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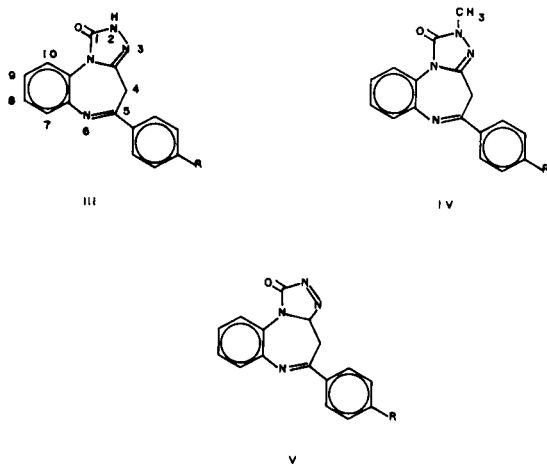
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Ethyl 3-[3*H*-1,5-benzodiazepin-2-yl]carbazates **II** were prepared in moderate yields from the title compounds and ethyl carbazate. The compounds **II** were easily transformed into 1*H*-s-triazolo[4,3-*a*][1,5]benzodiazepin-1-ones **III** via a one-step procedure. Reaction of triazolo-1,5-benzodiazepinones **III** with sodium hydride in methyl iodide gave a mixture of products from which were isolated two compounds **IV** and **V**. The structure of all products was confirmed by ir, <sup>1</sup>H nmr and mass spectrometry.

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Since the report that the fusion of a triazole ring to the *a* face of 1,4-benzodiazepines modified the biological behaviour of the parent molecule [4], there has been renewed interest in the preparations and pharmaceutical properties of other heterocyclic fused diazepine ring system [5]. However, there has been scant interest in the synthesis of compounds with a triazole ring fused to the 1,5-benzodiazepine system [6]. This induces us to report the synthesis and spectral data of closely related family of compounds of the general structure **III**, **IV** and **V** (Scheme 1).

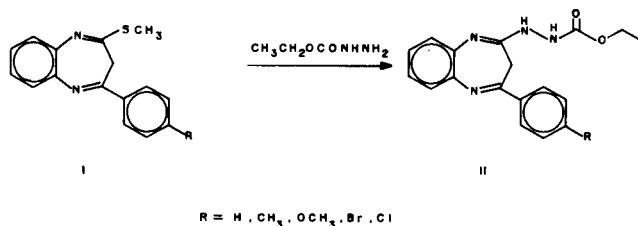
Scheme 1



Our key intermediates, **I**, were prepared similarly to literature methods [7]. The reaction of 2-methylthio-4-(*p*-R-phenyl)-3*H*-1,5-benzodiazepines **I** with ethyl carbazate in refluxing ethanol afforded **II** (Scheme 2). Spectroscopic evidence was consistent with the structure of **II**. In the infrared spectra the appearance of absorption bands at 3350 and 1710  $\text{cm}^{-1}$  [8] indicated the incorporation of an ethyl carbazate group into the 1,5-benzodiazepine framework. It was also confirmed with the <sup>1</sup>H-nmr spectra of **II**

derivatives which showed the characteristic signals for this group, an one-proton singlet at  $\delta$  9.0 (-NH) a quartet at  $\delta$  4.5 ( $J = 7$  Hz) and a triplet at  $\delta$  1.13 ( $J = 7$  Hz) for the methylene and methyl protons of the ethyl moiety.

Scheme 2



On other hand, the tricyclic triazolo-1,5-benzodiazepin-1-one **III** were formed in good yield by heating **II** at 197-207° for 30 minutes (Scheme 3). The infrared spectrum of compounds **III** displayed absorption at 3300 and 1700  $\text{cm}^{-1}$  which were assigned to -NH- and carbonyl moieties of the triazolenone ring. In the <sup>1</sup>H-nmr spectrum of **III** the peak arising from the 2-amide proton appeared as a broad singlet at  $\delta$  11.0-11.5, two doublets at  $\delta$  7.95 ( $J = 8$  Hz, 2H) and  $\delta$  7.3 ( $J = 8$  Hz, 2H), respectively, were assigned to the aromatic protons joined to the 5-(*p*-R-phenyl) moiety whereas a two-proton singlet at  $\delta$  4.1-3.8 was assigned to the methylene protons bonded to C<sub>4</sub> of the triazolo-1,5-benzodiazepin-1-one framework. The remaining aromatic protons in compounds **III** appeared as an unresolved multiplet at  $\delta$  8.4-7.3.

Scheme 3

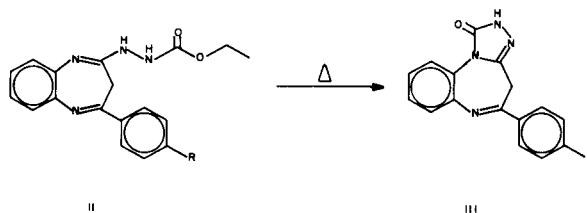


Table 1  
Physical, Analytical and Spectral Data for Compounds II

Compound No.	R	Mp °C	Yield %	Molecular Formula	Analyses %		Spectral Data
					C	H	
a	H	178-180	40	C <sub>18</sub> H <sub>18</sub> N <sub>4</sub> O <sub>2</sub>	67.06 (67.00)	5.63 (5.60)	ir (nujol): 3350, 1710, 1630 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.0 (bs, 1H), 8.0-7.1 (m, 10H), 4.5 (q, J = 7 Hz, 2H), 3.5 (s, 2H), 1.3 (t, J = 7 Hz, 3H)
b	Me	192-194	42	C <sub>19</sub> H <sub>20</sub> N <sub>4</sub> O <sub>2</sub>	67.84 (67.80)	5.99 (5.95)	ir (nujol): 3300, 1711, 1625 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.2 (bs, 1H), 8.05 (d, J = 9 Hz, 2H), 7.65-6.8 (m, 5H) 7.25 (d, J = 9 Hz, 2H), 4.2 (q, J = 7 Hz, 2H), 3.55 (s, 2H), 2.45 (s, 3H), 1.35 (t, J = 7 Hz, 3H)
c	OMe	186-187	48	C <sub>19</sub> H <sub>20</sub> N <sub>4</sub> O <sub>3</sub>	64.75 (64.72)	5.72 (5.70)	ir (nujol): 3320, 1710, 1627 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.0 (bs, 1H) 8.05 (d, J = 9 Hz, 2H), 7.65-6.8 (m, 5H), 6.9 (d, J = 9 Hz, 2H), 4.5 (q, J = 7 Hz, 2H), 3.85 (s, 3H), 3.5 (s, 2H), 1.3 (t, J = 7 Hz, 3H)
d	Br	195-197	50	C <sub>18</sub> H <sub>17</sub> BrN <sub>4</sub> O <sub>2</sub>	53.88 (53.85)	4.27 (4.24)	ir (nujol): 3310, 1712, 1630 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.1 (bs, 1H), 8.0 (d J 9 Hz, 2H), 7.65-6.9 (m, 5H), 7.1 (d, J = 9 Hz, 2H), 4.3 (q, J = 7 Hz, 2H), 3.5 (s, 2H), 1.3 (t, J = 7 Hz, 3H)
e	Cl	193-195	52	C <sub>18</sub> H <sub>17</sub> ClN <sub>4</sub> O <sub>2</sub>	60.59 (60.55)	4.80 (4.76)	ir (nujol): 3315, 1710, 1628 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.0 (bs, 1H), 8.0 (d J 9 Hz, 2H), 7.7-7.0 (m, 5H) 7.2 (d, 9 Hz, 2H), 4.4 (q, J = 7 Hz, 2H), 3.6 (s, 2H), 1.3 (t, J = 7 Hz, 3H)

Table 2  
Physical, Analytical and Spectral Data for Compounds III

Compound No.	R	Mp °C	Yield %	Molecular Formula	Analyses %		Spectral Data
					C	H	
a	H	253-255	74	C <sub>16</sub> H <sub>12</sub> N <sub>4</sub> O	69.55 (69.52)	4.38 (4.35)	ir (nujol): 3250, 1702, 1610 cm <sup>-1</sup> ; <sup>1</sup> H nmr (dimethyl-d <sub>6</sub> sulfoxide): δ 11.0 (bs, 1H), 8.4-7.3 (m, 9H) 4.10 (s, 2H); ms: M <sup>+</sup> at m/z 276
b	Me	280-282	72	C <sub>17</sub> H <sub>14</sub> N <sub>4</sub> O	70.33 (70.30)	4.86 (4.83)	ir (nujol): 3300, 1710, 1600 cm <sup>-1</sup> ; <sup>1</sup> H nmr (dimethyl-d <sub>6</sub> sulfoxide): δ 11.3 (bs, 1H), 8.2-7.3 (m, 4H) 7.95 (d, J = 9 Hz, 2H), 7.3 (d, J = 9 Hz, 2H), 3.9 (s, 2H), 2.4 (s, 3H); ms: M <sup>+</sup> at m/z 290
c	OMe	265-267	71	C <sub>17</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>	66.66 (66.62)	4.60 (4.58)	ir (nujol): 3350, 1703, 1620 cm <sup>-1</sup> ; <sup>1</sup> H nmr (dimethyl-d <sub>6</sub> sulfoxide): δ 11.2 (bs, 1H), 8.0-6.8 (m, 4H), 7.9 (d, J = 9 Hz, 2H), 6.8 (d, J = 9 Hz, 2H), 3.9 (bs, 5H); ms: M <sup>+</sup> at m/z 306
d	Br	298-300	75	C <sub>16</sub> H <sub>11</sub> BrN <sub>4</sub> O	54.10 (54.00)	3.12 (3.10)	ir (nujol): 3250, 1710, 1610 cm <sup>-1</sup> ; <sup>1</sup> H nmr (dimethyl-d <sub>6</sub> sulfoxide): δ 11.0 (bs, 1H), 8.5-7.3 (m, 4H) 8.0 (d, J = 9 Hz, 2H), 7.4 (d, J = 9 Hz, 2H), 4.0 (s, 2H); ms: M <sup>+</sup> at m/z 354
e	Cl	299-301	73	C <sub>16</sub> H <sub>11</sub> ClN <sub>4</sub> O	61.84 (61.81)	3.57 (3.55)	ir (nujol): 3300, 1711, 1620 cm <sup>-1</sup> ; <sup>1</sup> H nmr (dimethyl-d <sub>6</sub> sulfoxide): δ 11.0 (bs, 1H), 8.3-7.2 (m, 4H) 8.0 (d, J = 9 Hz, 2H), 7.1 (d, J = 9 Hz, 2H), 7.1 (d, J = 9 Hz, 2H), 7.1 (d, J = 9 Hz, 2H), 3.9 (s, 2H); ms: M <sup>+</sup> at m/z 310

Table 3  
Physical, Analytical and Spectral Data for Compounds IV

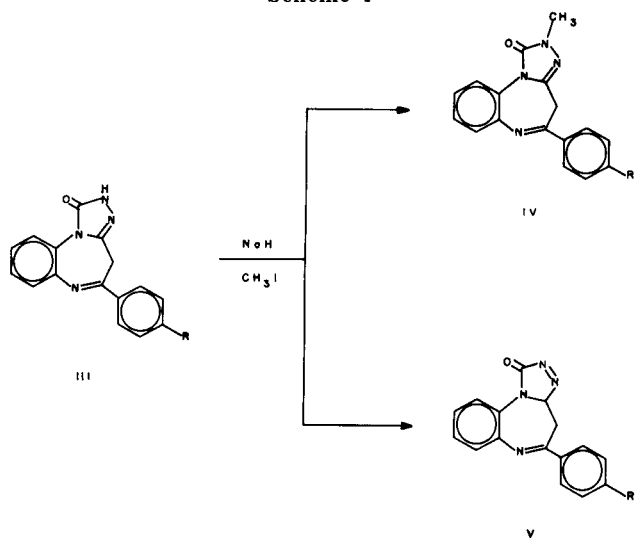
Compound No.	R	Mp °C	Yield %	Molecular Formula	Analyses %		Spectral Data
					C	H	
a	H	150-152	5.0	C <sub>17</sub> H <sub>14</sub> N <sub>4</sub> O	70.33 (70.30)	4.86 (4.80)	ir (chloroform): 1710, 1600 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 8.9 (bd, J = 8 Hz, 1H) 8.1-7.3 (m, 8H) 3.9 (s, 2H) 8.45 (s, 3H); ms: M <sup>+</sup> at m/z 290
b	Me	170-172	4.0	C <sub>18</sub> H <sub>16</sub> N <sub>4</sub> O	71.03 (69.96)	5.30 (5.23)	ir (chloroform): 1710, 1605 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.0 (bd, J = 8 Hz, 1H) 8.0 (H, J = 8 Hz, 2H) 7.9-7.2 (m, 3H), 7.0 (d, J = 8 Hz, 2H) 3.9 (s, 2H), 3.15 (s, 3H), 2.4 (s, 3H); ms: M <sup>+</sup> at m/z 304
c	OMe	154-156	9.0	C <sub>18</sub> H <sub>16</sub> N <sub>4</sub> O <sub>2</sub>	67.48 (67.40)	5.04 (4.97)	ir (chloroform): 1712, 1600 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 8.9 (bd, J = 8 Hz, 1H) 8.1 (d, J = 8 Hz, 2H), 8.0-7.25 (m, 3H), 6.95 (d, J = 8 Hz, 2H), 3.9 (bs, 5H), 3.45 (s, 3H); ms: M <sup>+</sup> at m/z 320
d	Br	148-150	4.0	C <sub>17</sub> H <sub>13</sub> BrN <sub>4</sub> O	55.30 (55.20)	3.55 (3.50)	ir (chloroform): 1710, 1600 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 9.0 (bd, J = 8 Hz, 1H) 8.1 (d, J = 8 Hz, 2H), 7.9-7.3 (M, 3H), 7.4 (d, J = 8 Hz, 2H), 3.95 (S, 2H), 3.5 (s, 3H); ms: M <sup>+</sup> at m/z 368
e	Cl	143-145	7.0	C <sub>17</sub> H <sub>13</sub> ClN <sub>4</sub> O	62.87 (62.84)	4.03 (4.00)	ir (chloroform): 1711, 1610 cm <sup>-1</sup> ; <sup>1</sup> H nmr (deuteriochloroform): δ 8.9 (bd, J = 8 Hz, 1H) 8.0 (d, J = 8 Hz, 2H), 7.9-7.3 (m, 3H), 7.0 (d, J = 8 Hz, 2H), 3.9 (s, 2H), 3.45 (s, 3H); ms: M <sup>+</sup> at m/z 324

Table 4  
Physical, Analytical and Spectral Data for Compounds V

Compound No.	R	Mp °C	Yield %	Molecular Formula	Analyses %		Spectral Data
					C	H	
a	H	159-160	4.0	C <sub>16</sub> H <sub>12</sub> N <sub>4</sub>	69.55 (69.50)	4.38 (4.35)	ir (chloroform): 1712 cm <sup>-1</sup> ; ms: M <sup>+</sup> at m/z 276 (100%), m/z 220 [M-56] <sup>+</sup> , (16%)
b	Me	171-172	3.5	C <sub>17</sub> H <sub>14</sub> N <sub>4</sub> O	70.33 (70.30)	4.86 (4.82)	ir (chloroform): 1712 cm <sup>-1</sup> ; ms: M <sup>+</sup> at m/z 290 (100%), m/z 250 [M-56] <sup>+</sup> , (17%)
c	OMe	188-190	3.0	C <sub>17</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>	66.66 (66.63)	4.60 (4.59)	ir (chloroform): 1710 cm <sup>-1</sup> ; ms: M <sup>+</sup> at m/z 306 (100%), m/z 250 [M-56] <sup>+</sup> , (18%)
d	Br	219-221	7.0	C <sub>16</sub> H <sub>11</sub> BrN <sub>4</sub> O	54.10 (54.00)	3.12 (3.08)	ir (chloroform): 1712 cm <sup>-1</sup> ; ms: M <sup>+</sup> at m/z 354 (100%), m/z 298 [M-56] <sup>+</sup> , (23%)
e	Cl	224-226	6.0	C <sub>16</sub> H <sub>11</sub> ClN <sub>4</sub> O	61.84 (61.80)	3.57 (3.55)	ir (chloroform): 1710 cm <sup>-1</sup> ; ms: M <sup>+</sup> at m/z 310 (100%), m/z 254 [M-56] <sup>+</sup> , (21%)

When triazolo-1,5-benzodiazepin-1-ones **III** were treated with sodium hydride and methyl iodide in refluxing benzene a mixture of compounds was obtained. From this mixture we could separate, by thin layer chromatography, two minor components **IV** and **V** (Scheme 4). Structural of these compounds rest on analytical and spectroscopic evidence (Tables 3 and 4).

Scheme 4

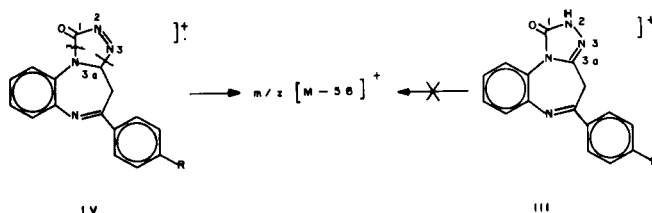


In the infrared spectra of compound **IV** a characteristic band for the triazolone group [8] was present (1712 cm<sup>-1</sup>) together with a band at 1600 assignable to the C=N group. In the <sup>1</sup>H nmr spectra of derivatives **IV** the presence of a three proton singlet at δ 3.5 indicated the incorporation of a methyl group at 2-nitrogen; a downfield one-proton doublet of doublets at δ 8.9-8.7 (*J* = 8 Hz, 1 Hz) was assigned to the methine proton bonded to C<sub>10</sub>. Two doublets at δ 8.1-8.3 (*J* = 8 Hz) and δ 6.9-7.2 (*J* = 8 Hz) respectively were assigned to the aromatic protons bonded to the 5-(*p*-R-phenyl) moiety whereas a two proton singlet at δ 3.8-4.0 was assigned to the methylene protons attached to C<sub>4</sub>.

On other hand, compounds **V** showed the same molecular ions in their mass spectra as compounds **III** (Tables 2 and 4) although their melting points are different, indicating that both of them are structural isomers. The appearance of an carbonyl absorption band at 1700 cm<sup>-1</sup> and the absence of an -NH- band at 3250-3350 cm<sup>-1</sup> in the infra-red spectra for **V** was consistent with the above assertion. Further evidence concerning the structure of the triazolobenzodiazepinones **V** has been derivated from their mass spectral data. While compounds **V** yield an intense ion at m/z [M-56]<sup>+</sup>, (23-16% relative intensity); the mass spectra of the compounds **III** were lacking this ion completely. The existence of a double bond between N(2) and N(3) in compounds **Va-e** could explained the high relative abundance of the ion at m/z [M-56]<sup>+</sup> since the rupture of the C(3a)-N(3) bond is an easy matter (Scheme 5). Contrary to this fact, compounds **IIIa-e** the presence of a double bond between C(3a) and N(3) hindered this rupture.

Further investigation of the products on the reaction of **III** compounds with methyl iodide in sodium hydride are presently being carried out.

Scheme 5



## EXPERIMENTAL

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

mass spectrometer.

Compounds **Ia-e** have been prepared following reported procedures [7]. The structures of compounds **Ia-e** were supported by ir and mass spectral data which are similar to those reported [9].

Compounds **IIa-e** have been prepared from the appropriate 2-thiomethyl-4-(*p*-R-phenyl)-3*H*-1,5-benzodiazepines, **I**, by treatment with ethyl carbazate [8]. The physical, analytical and spectra data for the synthesized compounds **IIa-e** are recorded in Table 1.

The compounds **IIIa-e** have been prepared following reported procedures [8]. The structures of compound **IIIa-e** were supported by ir, <sup>1</sup>H nmr and mass spectral data which appeared in Table 2.

Reaction of 2,4-Dihydro-5-(*p*-R-phenyl)-1*H*-s-triazolo[4,3-*a*]-[1,5]benzodiazepin-1-ones, **IIIa-e**, with methyl Iodide (Scheme 4).

Synthesis of 4*H*-2-Methyl-5-(*p*-R-phenyl)-1*H*-s-triazolo[4,3-*a*][1,5]benzodiazepin-1-ones, **IVa-e**, and 3*a*,4-Dihydro-5-(*p*-R-phenyl)-1*H*-s-triazolo[4,3-*a*][1,5]benzodiazepin-1-ones, **Va-e**.

#### General Procedure.

A mixture of **III a** (0.276 g, 1 mmole) and sodium hydride (50%, 0.048 g, 1 mmole) in dry dimethylformamide (15 ml) was stirred under ice cooling for 10 minutes; then a solution of methyl iodide (0.142 g, 1 mmole) in dry dimethylformamide (2 ml) was added and the mixture stirred for 3 hours. the resulting

suspension was diluted with ethylene chloride (30 ml) and washed with water (5 x 10 ml), dried over anhydrous sodium sulfate and concentrated (rotary evaporator) to afford a yellow oil. Silica tlc showed the presence of several compounds. Separation of compounds **IVa** and **Va** was achieved by preparative silica tlc (benzene/ethyl acetate, 60:40); **IVa** (yield-5%) mp 150-152°; **Va** (yield-4%) mp 159-160°. The physical, analytical and spectral data for compounds **IVa-e** and **Va-e**, are recorded in Tables 3 and 4, respectively.

#### REFERENCES AND NOTES

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