Tricyclic Heteroaromatic Systems. 5*H*-1,2,3-Triazolo[5,1-*c*] [1,4]benzodiazepine

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The synthesis of the new tricyclic system 5*H*-1,2,3-triazolo[5,1-*c*] [1,4]benzodiazepine, diaza-analogue of 5*H*-pyrrolo[2,1-*c*] [1,4]benzodiazepine, which is the common feature of some antitumor antibiotics, is reported. The structure of the new tricyclic system and of some of its key intermediates is assigned by means of a ^{13}C nmr study.

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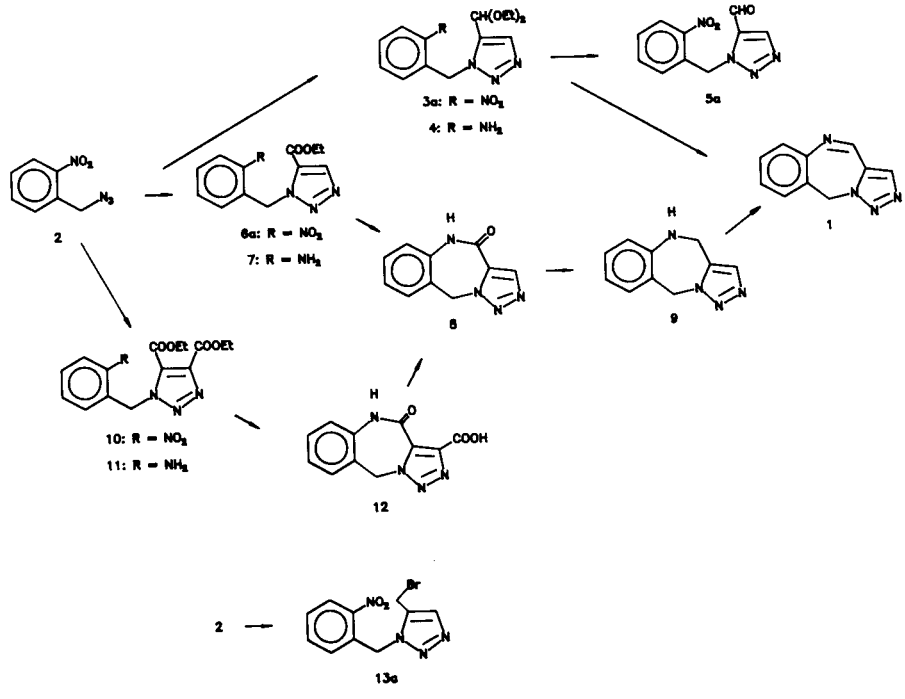
In recent years some researches in our laboratory have been directed toward the synthesis of potential antitumor agents containing a six-seven-five tricylic ring system [1-5], which are structurally related to the antitumor antibiotics anthramycin, tomaymycin and sibiromycin, whose common feature is the 5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine moiety.

Our continuing interest in the search for new antitumor drugs ensued from the hope that chemical modifications of the natural antibiotics would produce substances of biological interest; this now led us to the synthesis of another tricyclic system, namely the 5*H*-1,2,3-triazolo[5,1-*c*][1,4]benzodiazepine **1**, which can be considered a diaza-analogue of the 5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine.

The synthesis of the new tricyclic ring system **1** could be achieved by following one of the three 1,3-dipolar cycloaddition of acetylene derivatives to 2-nitrobenzylazide **2** [6], as outlined in Scheme 1.

The synthetic pathway with fewer steps is that allowing **2** to react with propiolaldehyde diethylacetal. In compliance with the literature, this unsymmetrical acetylene compound gave rise to the two isomeric triazoles **3a-b**, which were separated by column chromatography. The structures of the 1,5-isomer **3a** and that of the 1,4-**3b** were attributed by means of a ^{13}C nmr study (see ahead). To our great surprise, the ratio of the two isomeric products was in disagreement with the literature data. It is in fact reported that addition of azides to unsymmetrical acetylenes tends mainly to give the isomer with the electron-withdrawing or very bulky group at the 4-position [7-8]. In fact Sheehan and Robinson [9], using the same 1,3-dipolarophile and phenylazide, obtained 52% of 1,4-isomer and 23% of 1,5-isomer. In our hands the main product of the reaction was the 5-carbaldehyde diethylacetal **3a** (40% yield) while the less hindered 4-isomer **3b** was recovered with only 23% yield. Compound **3b** was



discarded while the catalytic reduction of **3a** gave the 1-(2-aminobenzyl) derivative **4**, which, heated for a few minutes at 180°, cyclized to give the 5*H*-1,2,3-triazolo-[5,1-*c*][1,4]benzodiazepine **1**.

Compounds **3a-b** was also hydrolyzed to the corresponding carbaldehyde derivatives **5a-b**. However numerous trials to reduce the nitro group of **5a** were unsuccessful since the starting nitro derivative was always recovered unchanged.

Thus with reaction of few steps the fundamental new tricyclic ring system **1** was prepared.

We were however intrigued by the reversed ratio of the two isomeric products **3a** and **3b**, and we thus allowed **2** to react with ethyl propiolate.

In this case the main product of the reaction, in agreement with the literature data, was the less hindered 4-isomer **6b**. However in the cycloaddition of phenylazide and methyl propiolate, in which the 1,4-disubstituted-1,2,3-triazolo was the major product, the isomer ratio was 7:1 [10], while in our case the 4-isomer **6b** and 5-isomer **6a** ratio was 3:1.

This finding and the reversed isomer distribution of the diacetal derivatives suggest that the presence of the 2-nitro group influences the mode of cycloaddition. In fact in the case of the weak electron-withdrawing diethylacetal the isomer distribution is completely reversed with respect to the reported one, while in the case of the strong electron-withdrawing carboxylate group the ratio is not so strongly in favour of the 1,4-isomer. This is in agreement with the literature data [11] in which it is reported that the ratio of 1,4- and 1,5-isomer ensuing from the cycloaddition of 4-nitrobenzylazide to ethyl propiolate was 7:3.

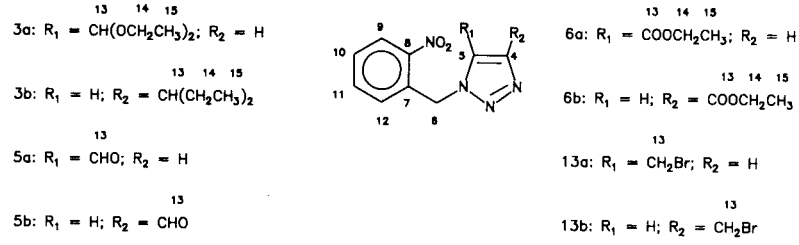
Since the total yield of the reaction between **2** and ethyl propiolate was good (over 90%) we were able to carry on the reaction to the tricyclic compound **1**. Thus compound **6b** was discarded, while **6a** was reduced to the 2-aminobenzyl derivative **7** which was cyclized to the lactam **8**. Lithium aluminium hydride in boiling tetrahydrofuran effected the reduction of the lactam **8** to the secondary amine **9** which was dehydrogenated to yield the target compound **1**.

At last, to further test the influence of the nitro group on the cycloaddition regiochemical mode, we allowed **2** to react with propargyl bromide. It is reported [12] that the latter dipolarophile reacted with benzyl azide with very poor yield to give only the 4-isomer. In our hands, from the reaction of 2-nitrobenzylazide **2** and the weaker dipolarophile propargyl bromide we recovered the 4-isomer **13b** (21% yield) and even a small amount (5%) of 5-isomer **13a**. This finding confirms that the ortho nitro group of benzylazide influences the regiochemical mode of cycloaddition. Of course, the small amount of **13a** and the poor total yield of the reaction deterred us from going on with this synthetic pathway.

The question of the regiochemistry of the cycloaddition was simply avoided by allowing **2** to react with diethyl acetylenedicarboxylate. The resulting adduct **10** was

Table 1

^{13}C Chemical Shift Assignments (ppm)



No.	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	Coupling Constant (Hz)
3a	133.18	135.25	48.97	131.40	146.90	124.51	128.32	133.41	128.32	94.31	61.64	14.20	$^1J_{C_4H_4}$ = 195.3
3b	147.42	122.84	50.46	130.29	147.28	125.02	129.37	134.03	130.14	96.49	61.42	14.85	$^1J_{C_5H_5}$ = 195.3
5a	140.64	133.64	50.77	130.17	147.50	125.08	128.44	133.80	129.04	178.08			$^1J_{C_4H_4}$ = 196.2
5b	147.81	126.10	51.16	129.00	147.81	125.53	130.24	134.37	131.15	184.64			$^1J_{C_5H_5}$ = 193.3
6a	137.64	130.85	50.27	128.25	147.12	124.74	127.97	133.64	128.59	157.52	61.60	13.50	$^1J_{C_4H_4}$ = 197.2
6b	140.29	128.25	50.84	129.44	147.31	125.20	129.80	134.20	130.60	160.22	61.01	13.97	$^1J_{C_5H_5}$ = 198.0
13a	134.10	133.59	48.80	130.10	147.12	125.30	129.28	134.10	129.28	16.22			$^1J_{C_4H_4}$ = 194.0
13b	144.79	123.68	50.66	129.95	147.29	125.13	129.59	134.16	130.41	21.24			$^1J_{C_5H_5}$ = 195.0

reduced to **11** which was cyclized to the acid **12**. The acid function was removed by thermal decarboxylation to give the lactam **8** which was worked up as previously described to the target compound **1**.

Even if the use of diethyl acetylenedicarboxylate produces a single adduct, this synthetic route leading to **1** takes more steps than the one in which propiolaldehyde diethylacetal is used as 1,3-dipolarophile.

^{13}C Nuclear Magnetic Resonance Study.

In view of the fact that in the ^{1}H-nmr spectra the chemical shifts of the H-4 and H-5 of 1,5- and 1,4-disubstituted triazoles are quite similar (see Experimental), the structures of the regioisomers were attributed by means of a ^{13}C-nmr study.

The ^{13}C chemical shift assignments of the adducts **3a-b**, **5a-b**, **6a-b** and **13a-b** are listed in Table 1. An arbitrary numbering is used to identify all carbon atoms. The assignments are established as follows: first of all, the triazole CH must be distinguished from the phenyl ones. That can be accomplished by means of the triazole CH geminal coupling constant which, having a stronger "s" nature than those of the phenyl CH's (larger than 190 Hz), is easily identified.

The position of the triazole CH in the heterocyclic ring is given by the chemical shift value of its carbon atom. In fact, it is well known [13-14] that in 1-substituted triazoles the C-4 is more deshielded than the C-5. Thus whether the triazole CH is at the 4- or 5-position is easily observed.

The steric compression due to the presence of a substituent in the 5-position of the triazole moiety on the adjacent benzyl carbon atom (C-6) should be noted. It is evident that, since this steric compression is mediated by the electronic clouds of the protons, the C-6 of compounds **3a** and **13a** is more shielded than that of the other two 5-isomers **5a** and **6a**.

The steric compression due to the presence of the 5-substituent is present even in the phenyl carbon atoms, which appear on the whole more shielded than those of the corresponding 4-isomers.

The ^{13}C chemical shifts of the new tricyclic compound **1** is also reported in the Experimental.

EXPERIMENTAL

All melting points were determined on a Gallenkamp capillary melting point apparatus.

The ^{1}H-nmr spectra were recorded with a Varian EM-360 instrument, chemical shifts are reported in δ (ppm) downfield from internal tetramethylsilane (TMS).

The natural abundance ^{13}C nmr spectra were run on a Varian FT-80A spectrometer at 20 MHz in the Fourier transform mode. All samples were recorded in 10 mm o.d. tubes at probe temperature (35°) with concentrations of approximately 10% (w/v) in deuteriochloroform, which provided the deuterium signal for the field frequency lock. Chemical shifts were measured relative to the central peak of the solvent (deuteriochloroform = 76.9 ppm) and corrected to internal TMS. Typical acquisition parameters included: a spectral width of 5000 Hz, a flip angle of 42° and an interpulse delay between acquisitions of 510 μ seconds. Chemical shift values were reproducible to better than ± 0.05 ppm. The decoupled spectra were obtained without pulse delay and with a digitation of 2 points per cycle. The coupled spectra with nuclear Overhauser effect (nOe) were obtained by putting the decoupler on during a pulse delay of 2 seconds and off during an acquisition time of 1 second. The digitization of the coupled spectra was 2 points per cycle.

Silica gel plates (Merck F_{254}) and silica gel 60 (Merck, 70-230 mesh) were used for analytical and column chromatography.

1-(2-Nitrobenzyl)-1,2,3-triazole-5-carbaldehyde Diethylacetal (**3a**) and 1-(2-Nitrobenzyl)-1,2,3-triazole-4-carbaldehyde Diethyl acetal (**3b**).

To a solution of 2-nitrobenzylazide **2** [6] (2.4 g, 13.4 mmoles) in benzene (15 ml) propiolaldehyde diethylacetal (97%, 1.8 ml, 13.4 mmoles) was added. The mixture was refluxed for 30 hours. Evaporation of the solvent afforded an oil (3.52 g) which was chromatographed on a silica gel column (eluting system chloroform/ethylacetate, 8:2).

Compound **3a**.

Evaporation of the central eluates yielded an oil (1.6 g, 40% yield); ^{1}H-nmr (deuteriochloroform): 8.3-8.0 (m, 1H, benzene proton), 7.78 (s, 1H, H-4), 7.7-7.3 (m, 2H, benzene protons), 7.0-6.7 (m, 1H, benzene proton), 6.11 (s, 2H, benzyl protons), 5.59 (s, 1H, acetal proton), 3.8-3.1 (m, 4H, $2CH_2$), 1.06 (t, 6H, $2CH_3$).

Compound **3b**.

Evaporation of the last eluates afforded a solid residue which was recrystallized from cyclohexane, mp 93-96°, 0.9 g, 23% yield; ^{1}H-nmr (deuteriochloroform): 8.3-8.1 (m, 1H, benzene proton), 7.76 (s, 1H, H-5), 7.7-7.0 (m, 3H, benzene protons), 5.98 (s, 2H, benzyl protons), 5.78 (s, 1H, acetal proton), 3.71 (q, 4H, $2CH_2$), 1.23 (t, 6H, $2CH_3$).

Anal. Calcd. for $C_{14}H_{18}N_4O_4$ (306.36): C, 54.88; H, 5.93; N, 18.29. Found: C, 54.54; H, 5.87; N, 18.35.

1-(2-Nitrobenzyl)-1,2,3-triazole-5-carbaldehyde (**5a**) and 1-(2-Nitrobenzyl)-1,2,3-triazole-4-carbaldehyde (**5b**).

A suspension of **3a** or **3b** (1 g, 3.3 mmoles) in the minimum amount of aqueous ethanol (1:1) was acidified with 6 *M* hydrochloric acid and then refluxed for 30 minutes.

Coumpound **5a**.

Precipitated after the evaporation of the ethanol at reduced pressure. It was recrystallized from water to give colorless crystals, mp 105-108°, 79% yield; ^{1}H-nmr (deuteriochloroform): 10.01 (s, 1H, aldehyde proton), 8.37 (s, 1H, H-4), 8.3-8.0 (m, 1H, benzene proton), 7.7-7.3 (m, 2H, benzene protons), 7.0-6.6 (m, 1H, benzene proton), 6.32 (s, 2H, CH_2 benzyl).

Anal. Calcd. for $C_{10}H_8N_4O_3$ (232.22): C, 51.72; H, 3.48; N, 24.13. Found: C, 51.65; H, 3.37; N, 24.27.

Compound **5b**.

Precipitated after cooling the aqueous ethanolic solution. It was recrystallized from chloroform, mp 151-154°, 53% yield; ^{1}H-nmr (deuteriochloroform): 10.20 (s, 1H, aldehyde proton), 8.4-8.1 (m,

2H, 1 benzene proton + H-5), 7.8-7.3 (m, 3H, benzene protons), 6.02 (s, 2H, CH_2 benzyl). Found: C, 51.59; H, 3.45; N, 24.27.

5H-1,2,3-Triazolo[5,1-c][1,4]benzodiazepine (1)

Method A.

To a solution of **3a** (1.1 g, 3.6 mmoles) in ethyl acetate (100 ml) palladium on barium sulfate (10%, 250 mg) was added. The mixture was hydrogenated in a Parr apparatus at 35 psi for 24 hours. Removal of the catalyst and evaporation of the solvent afforded a yellow oil (0.7 g, 70% yield) which was the 1-(2-aminobenzyl)-1,2,3-triazole-5-carbaldehyde diethylacetal (**4**); ^{1}H-nmr (deuteriochloroform): 7.70 (s, 1H, H-4), 7.4-6.5 (m, 4H, benzene protons), 5.62 (s, 1H, diacetal proton), 5.55 (s, 2H, benzyl protons), 4.3 (br s, 2H, NH_2), 3.55 (q, 4H, $2CH_2$), 1.22 (t, 6H, $2CH_3$). Compound **4** was heated in an open tube at 180° for 5 minutes under a nitrogen flow to allow the escape of the evolving ethanol. The crude residue was taken up with hot cyclohexane and chromatographed on a silica gel column (eluting system cyclohexane/ethyl acetate, 3:7). Evaporation of the central eluates afforded a yellow oil which by recrystallization from cyclohexane yielded yellow crystals, 36% yield.

Method B.

A mixture of **9** (0.08 g, 0.43 mmoles) and Pd/C (10%, 300 mg) was heated at 170° at reduced pressure (0.1 mm Hg) for 5 hours. The residue was taken up with chloroform. The catalyst was filtered off and the solvent evaporated at reduced pressure. The residue was recrystallized from cyclohexane, 25% yield, mp 145-148°; ^{1}H-nmr (deuteriochloroform): 8.68 (s, 1H, H-11), 7.93 (s, 1H, H-1), 7.7-7.2 (m, 4H, benzene protons), 5.52 (s, 2H, H-5); ^{13}C-nmr (deuteriochloroform): 146.13 (C-9a), 145.01 (C-11, $^1J_{C11H11}$ = 186.2 Hz), 134.20 (C-1, $^1J_{C1H1}$ = 195.0 Hz), 130.85 (C-11a), 129.62 (C-7), 128.98 (C-6), 128.78 (C-8), 128.49 (C-9), 125.50 (C-5a), 51.87 (C-5).

Anal. Calcd. for $C_{10}H_8N_4$ (184.22): C, 65.19; H, 4.39; N, 30.42. Found: C, 65.00; H, 4.31; N, 30.53.

Ethyl 1-(2-Nitrobenzyl)-1,2,3-triazole-5-carboxylate (**6a**) and Ethyl 1-(2-Nitrobenzyl)-1,2,3-triazole-4-carboxylate (**6b**).

To a solution of **2** (9.6 g, 5.4 mmoles) in benzene (100 ml) ethyl propiolate (8 ml, 79 mmoles) was added. The mixture was refluxed for 24 hours. Upon cooling the triazole-4-carboxylate **6b** (9.43 g) precipitated. However the presence of compound **6b** in the mother liquor was detected by tlc. Thus the solvent was evaporated at reduced pressure and the residue was chromatographed on a silica gel column (eluting system cyclohexane/ethyl acetate, 1:1).

Compounds **6a**.

Evaporation of the central eluates afforded an oil, which by recrystallization from ethanol/water gave yellow crystals, mp 73-75°, 24% yield; ^{1}H-nmr (deuteriochloroform): 8.3-8.0 (m, 2H, benzene proton + H-4), 7.7-7.4 (m, 2H, benzene protons), 6.9-6.6 (m, 1H, benzene proton), 6.32 (s, 2H, benzyl protons), 4.29 (q, 2H, CH_2), 1.25 (t, 3H, CH_3).

Anal. Calcd. for $C_{12}H_{12}N_4O_4$ (276.28): C, 52.16; H, 4.39; N, 20.28. Found: C, 52.34; H, 4.48; N, 20.51.

Compound **6b**.

Evaporation of the last eluates afforded a second crop of compound **6b**. Recrystallization from ethanol/water gave yellow crystals, mp 142-143°, 68% total yield; ^{1}H-nmr (deuteriochloroform): 8.32 (s, 1H, H-5), 8.3-8.1 (m, 1H, benzene proton), 7.8-7.5 (m, 2H, benzene protons), 7.4-7.1 (m, 1H, benzene proton), 6.01 (s, 2H, benzyl protons), 4.42 (q, 2H, CH_2), 1.39 (t, 3H, CH_3).

Anal. Calcd. for $C_{12}H_{12}N_4O_4$ (276.28): C, 52.16; H, 4.39; N, 20.28. Found: C, 52.31; H, 4.26; N, 20.48.

10,11-Dihydro-5*H*-1,2,3-triazolo[5,1-c][1,4]benzodiazepin-11-one (**8**).

Method A.

To a solution of **6a** (2.3 g, 8.3 mmoles) in ethyl acetate (50 ml) palladium on barium sulfate (10%, 230 mg) was added. The mixture was hydrogenated at atmospheric pressure for 12 hours. Removal of the catalyst and evaporation of the solvent afforded a yellow oil which was the ethyl 1-(2-aminobenzyl)-1,2,3-triazole-5-carboxylate **7**, 1.1 g, 54% yield; ^{1}H-nmr (deuteriochloroform): 8.10 (s, 1H, H-4), 7.7-6.5 (m, 4H, benzene protons), 5.87 (s, 2H, benzyl protons), 4.42 (q, 2H, CH_2), 1.39 (t, 3H, CH_3).

A mixture of the 2-amino derivative **7** (1.13 g, 4.59 mmoles), anhydrous *N,N*-dimethylformamide (10 ml) and sodium hydride (80%, 0.3 g) was stirred at room temperature overnight. Ice and norite were then added to the mixture which was heated and filtered. Upon cooling a precipitate was formed which was collected and recrystallized from ethanol/water, 46% yield.

Method B.

A solution of the acid **12** (2.2 g, 9 mmoles) in N,N-dimethylformamide (12 ml) was refluxed for 1 hour. Water was added to the cooled solution until a white precipitate was obtained. The crude title compound was recrystallized from ethanol/water, 95% yield, mp 255-257°; ^{1}H nmr (dimethylsulfoxide-d_6): 10.9 (br s, 1H, NH), 8.32 (s, 1H, H-1), 7.9-7.0 (m, 4H, benzene protons), 5.87 (s, 2H, H-5).

Anal. Calcd. for $C_{10}H_8N_4O$ (200.22): C, 59.98; H, 4.04; N, 27.99. Found C, 60.12; H, 4.13; N, 28.15.

10,11-Dihydro-5*H*-1,2,3-triazolo[5,1-c][1,4]benzodiazepine (**9**).

A solution of **8** (1 g, 5 mmoles) and lithium aluminium hydride (1.5 g, 40 mmoles) in freshly distilled tetrahydrofuran (60 ml) was refluxed for 12 hours. Ice was added to the cooled solution which was then filtered and extracted with ethyl acetate. The organic solvent was evaporated at reduced pressure and the residue was purified through a silica gel column (eluting system cyclohexane/ethyl acetate, 1:9). Evaporation of the central eluates gave white crystals, mp 143-145°, 26% yield; ^{1}H-nmr (deuteriochloroform): 7.51 (s, 1H, H-1), 7.4-6.6 (m, 4H, benzene protons), 5.68 (s, 2H, H-5), 4.56 (s, 2H, H-11), 4.1 (br s, 1H, NH).

Anal. Calcd. for $C_{10}H_{10}N_4$ (186.24): C, 64.49; H, 5.42; N, 30.09. Found: C, 64.61; H, 5.31; N, 29.99.

Diethyl 1-(2-Nitrobenzyl)-1,2,3-triazole-4,5-dicarboxylate (**10**).

A solution of **2** (18.2 g, 102 mmoles) and diethyl acetylendicarboxylate (21 g, 123 mmoles) in benzene (200 ml) was refluxed for 24 hours. Evaporation of the solvent afforded an oil which when recrystallized from ethanol gave white crystals, mp 50-61°, 65% yield; ^{1}H-nmr (deuteriochloroform): 8.3-8.0 (m, 1H, benzene proton), 7.8-7.3 (m, 2H, benzene protons), 7.1-6.8 (m, 1H, benzene proton), 6.27 (s, 2H, benzyl protons), 4.7-4.1 (m, 4H, $2CH_2$), 1.6-0.9 (m, 6H, $2CH_3$).

Anal. Calcd. for $C_{15}H_{16}N_4O_6$ (348.35): C, 51.72; H, 4.64; N, 16.09. Found: C, 51.56; H, 4.51; N, 16.31.

10,11-Dihydro-5*H*-1,2,3-triazolo[5,1-*c*][1,4]benzodiazepine-1-carboxylic Acid (**12**).

To a solution of **10** (2 g, 5.7 mmoles) in ethyl acetate (200 ml) palladium on barium sulfate (10%, 200 mg) was added. The mixture was hydrogenated at atmospheric pressure for 4 hours. Removal of the catalyst and evaporation of the solvent afforded the diethyl 1-(2-aminobenzyl)-1,2,3-triazolo-4,5-dicarboxylate (**11**) which was purified through a silica gel column (eluting system chloroform/methanol, 9:1). 1.5 g, 83% yield; ^{1}H-nmr (deuteriochloroform): 7.4-6.5 (m, 4H, benzene protons), 5.71 (s, 2H, benzyl protons), 4.7-4.1 (m, 6H, $2CH_2$ + NH_2), 1.6-1.1 (m, 6H, $2CH_3$).

A solution of the 2-aminobenzyl derivative **11** (1.4 g, 4.4 mmoles) and sodium hydride (80%, 0.25 g) in anhydrous *N,N*-dimethylformamide (16 ml) was stirred overnight. The mixture was treated with ice until complete precipitation of the sodium salt took place. The latter was collected by suction, washed with acetone and diethyl ether and then dissolved in water. The solution was acidified with 6 *M* hydrochloric acid. The resulting precipitate was collected and recrystallized from *N,N*-dimethylformamide/water, mp 232° dec, 64% yield; ^{1}H-nmr (dimethylsulfoxide-d_6): 11.3 (br s, 1H, COOH), 7.8-7.0 (m, 5H, 4 benzene protons + NH), 5.88 (s, 2H, H-5).

Anal. Calcd. for $C_{11}H_8N_4O_3$ (244.23): C, 54.09; H, 3.31; N, 22.95. Found: C, 53.84; H, 3.17; N, 23.07.

1-(2-Nitrobenzyl)-5-bromomethyl-1,2,3-triazole (**13a**) and 1-(2-Nitrobenzyl)-4-bromomethyl-1,2,3-triazole (**13b**).

To a solution of **2** (3 g, 16.8 mmoles) in benzene (35 ml) propargyl bromide (97%, 2 ml, 21 mmoles) was added. The solution was refluxed for 24 hours. Evaporation of the solvent afforded an oil which, by recrystallization from ethanol, gave 0.72 g of 4-bromomethyl derivative **13b**. However the presence of compound **13b** was again detected by tlc in the ethanol mother liquor. Thus the ethanolic solution was brought to dryness at reduced pressure. The residue was chromatographed on a silica gel column (eluting system cyclohexane/ethyl acetate/benzene, 4:4:2). Evaporation of the central eluates afforded a second crop (0.34 g) of 4-isomer **13b**, mp 109-111°, 21% total yield; ^{1}H-nmr (deuteriochloroform): 8.3-8.1 (m, 1H, benzene proton), 7.81 (s, 1H, H-5), 7.7-7.4 (m, 2H, benzene protons), 7.3-7.0 (m, 1H, benzene proton), 5.96 (s, 2H, benzyl protons), 4.59 (s, 2H, CH_2Br).

Anal. Calcd. for $C_{10}H_9BrN_4O_2$ (297.14): C, 40.42; H, 3.06; N, 18.86. Found: C, 40.13; H, 2.89; N, 18.53.

Evaporation of the last eluates afforded the 5-bromomethyl derivative **13a**, mp 121-124°, 5% yield; ^{1}H-nmr (deuteriochloroform): 8.4-8.0 (m, 1H, benzene proton), 7.80 (s, 1H, H-4), 7.7-7.4 (m, 2H, benzene protons), 7.1-6.7 (m, 1H, benzene proton), 6.05 (s, 2H, benzyl protons), 4.47 (s, 2H, CH_2Br).

Anal. Calcd. for $C_{10}H_9BrN_4O_2$ (297.14): C, 40.42; H, 3.06; N, 18.86. Found: C, 40.21; H, 3.12; N, 19.02.

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