—Ar), 7.98 (d, *J* = 14.5 Hz, 1H, —CH=C=Ar). ^{13}C NMR (DMSO-d_6) δ: 22.3, 111.8, 119.1, 120.2, 121.9, 125.2, 126.2, 127.3, 127.9, 128.0, 128.3, 133.1, 134.6, 140.7, 163.6, 164.6, 165.8. MS *m*/*z*: 262 (M^+).

2-Ethyl-3-α-styryl-quinazolin-4(3H)-one (4′a). IR (KBr, ν, cm^{-1}): 3360, 3245, 3090, 2948, 1668, 1584, 1527, 1205. ^{1}H NMR (DMSO-d_6) δ: 1.92 (t, 3H, CH_3), 2.70 (q, 2H, CH_2), 7.21–7.70 (m, 9H, ArH), 7.74 (d, *J* = 14.2 Hz, 1H, =C=CH—Ar), 7.82 (d, *J* = 14.2 Hz, 1H, —CH=C=Ar). ^{13}C NMR (DMSO-d_6) δ: 5.9, 24.0, 111.9, 120.0, 121.7, 125.4, 125.9, 127.1, 128.0, 128.2, 128.4, 128.9, 133.0, 134.8, 140.9, 163.8, 164.9, 165.0. MS *m*/*z*: 276 (M^+).

3-[5-(3,4-Dimethoxyphenyl)-3-oxopyrazolidin-4-yl]-2-methylquinazolin-4(3H)-one (5c). IR (KBr, ν, cm^{-1}): 3432, 3376, 3225, 2980, 2870, 1715, 1670, 1668, 1320, 1270, 1248. ^{1}H NMR (DMSO-d_6) δ: 2.11 (s, 3H, CH_3), 2.86 (d, 1H, CH), 2.94 (d, 1H, CH), 3.70 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 6.81–7.50 (m, 7H, ArH), 8.23 (s, 1H, NH, D_2O exchangable), 8.54 (s, 1H, NH, D_2O exchangable). MS *m*/*z*: 380 (M^+).

2-Methyl-3-[α-(N-piperidinylcarbonyl)-4-methyl-α-styryl]-quinazolin-4(3H)-ones (6b$_i$) (X = CH$_2$). IR (KBr, ν, cm^{-1}): 3435, 3320, 3228, 1720, 1680, 1665, 1270, 1262, 1232. ^{1}H NMR (DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 1.90–3.10 (m, 10H, 5 × CH_2), 6.82 (s, 1H, =C=CH—Ar), 7.10–7.51 (m, 8H, ArHs). ^{13}C NMR (DMSO-d_6) δ: 22.0, 24.1, 24.6, 26.8, 26.8, 43.5, 43.5, 119.9, 121.6, 122.0, 125.4, 125.4, 126.9, 127.3, 128.5, 129.8, 129.8, 131.5, 132.5, 134.8, 136.7, 145.8, 164.5, 165.8. MS *m*/*z*: 387 (M^+).

2-Methyl-3-[α-(N-pyrolidinylcarbonyl)-β-(2-furyl)vinyl]quinazolin-4(3H)-ones (6d$_{ii}$) (X = 0). IR (KBr, ν, cm^{-1}): 3392, 3242, 3115, 1718, 1690, 1685, 1275, 1260, 1235. ^{1}H NMR (DMSO-d_6) δ: 2.21 (s, 3H, CH_3), 1.78–3.22 (m, 8H, 4 × CH_2), 6.91 (s, 1H, =C=CH—Ar), 7.20–7.64 (m, 7H, ArH, HetH). MS *m*/*z*: 333 (M^+).

2-Methyl-3-[α-(N-morpholinylcarbonyl)-β-(3-indolyl)vinyl]-quinazolin-4(3H)-ones (6e$_{iii}$) (X = O). IR (KBr, ν, cm^{-1}): 3425, 3230, 3095, 2968, 1708, 1692, 1645, 1290, 1268, 1225. ^{1}H NMR (DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 1.69–3.72 (m, 8H, 4 × CH_2), 6.89 (s, 1H, =C=CH—Ar), 7.20–7.98 (m, 9H, ArH, HetH), 9.20 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 22.2, 42.8, 43.5, 67.9, 68.2, 110.8, 111.3, 119.6, 120.5, 120.4, 121.8, 122.5, 125.1, 126.8, 127.0, 128.5, 129.5, 130.3, 133.1, 133.5, 136.6, 145.6, 163.8, 165.9. MS *m*/*z*: 415 (M^+).

3-Benzylidene-4-benzoyl-1H-[1,4]benzodiazepine-2,5(3H,4H)-dione (7a). IR (KBr, ν, cm^{-1}): 3296, 3205, 3010, 3330, 1685, 1660, 1640, 1465, 1220. ^{1}H NMR (DMSO-d_6) δ: 7.21–7.80 (m, 14H, ArH), 7.95 (s, 1H, =C=CH—Ar), 9.64 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 121.3, 122.5, 123.0, 124.6, 125.3, 126.2, 126.7, 127.3, 127.9, 128.0, 128.3, 128.6, 128.8, 128.9, 129.5, 129.8, 132.0, 134.6, 137.6, 138.8, 162.6, 163.6, 164.9. MS *m*/*z*: 368 (M^+).

3-(4-Methylbenzylidene)-4-benzoyl-1H-[1,4]benzodiazepine-2,5(3H,4H)-dione (7b). IR (KBr, ν, cm^{-1}): 3445, 3316, 3250, 2965, 1720, 1651, 1648, 1454, 1212. ^{1}H NMR (DMSO-d_6) δ: 2.30 (s, 3H, CH_3), 7.23–7.88 (m, 13H, ArH), 7.95 (s, 1H, =C=CH—Ar), 9.56 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 24.1, 121.5, 122.6, 123.1, 124.8, 125.2, 126.5, 126.8, 127.3, 127.6, 127.8, 127.9, 128.5, 128.9, 129.2, 129.5, 131.3, 132.5, 134.8, 135.5, 138.9, 162.1, 163.5, 164.8. MS *m*/*z*: 382 (M^+).

3-Benzylidene-4-(4-methylbenzoyl)-1H-[1,4]benzodiazepine-2,5(3H,4H)-dione (7′a) IR (KBr, ν, cm^{-1}): 3510, 3276, 3245, 2970, 1720, 1656, 1632, 1467, 1216. ^{1}H NMR (DMSO-d_6) δ: 2.30 (s, 3H, CH_3), 7.10–7.79 (m, 13H, ArH), 7.90 (s, 1H, =C=CH—Ar), 9.8 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 24.5, 121.8, 122.9, 123.5, 124.1, 125.5, 126.6, 126.9, 127.5, 127.7, 128.1, 128.6, 128.9, 129.3, 129.8, 131.8, 132.5, 133.6, 135.7, 137.9, 142.5, 162.8, 164.6, 164.5. MS *m*/*z*: 382 (M^+).

3-(4-Methylbenzylidene)-4-(4-methylbenzoyl)-1H-[1,4]benzodiazepine-2,5(3H,4H)-dione (7′b). IR (KBr, ν, cm^{-1}): 3270 (NH); 1680, 1642, 1632 (C = 0); 1212 (C—N). ^{1}H NMR (DMSO-d_6) δ: 2.20 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 7.10–7.91 (m, 12H, ArH), 7.95 (s, 1H, =C=CH—Ar), 9.50 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 23.7, 24.1, 121.2, 122.8, 123.5, 124.2, 126.2, 126.7, 127.1, 127.5, 127.7, 127.9, 129.3, 129.5, 129.8, 129.9, 131.5, 132.3, 133.8, 135.9, 138.7, 140.5, 162.6, 163.9, 164.5. MS *m*/*z*: 396 (M^+).

7-Benylidene-9-Phenyl-6,7-dihydro-5H-[1,4]benzodiazepino-[5,4-b][1,3,5]benzo triazepin-6-one (8a). IR (KBr, ν, cm^{-1}): 3390, 3325, 3276, 2986, 1697, 1685, 1660,1450, 1278, 1275, 1220. ^{1}H NMR (DMSO-d_6) δ: 7.10–7.32 (m, 9H, ArH), 7.52–7.80 (m, 9H, ArH), 7.84 (s, 1H, =C=CH—Ar), 9.20 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 107.6, 119.8, 121.4, 122.8, 123.4, 124.2, 126.2, 126.4, 126.7, 126.8, 126.9, 128.0, 128.3, 128.4, 128.6, 128.9, 129.2, 129.6, 129.8, 130.6, 134.8, 135.8, 136.6, 143.5, 144.9, 147.3, 163.2, 164.5, 165.3. MS *m*/*z*: 440 (M^+).

7-(2-Furylmethylidene)-9-Phenyl-6,7-dihydro-5H-[1,4]benzodiazepino[5,4-b][1,3,5]benzotriazepin-6-one (8d). IR (KBr, ν, cm^{-1}): 3410, 3365, 3110, 2835, 1690, 1665, 1632, 1468, 1280, 1266, 1230. ^{1}H NMR (DMSO-d_6) δ: 6.50–6.82 (m, 3H, ArH), 7.22–7.71 (m, 13H, ArH), 7.86 (s, 1H, =C=CH—Ar), 9.41 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 107.6, 108.3, 120.6, 121.5, 123.1, 123.5, 124.0, 124.3, 126.2, 126.7, 126.9, 128.2, 128.5, 128.7, 128.9, 129.2, 130.0, 130.3, 136.1, 139.3, 143.5, 144.6, 144.8, 146.5, 163.5, 164.2, 164.6. MS *m*/*z*: 430 (M^+).

17-(Indol-3-yl)-19-phenyl-10,16,17,17a-tetrahydro[1,5]benzodiazepino[2′,3′:2,3] [1,4] benzodiazepino[5,4-b][1,3,5]benzotriazepine (9e). IR (KBr, ν, cm^{-1}): 3415, 3340, 3170, 2982, 2870, 1695, 1642, 1628, 1285, 1242, 1228. ^{1}H NMR (DMSO-d_6) δ: 4.51 (d, 1H, CH), 4.58 (d, 1H, CH), 6.34–6.80 (m, 5H, ArH), 6.85–7.10 (m, 8H, ArH), 7.24–7.65 (m, 9H, ArH), 9.10 (s, 1H, NH, D_2O exchangable), 9.40 (s, 1H, NH, D_2O exchangable), 9.62 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 49.3, 52.7, 110.8, 113.6, 116.5, 116.8, 118.1, 118.4, 118.8, 119.2, 120.5, 121.8, 122.5, 122.9, 123.7, 125.2, 125.8, 127.1, 127.6, 127.8, 128.2, 128.5, 128.7, 128.7, 130.5, 131.2, 132.6, 133.9, 134.4, 134.7, 135.8, 136.3, 145.5, 146.9, 164.2, 164.5, 172.8. MS *m*/*z*: 568 (M^+).

13-Benzoyl-12-(3,4-dimethoxyphenyl)-5,11,12,12a,13,14-hexahydro[1,5]benzo diazepino[2,3-b][1,4]benzodiazepin-14-one (10c) IR (KBr, ν, cm^{-1}): 3450, 3230, 3205, 3110, 2975, 1725, 1708, 1272, 1260, 1225. ^{1}H NMR (DMSO-d_6) δ: 3.70 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 4.80 (d, 1H, CH), 4.86 (d, 1H, CH), 6.52–7.0 (m, 4H, ArH), 7.05–7.30 (m, 3H, ArH), 7.36–7.84 (m, 9H, ArH), 8.25 (s, 1H, NH, D_2O exchangable), 8.48 (s, 1H, NH, D_2O exchangable). ^{13}C NMR (DMSO-d_6) δ: 49.2, 52.3, 55.8, 56.2, 114.5, 115.6, 116.8, 118.1, 118.5, 118.8, 120.5, 123.8, 127.1, 127.6, 127.9, 128.2, 128.4, 128.6, 128.9, 132.7, 133.5, 134.8, 136.5, 137.2, 142.7, 145.8, 146.2, 147.4, 148.7, 163.8, 164.5. MS *m*/*z*: 518 (M^+).

Acknowledgments. The authors are thankful to the Department of Chemistry, University of Jammu, Jammu, and IIIM Jammu for providing research and library facilities.

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