Heterocyclic Variants of the 1,5-Benzodiazepine System. V. Derivatives of 2-(*ortho*-R_1-Anilino)-4-(*p*-R_2-phenyl)-3*H*-1,5-benzodiazepines

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Mono-*N*-methylation of 2-(*ortho*-R_1-anilino)-4-(*p*-R_2-phenyl)-3*H*-1,5-benzodiazepines **IV** is achieved in moderate yield with sodium hydride in methyl iodide. Reaction of the *N*-methyl derivatives **I** with methoxyacetyl chloride gave the compounds **II** and **III**. The structure of all products was confirmed by ir, ^{1}H-nmr and mass spectrometry.

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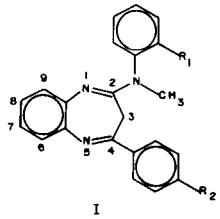
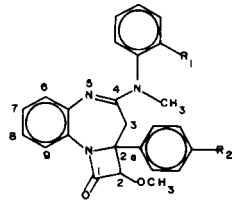
In our continuing search for superior central nervous system drugs [3], a variety of 1,5-benzodiazepines of general formula **I, II** and **III** were prepared (Scheme 1). Some of these, **I**, are close analogs of benzodiazepines known to have anxiolytic activity [4] and others, **II** and **III**, are more remote analogs made in order to explore new avenues of activity.

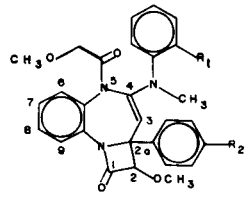
Scheme 1



I



II



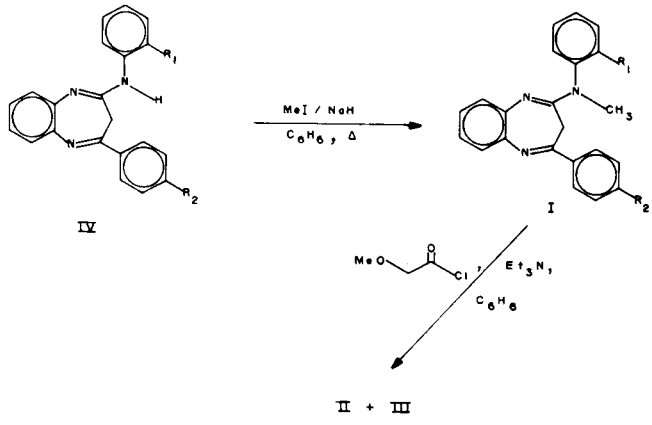
III

	R_1	R_2
a	H	H
b	CH_3	H
c	OCH_3	H
d	Cl	H
e	Br	H
f	H	CH_3
g	CH_3	CH_3
h	OCH_3	CH_3

	R_1	R_2
i	Cl	CH_3
j	Br	CH_3
k	H	Cl
l	CH_3	Cl
m	OCH_3	Cl
n	Cl	Cl
o	Br	Cl

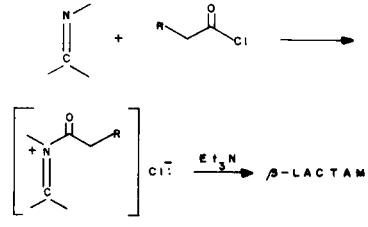
Our key intermediates, **IV**, were prepared similarly to literature methods [5]. Treatment of 2-(*ortho*-R_1-anilino)-4-(*p*-R_2-phenyl)-3*H*-1,5-benzodiazepines **IV** with sodium hydride and methyl iodide in refluxing benzene afforded **I** (Scheme 2).

Scheme 2



IV I II + III

Scheme 3



V

Structural assignment of **I** derivatives was made on spectroscopic grounds. In the infra-red spectra of **I** the appearance of an absorption band at 1610 cm^{-1} was consistent with the presence of an imine group [6]. In the ^{1}H nmr spectra of **I** a broad singlet in the region at δ 2.95-3.6 was assigned to methylene protons joined to C_3 [7] and *N*-methyl protons, respectively. The remaining aromatic protons in **I** were assigned to signal in the region at δ 6.75-7.5 (multiplet). Further confirmation of the structure of **I** is derived from their mass spectral data. All the compounds showed the molecular ion and their base peak is the ion at m/z [M^+-(*ortho*-R_1)] [8].

On the other hand, reaction of imine compounds with substituted acetyl chloride in dried benzene, in the

Table 1

Physical and Analytical Data of Compounds **I**

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses, % C	H
a	H	H	192-193	63	$C_{22}H_{19}N_3$	81.20 (81.00)	5.88 (5.89)
b	Me	H	52-53	56	$C_{23}H_{21}N_3$	81.38 (81.30)	6.23 (6.21)
c	OMe	H	50-51	88	$C_{23}H_{21}N_3O$	77.71 (77.68)	5.95 (6.01)
d	Cl	H	35-36	46	$C_{22}H_{18}ClN_3$	73.42 (73.38)	5.04 (5.0)
e	Br	H	118-119	71	$C_{22}H_{18}BrN_3$	65.35 (65.30)	4.48 (4.5)
f	H	Me	202-203	75	$C_{23}H_{21}N_3$	81.38 (81.29)	6.23 (6.23)
g	Me	Me	68-69	57	$C_{24}H_{23}N_3$	81.55 (81.57)	6.55 (6.53)
h	OMe	Me	62-63	61	$C_{24}H_{23}N_3O$	78.02 (78.00)	6.44 (6.45)
i	Cl	Me	78-80	36	$C_{23}H_{20}ClN_3$	73.88 (73.85)	5.39 (5.40)
j	Br	Me	164-165	52	$C_{23}H_{20}BrN_3$	66.03 (66.1)	4.82 (4.80)
k	H	Cl	214-215	56	$C_{22}H_{18}ClN_3$	73.42 (73.39)	5.04 (5.0)
l	Me	Cl	158-160	72	$C_{23}H_{20}ClN_3$	73.88 (73.85)	5.39 (5.35)
m	OMe	Cl	155-156	77	$C_{23}H_{20}ClN_3O$	70.85 (70.80)	5.17 (5.17)
n	Cl	Cl	152-153	50	$C_{22}H_{17}Cl_2N_3$	67.01 (66.95)	4.34 (4.32)
o	Br	Cl	150-151	57	$C_{22}H_{17}BrClN_3$	60.22 (60.15)	3.90 (3.9)

Table 2

Physical, Analytical and Spectral Data for Compounds **II**

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses, % C	H	Spectral Data
a	H	H	58-59	36	$C_{25}H_{23}N_3O_2$	75.54 (75.49)	5.83 (5.81)	ir (chloroform): 1755, 1641 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.5-6.85 (m, 13H), 4.5 (s, 1H), 3.4 (d, J = 14 Hz, 1H), 3.15 (s, 3H), 3.05 (s, 3H), 2.8 (d, J = 14 Hz, 1H); ms: M^+ at m/z 397.
b	Me	H	70-71	29	$C_{26}H_{25}N_3O_2$	75.88 (75.83)	6.12 (6.10)	ir (chloroform): 1750, 1635 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.65-6.75 (m, 12H), 4.45 (s, 1H), 3.65 (d, J = 14 Hz, 1H), 3.21 (s, 3H), 3.15 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.35 (s, 3H); ms: M^+ at m/z 411.
c	OMe	H	67-68	39	$C_{26}H_{25}N_3O_3$	73.04 (73.0)	5.89 (5.87)	ir (chloroform): 1751, 1635 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.5-6.85 (m, 12H), 4.51 (s, 1H), 3.82 (s, 3H), 3.4 (d, J = 14 Hz, 1H), 3.15 (s, 3H), 3.05 (s, 3H), 2.8 (d, J = 14 Hz, 1H); ms: M^+ at m/z 427.
d	Cl	H	162-163	26	$C_{25}H_{22}ClN_3O_2$	69.51 (69.45)	5.13 (5.13)	ir (chloroform): 1755, 1645 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.3 (m, 1H), 7.6-6.75 (m, 12H), 4.52 (s, 1H), 3.45 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.1 (s, 3H), 2.8 (d, J = 14 Hz, 1H); ms: M^+ at m/z 431.
e	Br	H	175-176	28	$C_{25}H_{22}BrN_3O_2$	63.03 (62.98)	4.65 (4.63)	ir (chloroform): 1751, 1625 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.65-6.8 (m, 12H), 4.51 (s, 1H), 3.5 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.1 (s, 3H), 2.8 (d, J = 14 Hz, 1H); ms: M^+ at m/z 475.

Table 2 (continued)

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses, % C	H	Spectral Data
f	H	Me	184-185	21	$C_{26}H_{25}N_3O_2$	75.88 (75.83)	6.12 (6.12)	ir (chloroform): 1752, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.3 (m, 1H), 7.5-6.8 (m, 12H), 4.5 (s, 1H), 3.6 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.15 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.35 (s, 3H); ms: M^+ at m/z 411.
g	Me	Me	162-163	25	$C_{27}H_{27}N_3O_2$	76.20 (76.15)	6.39 (6.38)	ir (chloroform): 1750, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.6-6.8 (m, 11H), 4.45 (s, 1H), 3.5 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.15 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.37 (s, 3H), 2.35 (s, 3H); ms: M^+ at m/z 425.
h	OMe	Me	86-87	36	$C_{27}H_{27}N_3O_3$	73.44 (73.40)	6.16 (6.14)	ir (chloroform): 1752, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.5-6.75 (m, 11H), 4.5 (s, 1H), 3.82 (s, 3H), 3.4 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.1 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.3 (s, 3H); ms: M^+ at m/z 441.
i	Cl	Me	187-189	79	$C_{26}H_{24}ClN_3O_2$	70.02 (69.95)	5.42 (5.42)	ir (chloroform): 1768, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.6-6.8 (m, 11H), 4.5 (s, 1H), 3.45 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.1 (s, 3H), 2.8 (d, J = 14 Hz, 1H), 2.31 (s, 3H); ms: M^+ at m/z 445.
j	Br	Me	115-116	21	$C_{26}H_{24}BrN_3O_2$	63.67 (63.63)	4.93 (4.91)	ir (chloroform): 1755, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.65-6.71 (m, 11H), 4.51 (s, 1H), 3.5 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.1 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.3 (s, 3H); ms: M^+ at m/z 489.
k	H	Cl	162-163	26	$C_{25}H_{22}ClN_3O_2$	69.51 (69.48)	5.13 (5.13)	ir (chloroform): 1752, 1631 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.6-6.75 (m, 12H), 4.5 (s, 1H), 3.45 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.1 (s, 3H), 2.8 (d, J = 14 Hz, 1H); ms: M^+ at m/z 431.
l	Me	Cl	180-181	17	$C_{26}H_{24}ClN_3O_2$	70.02 (69.94)	5.42 (5.42)	ir (chloroform): 1751, 1625 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.65-6.7 (m, 11H), 3.45 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.15 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.3 (s, 3H); ms: M^+ at m/z 445.
m	OMe	Cl	90-91	22	$C_{26}H_{24}ClN_3O_3$	67.60 (67.57)	5.23 (5.21)	ir (chloroform): 1750, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.6-6.8 (m, 11H), 4.5 (s, 1H), 3.8 (s, 3H), 3.4 (d, J = 14 Hz, 1H), 3.15 (s, 3H), 3.05 (s, 3H), 2.75 (d, J = 14 Hz, 1H); ms: M^+ at m/z 461.
n	Cl	Cl	52-53	83	$C_{25}H_{21}Cl_2N_3O_2$	64.38 (64.35)	4.53 (4.53)	ir (chloroform): 1755, 1625 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.3 (m, 1H), 7.7-6.8 (m, 11H), 4.5 (s, 1H), 3.45 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.15 (s, 3H), 2.8 (d, J = 14 Hz, 1H); ms: M^+ at m/z 465.
o	Br	Cl	205-206	35	$C_{25}H_{21}BrClN_3O_2$	58.78 (58.73)	4.14 (4.12)	ir Chloroform): 1751, 1626 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.25 (m, 1H), 7.6-6.8 (m, 11H), 4.5 (s, 1H), 3.5 (d, J = 14 Hz, 1H), 3.2 (s, 3H), 3.15 (s, 3H), 2.75 (d, J = 14 Hz, 1H); ms: M^+ at m/z 509.

presence of triethylamine, is reported to give β-lactam derivatives [9]. When *N*-methyl-1,5-benzodiazepines **I** were treated with methoxyacetyl chloride under these conditions, a mixture of products, **II** and **III**, was obtained (Scheme 2); the mixture of **II** and **III** was separated by thin layer chromatography. Structural assignment of these compounds rest on analytical and spectroscopic evidences (Table 2 and 3).

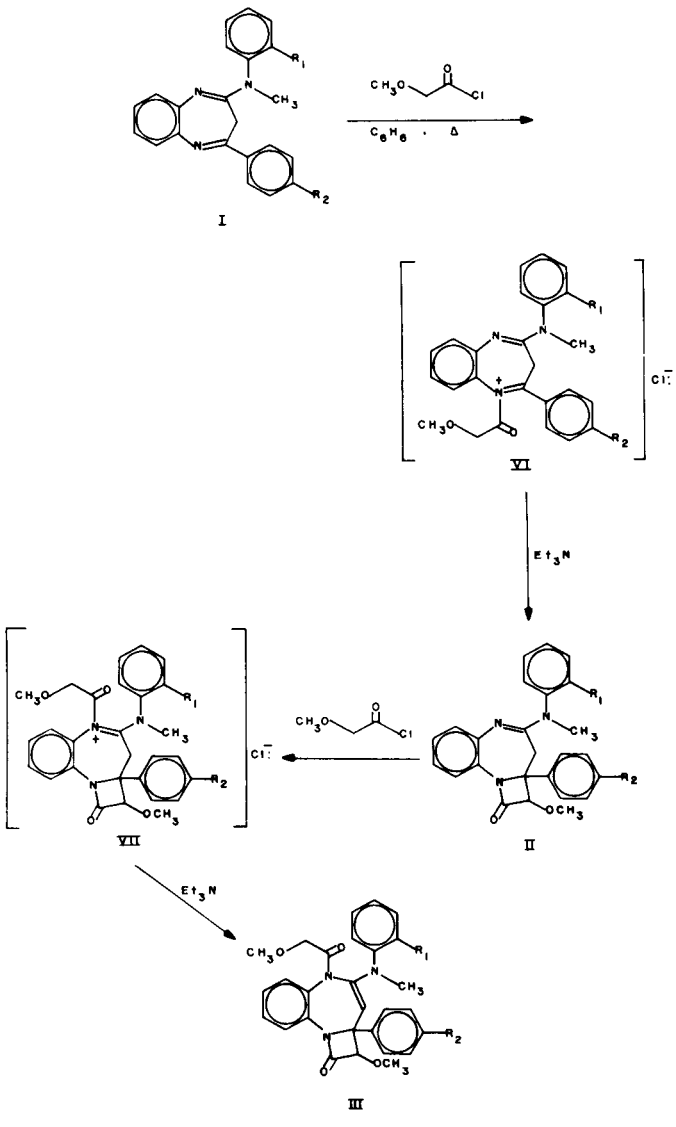
In the infrared spectra of compound **II**, a characteristically band for the β-lactam group [10] was present (1750 cm^{-1}) together with a band at 1620 cm^{-1} assignable to the -C=N- group. In the ^1H nmr spectra of **II** derivatives the presence of a three-proton singlet at δ 3.2 confirmed the incorporation of an aliphatic methoxy group; a downfield one-proton singlet at δ 4.5 was assigned to the methine proton attached to the carbon bearing the methoxy group. Likewise another three-proton singlet at δ 3.15 was assigned to the *N*-methyl protons. Two doublets at δ 2.6-2.8 (J = 14 Hz) and δ 3.6-3.4 (J = 14 Hz) respectively were assigned to the methylene protons joined to C_3 whereas a multiplet at δ 8.2-8.4 was assigned to the aromatic proton joined to C_9 [11]. The remaining

Table 3

Physical, Analytical and Spectral Data for Compounds **III**

Compound No.	R_1	R_2	Mp °C	Yield %	Molecular Formula	Analyses, % C	Analyses, % H	Spectral Data
a	H	H	187-188	41	$C_{28}H_{27}N_3O_4$	71.62 (71.56)	5.79 (5.75)	ir (chloroform): 1750, 1705 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.4 (bd, J = 10 Hz, 1H), 7.56-6.22 (m, 14H), 5.5 (s, 1H), 4.75 (s, 2H), 3.33 (s, 3H), 3.18 (s, 3H), 2.92 (s, 3H); ms: M^+ at m/z 469.
b	Me	H	194-195	37	$C_{29}H_{29}N_3O_4$	72.02 (71.98)	6.04 (6.0)	ir (nujol): 1764, 1698 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.32 (bd, J = 10 Hz, 1H), 7.5-6.3 (m, 13H), 5.4 (s, 1H), 4.74 (s, 2H), 3.31 (s, 3H), 3.1 (s, 3H), 2.84 (s, 3H), 2.35 (s, 3H); ms: M^+ at m/z 483.
c	OMe	H	70-71	39	$C_{29}H_{29}N_3O_5$	69.72 (69.70)	5.85 (5.84)	ir (chloroform): 1755, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.35 (bd, J = 10 Hz, 1H), 7.45-6.3 (m, 13H), 5.3 (s, 1H), 4.72 (s, 2H), 3.4 (s, 3H), 3.28 (s, 3H), 3.0 (s, 3H), 2.86 (s, 3H); ms: M^+ at m/z 499.
d	Cl	H	194-195	28	$C_{28}H_{26}ClN_3O_4$	66.72 (66.70)	5.20 (5.20)	ir (chloroform): 1753, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.4 (bd, J = 10 Hz, 1H), 7.6-6.3 (m, 13H), 5.41 (s, 1H), 4.75 (s, 2H), 3.32 (s, 3H), 3.2 (s, 3H), 2.9 (s, 3H); ms: M^+ at m/z 503.
e	Br	H	153-154	37	$C_{28}H_{26}BrN_3O_4$	61.32 (61.29)	4.80 (4.8)	ir (chloroform): 1753, 1697 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.35 (bd, J = 10 Hz, 1H), 7.56-6.28 (m, 13H), 5.44 (s, 1H), 4.8 (s, 2H), 3.31 (s, 3H), 3.21 (s, 3H), 2.91 (s, 3H); ms: M^+ at m/z 547.
f	H	Me	184-185	27	$C_{29}H_{29}N_3O_4$	72.02 (72.0)	6.04 (6.01)	ir (chloroform): 1752, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.32 (bd, J = 10 Hz, 1H), 7.6-6.3 (m, 13H), 5.4 (s, 1H), 4.75 (s, 2H), 3.31 (s, 3H), 3.15 (s, 3H), 2.96 (s, 3H), 2.32 (s, 3H); ms: M^+ at m/z 483.
g	Me	Me	210-211	32	$C_{30}H_{31}N_3O_4$	72.41 (72.39)	6.28 (6.26)	ir (chloroform): 1760, 1696 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.35 (bd, J = 10 Hz, 1H), 7.58-6.28 (m, 12H), 5.42 (s, 1H), 4.74 (s, 2H), 3.32 (s, 3H), 3.18 (s, 3H), 2.94 (s, 3H), 2.34 (s, 6H); ms: M^+ at m/z 497.
h	OMe	Me	70-71	25	$C_{30}H_{31}N_3O_5$	70.15 (70.0)	6.08 (6.0)	ir (chloroform): 1754, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.4 (bd, J = 10 Hz, 1H), 7.56-6.23 (m, 12H), 5.5 (s, 1H), 4.75 (s, 2H), 3.4 (s, 3H),, 3.28 (s, 3H), 3.0 (s, 3H), 2.88 (s, 3H); ms: M^+ at m/z 513.
j	Br	Me	62-63	29	$C_{29}H_{26}BrN_3O_4$	61.92 (61.89)	5.01 (5.0)	ir (chloroform): 1762, 1710 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.33 (bd, J = 10 Hz, 1H), 7.6-6.3 (m, 12H), 5.4 (s, 1H), 4.76 (s, 2H), 3.31 (s, 3H), 3.18 (s, 3H), 2.94 (s, 3H), 2.35 (s, 3H); ms: M^+ at m/z 561.
k	H	Cl	218-219	32	$C_{28}H_{26}ClN_3O_4$	66.72 (66.70)	5.20 (5.18)	ir (chloroform): 1755, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.4 (bd, J = 10 Hz, 1H), 7.56-6.28 (m, 13H), 5.41 (s, 1H), 4.75 (s, 2H), 3.33 (s, 3H), 3.21 (s, 3H), 2.91 (s, 3H); ms: M^+ at m/z 503.
l	Me	Cl	173-174	16	$C_{29}H_{28}ClN_3O_4$	67.24 (67.20)	5.45 (5.43)	ir (chloroform): 1752, 1698 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.4 (bd, J = 10 Hz, 1H), 7.56-6.3 (m, 12H), 5.3 (s, 1H), 4.74 (s, 2H), 3.34 (s, 3H), 3.15 (s, 3H), 3.0 (s, 3H), 2.32 (s, 3H); ms: M^+ at m/z 517.
m	OMe	Cl	140-141	36	$C_{29}H_{28}ClN_3O_5$	65.22 (65.20)	5.28 (5.26)	ir (chloroform): 1753, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.3 (bd, J = 10 Hz, 1H), 7.6-6.25 (m, 12H), 5.31 (s, 1H), 4.76 (s, 2H), 3.4 (s, 3H), 3.3 (s, 3H), 3.0 (s, 3H), 2.85 (s, 3H); ms: M^+ at m/z 533.
o	Br	Cl	185-186	25	$C_{28}H_{25}BrClN_3O_4$	57.69 (57.65)	4.32 (4.31)	ir (chloroform): 1753, 1700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.35 (bd, J = 10 Hz, 1H), 7.65-6.3 (m, 12H), 5.3 (s, 1H), 4.8 (s, 2H), 3.35 (s, 3H), 3.2 (s, 3H), 2.93 (s, 3H); ms: M^+ at m/z 581.

Scheme 4



aromatic protons in compounds **II** appeared as unresolved multiplet at δ 6.8-7.6. Further evidence of the structure of **II** is derived from their mass spectral data. All the compounds showed the molecular ion and their base peak is formed by the loss of a methoxyketene unit and the *ortho*-R_1 substituent {m/z [M^+-(72 + R_1)]} [8,11].

The infrared spectrum of compounds **III** showed two stronger carbonyl absorptions at 1750 (β-lactam) and 1700 cm^{-1} (amide group) which indicated the incorporation of two acetyl groups. Likewise, in the ^1H nmr spectra of **III** the presence of two three-proton singlet at δ 3.15 and δ 3.3 confirmed the incorporation of two aliphatic methoxy groups; a downfield one proton singlet at δ 5.4 and two proton singlet at δ 4.66 were assigned to the methine proton and methylene protons attached to the carbons bearing the methoxy groups, respectively. Two other singlets at δ 6.5 (b) and δ 2.85 were assigned to the proton joined to C_3 and the *N*-methyl protons respectively, whereas a doublet of doublets at δ 8.4 (J = 10 Hz, 1 Hz) was assigned in turn to the proton joined to C_9. The remaining aromatic protons in compound **III** appeared as an unresolved multiplet at δ 7.45-6.35. Definitive evidence for the structure of compound **III** in the solid state was obtained by single-crystal X-ray diffraction of compound **IIIk** [12].

As shown by investigations of the mechanism of the reaction of an imine derivate with substituted acetyl chloride [13], this reaction may take place through the intermediate **V** (Scheme 3), when the substituted acetylchloride is added first to the solution of the imine derivative; therefore the formation of compounds **II** and **III** is consistent with the intermediary of acylimmonium ions **VI** and **VII** (Scheme 4).

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Nicolet FT-55X spectrophotometer. The ^1H nmr spectra were recorded on a Varian FT-80 spectrometer operating at 80 MHz, in deuteriochloroform solution containing tetramethylsilane as internal standard with chemical shifts (δ) expressed downfield from TMS. Mass spectra were obtained with a Hewlett-Packard 59854-A quadropole mass spectrometer.

The compounds **IVa-o** have been prepared following reported procedures [5]. The structures of compounds **IVa-o** were supported by ir and mass spectral data which are similar to the reported [8].

The compounds **Ia-o** have been prepared from the appropriate 2-(*ortho*-R_1-anilino)-4-(*p*-R_2-phenyl)-3*H*-1,5-benzodiazepines, **IV**, by sodium hydride-methyl iodide alkylation [11].

The structures of compounds **Ia** to **Io** were supported by ir, ^1H nmr and mass spectral data. The ir spectra for all compounds show a strong band at 1610 cm^{-1} in accordance with Sternbach's findings for similar moieties [6]. The ^1H nmr spectra (δ) of 1,5-benzodiazepine **I** derivatives show a broad singlet between 3.2-3.6, which may be attributed to 2-N-CH_3 protons and the methylene protons of position 3. We also observed a multiplet between 6.75-7.5 for aromatic protons. All compounds **I** show the molecular ion and their base peak is the ion at m/z [M^+-(*ortho*-R_1)]. In Table 1, physical data for the new compounds are recorded. All the compounds investigated gave satisfactory elemental analysis.

Reaction of 2-[*ortho*-R_1-(*N*-methylanilino)]-4-(*para*-R_2-phenyl)-3*H*-1,5-benzodiazepines, **Ia-o**, with methoxyacetyl chloride.

Synthesis of 2a-(*p*R_2-phenyl)-2-methoxy-4-[*ortho*-R_1-(*N*-methylanilino)]-1,2,2a-3-tetrahydroazeto[1,2-*a*][1,5]benzodiazepin-1-one, **IIa-o**, and 2a-(*p*-R_2-phenyl)-2-methoxy-5-(2-methoxyacetyl)-4-[*ortho*-R_1-(*N*-methylanilino)]-1,2,2a,5-tetrahydroazeto[1,2-*a*][1,5]benzodiazepin-1-one, **IIIa-o**.

General Procedure.

Compound **Ia** (0.88 g, 2.7 mmoles) was dissolved in benzene (100 ml) and 11 mmoles (1.2 g) of methoxyacetyl chloride was added. The mixture was refluxed for 2 hours, and a solution of triethylamine (1.12 g, 11 mmoles) in 10 ml of benzene was added dropwise, with stirring, during 20 minutes. The reaction mixture was heated for 2 hours, then it was allowed to cool. The resulting solution was washed with a 5% aqueous hydrochloric acid (3 x 20 ml), water (3 x 20 ml), dried over anhydrous sodium sulfate and concentrated (rotary evaporator) to afford a yellow oil. Silica tlc showed the presence of two compounds. Separation of this mixture was achieved by preparative silica tlc (hexane/ethyl acetate,

70:30): **IIa** (0.375 g, 35%), mp 58°; **IIIa** (0.380 g, 30%), mp 187°. The physical, analytical and spectral data for synthesized compounds **IIa-o** and **IIIa-o**, are recorded on Tables 2 and 3, respectively.

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