Pyrrolo[1,4]benzodiazepines. IV. Synthesis of *E*- and *Z*-5,11-Dioxo-11a-ethoxycarbonyl-2-ethylidene-1,2,3,10,11,11a-hexahydro-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine

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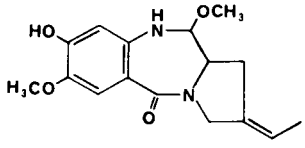
Received January 23, 1989

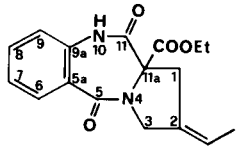
Preparation of the title compound starting from 4-acetyl-2,2-diethoxycarbonyl-2,3-dihydro-1-(2-nitrobenzoyl)-1*H*-pyrrole by selective reduction is described; its *E* and *Z* forms were isolated and their geometrical structure assigned on the basis of ^1H and ^{13}C nmr spectral data.

J. Heterocyclic Chem., **26**, 1023 (1989).

In the course of our studies on 5*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine derivatives we were able to insert the vinylic moiety at the 2 position of the tricyclic system: the key intermediate was 4-acetyl-2,2-diethoxycarbonyl-2,3-dihydro-1-(2-nitrobenzoyl)-1*H*-pyrrole (**3**) (see Scheme 1), as previously reported [1]. In the same work we tried to obtain the corresponding 2-ethylidene derivative, whose structure is more similar to that of the antitumor antibiotic tomaymycin (**1**) [2,3], but our attempts were unsuccessful.



1 Tomaymycin



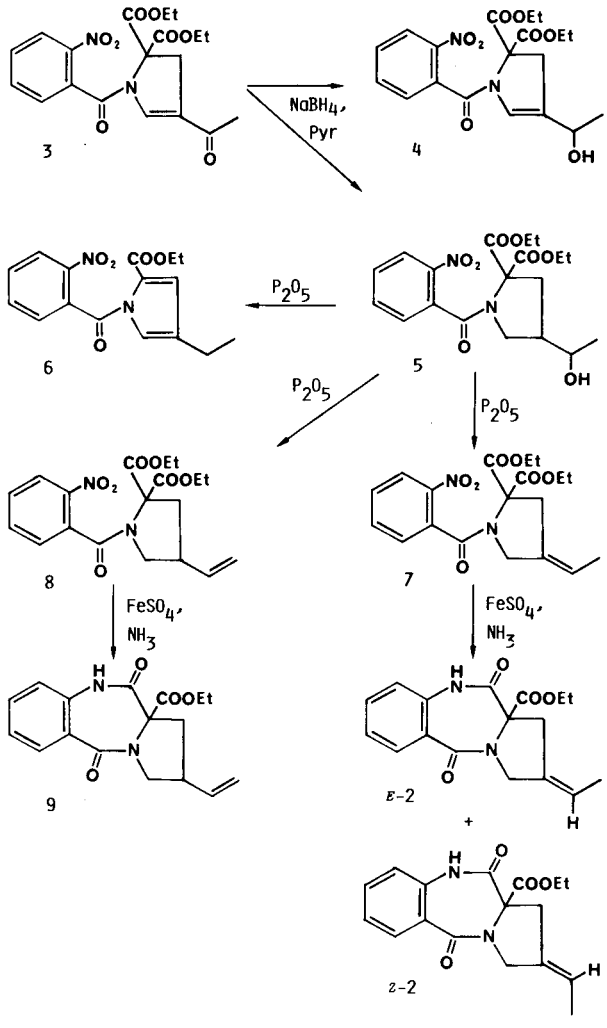
2

In the present paper we wish to report the preparation of the desired compound **2**, namely 5,11-dioxo-11a-ethoxycarbonyl-2-ethylidene-1,2,3,10,11,11a-hexahydro-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine. Also in this case we have used compound **3** as the starting material, but we have followed a different synthetic pathway.

The first step of such new synthetic method (Scheme 1) involves the selective reduction of the conjugated -CH=C-C=O system in order to obtain the 2-hydroxyethylpyrrolidine **5**. In our previous experiments [1] such reduction was accomplished by sodium borohydride, using aqueous tetrahydrofuran as the solvent: only the pyrroline derivative **4** was obtained under such conditions. Now, we have carried out the same reaction using pyridine instead of tetrahydrofuran: a mixture of both reduced products was obtained, but only a small amount of the partially reduced compound **4** was isolated, whereas the required **5** was predominant in the mixture.

The complete reduction of the unsaturated conjugated system of **3** was clearly confirmed by the spectral features of **5** in comparison with those of **3** and **4**, which are reported in detail in the experimental section. In this respect, the following remarks are particularly significant:

Scheme 1



a) as regards ^{13}C nmr spectra, the signal at δ 192.47 due to acetyl CO in the spectrum of **3** disappeared in the spectra of **4** and **5**, whereas a signal at δ 64.41 and 67.97, respectively, appeared, due to the sp^3 carbon atom of the CHOH group; moreover, the signals at δ 127.19 (4-C) and 123.57 (5-CH) in the spectrum of **4** were replaced in the spectrum

of **5** by two signals at δ 44.95 (4-CH) and 51.88 (5-CH_2), respectively, due to the hydrogenation of the pyrroline double bond; b) the ^1H nmr spectrum of **5** was characterized by the presence of two pairs of double doublets due to the methylenic geminal protons in the 3 and 5 positions, which coupled with the proton in the 4 position; moreover, the presence of the OH group was indicated by the broad signal at δ 2.00 exchangeable with deuterium oxide.

Compound **5** was then refluxed in anhydrous benzene in the presence of phosphorus pentoxide: products **6**, **7** and **8** were obtained in the mixture, with approximately 6%, 30% and 20% yield, respectively. The most abundant component was the required ethylidene derivative **7**, whereas the vinyl isomer **8** was formed in a smaller amount; their structures were unequivocally confirmed by spectral data. In particular, compound **8** showed the characteristic system of signals due to the presence of the vinyl moiety, whereas the presence of the ethylidene group at the 2 position of compound **7** was evident, as detailed in the Experimental. It has to be pointed out that many signals appeared doubled in both the ^1H and ^{13}C nmr spectra of **7**, because of the presence of the *E* and *Z* forms in the mixture.

The third minor component of the mixture obtained by dehydration of **5** was **6**: this pyrrole derivative was formed both by dehydration and formate elimination.

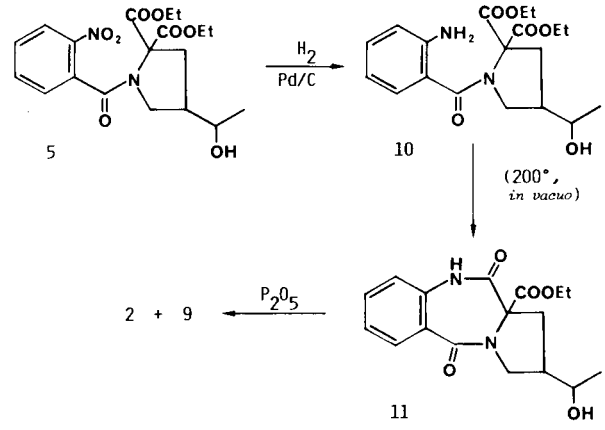
Both **7** and **8** were then cyclized to the corresponding pyrrolobenzodiazepines by treatment with ferrous sulfate in ammonia solution as the reducing agent. In the case of compound **8**, we obtained 5,11-dioxo-11a-ethoxycarbonyl-1,2,3,10,11,11a-hexahydro-2-vinyl-5*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine (**9**), whose proposed structure was in good agreement with spectral data. Also in this case we observed a number of double signals in both ^1H and ^{13}C nmr spectra, due to the presence of two chiral carbon atoms (2 and 11a): consequently, compound **9** is a mixture of two diastereoisomeric racemates (2*R*,11a*R*-2*S*,11a*S*; 2*R*,11a*S*-2*S*,11a*R*).

The reducing treatment of **7** afforded compound **2** as a mixture of two geometrical isomers, which were separated by repeated preparative tlc on silica gel. Both *E* and *Z* forms showed spectral features which were in close agreement with their proposed chemical structure. Particularly, we could distinguish between the two products on the basis of the chemical shift values of 1-CH_2 (δ 37.05 and 41.04) and 3-CH_2 (δ 53.88 and 50.57) in the ^{13}C nmr spectra of the *E* and *Z* isomers, respectively, which displayed the typical differences due to the change of the configuration of the ethylidene function at 2-C [4].

Confirmatory evidence arose from nuclear Overhauser enhancement difference spectral studies (nOeds) performed on the *E* isomer. Irradiation at the frequence of the ethylidene CH_3 (δ 1.72) produced a relevant enhancement of both the signals of 1-CH_2 protons at δ 4.05 (15%) and 2.24 (9%), whereas the signals of 3-CH_2 were almost completely unaffected. On the other hand, the positive effects observed for the signals at δ 4.55 (6%) and 4.39 (16%), by irradiation at δ 5.58, clearly indicated that the vinylic proton is in nOe proximity with those linked to 3-C (no enhancement of 1-CH_2 signals was detected in this experiment).

The availability of the key intermediate **5** allowed us to prepare compound **11** (see Scheme 2), which we had already prepared with a different synthetic method [1]. In the present case, compound **11** was obtained by catalytic hydrogenation of **5** to afford the amino derivative **10** which was then cyclized to **11** by heating at 200° *in vacuo*. In our preceding experiments [1], we were not able to obtain the ethylidene derivative **2** by dehydration of **11**; now, we have repeated such attempts, using phosphorus pentoxide in boiling benzene solution and prolonging the reaction time to many hours. In this manner we have been able to obtain **2**, but in very small amount and in mixture with the vinyl derivative **9**, as clearly indicated by the spectrometric examination of the mixture.

Scheme 2



In conclusion, the synthetic procedure depicted in Scheme 1 remains the only efficient method to obtain an analog of tomaymycin bearing the ethylidene moiety in the 2 position of the tricyclic system.

EXPERIMENTAL

Precoated silica gel Whatman K6F plates were used for thin layer chromatographic controls; detection of components was made by either uv light or treatment with iodine vapors. Chromatographic separations were performed on columns packed with silica gel 60 from Merck (70-230 mesh ASTM). Melting points were determined with a Kofler hot stage microscope and are uncorrected. Elemental analyses were performed on a Perkin-Elmer Elemental Analyzer Model 240. The ^1H and ^{13}C nmr spectra were obtained on a Bruker WM instrument operating at 250.13 and 62.96 MHz for ^1H and ^{13}C observations, respectively, in deuteriochloroform solutions using a 5 mm $^1H/^{13}C$ dual tuned probe. The nOeds experiments were performed with the aid of a

Bruker microprogram on a sample previously degassed by bubbling argon through the solution for 40 minutes.

4-Acetyl-2,2-diethoxycarbonyl-2,3-dihydro-1-(2-nitrobenzoyl)-1*H*-pyrrole (**3**).

This compound was prepared following Massa *et al.* [1]; ^{1}H nmr: δ 8.28 (splitting d, 1H), 7.84 (splitting t, 1H) and 7.72 (m, 2H) (aromatic protons), 6.82 (s, 1H, H-5), 4.38 (q, 4H, two ethyl CH_2), 3.50 (s, 2H, 3-CH_2), 2.15 (s, 3H, $COCH_3$), 1.38 (double t, 6H, two ethyl CH_3); ^{13}C nmr: δ 192.47 (acetyl CO), 166.86 (two carbethoxyl CO), 164.01 (CO-N), 146.00 (C-NO_2), 137.27, 134.52, 131.29 and 129.10 (benzenic CH), 130.00 (benzenic 1-C), 124.87 (5-CH), 122.89 (4-C), 74.00 (2-C), 62.94 (two ethyl CH_2), 39.26 (3-CH_2), 26.28 (acetyl CH_3), 13.87 (two ethyl CH_3).

2,2-Diethoxycarbonyl-2,3-dihydro-4-(1-hydroxyethyl)-1-(2-nitrobenzoyl)-1*H*-pyrrole (**4**).

A solution of 5.7 g (0.014 mole) of **3** in 60 ml of anhydrous pyridine was added with 0.8 g (0.02 mole) of sodium borohydride; the mixture was stirred for 30 minutes at room temperature, then poured into crushed ice and acidified with diluted hydrochloric acid. The acid solution was extracted three times with chloroform; the organic extracts were combined, dried on sodium sulfate, evaporated up to a small volume and then chromatographed on a silica gel column eluting with diethyl ether. Fractions containing compound **4** alone were combined and evaporated *in vacuo* to dryness; the residue was recrystallized from benzene to afford 0.5 g of **4** (yield 8.8%), mp 128-129°; ^{1}H nmr: δ 8.21 (splitting d, 1H), 7.76 (splitting t, 1H) and 7.63 (m, 2H) (aromatic protons), 5.92 (s, 1H, H-5), 4.37* (m, 5H, two ethyl CH_2 and hydroxyethyl CH), 3.32 (s, 2H, 3-CH_2), 1.92 (broad s, 1H, OH; exchanged with deuterium oxide), 1.38* (t, 6H, two ethyl CH_3); 1.27* (d, 3H, hydroxyethyl CH_3), J_{CH,CH_3} = 6 Hz; the asterisked assignments were supported by selective decoupling experiments; ^{13}C nmr: δ 167.71 (two carbethoxyl CO), 162.84 (CO-N), 145.59 (C-NO_2), 134.22, 130.49, 129.14 and 124.57 (benzenic CH), 131.69 (benzenic 1-C), 127.19 (4-C), 123.57 (5-CH), 72.55 (2-C), 64.41 (CH-OH), 62.60 (two ethyl CH_2), 40.22 (3-CH_2), 22.01 (hydroxyethyl CH_3), 13.91 (two ethyl CH_3).

Anal. Calcd. for $C_{19}H_{22}N_2O_8$: C, 56.15; H, 5.46; N, 6.89. Found: C, 56.22; H, 5.50; N, 6.83.

2,2-Diethoxycarbonyl-4-(1-hydroxyethyl)-1-(2-nitrobenzoyl)pyrrolidine (**5**).

A second group of fractions eluted from the above mentioned column afforded 1.4 g (yield 25%) of product **5**, mp 85-87° (from benzene added with a little amount of chloroform); ^{1}H nmr: δ 8.20 (splitting d, 1H), 7.75 (splitting t, 1H) and 7.60 (m, 2H) (aromatic protons), 4.35 (m, 4H, two ethyl CH_2), 3.66* (m, 1H, hydroxyethyl CH), 3.32 (dd, 1H) and 3.15 (dd, 1H) (5-CH_2 geminal protons, J_{gem} = 10 Hz), 2.80 (dd, 1H) and 2.40 (dd, 1H) (3-CH_2 geminal protons, J_{gem} = 11 Hz), 2.28* (m, 1H, H-4), 2.00 (broad s, 1H, OH, exchanged with deuterium oxide), 1.37 and 1.35 (two t, 6H, two ethyl CH_3), 1.08* (d, 3H, hydroxyethyl CH_3, J = 6 Hz), the asterisked assignments were supported by selective decoupling experiments; ^{13}C nmr: δ 168.32 and 168.24 (two carbethoxyl CO), 165.58 (CO-N), 145.13 (C-NO_2), 134.29, 129.92, 128.64 and 124.46 (benzenic CH), 133.23 (benzenic 1-C), 72.44 (2-C), 67.97 (CH-OH), 62.30 (two ethyl CH_2), 51.88 (5-CH_2), 44.95 (4-CH), 37.94 (3-CH_2), 22.22 (hydroxyethyl CH_3), 14.02 and 13.96 (two ethyl CH_3), the proposed assignments were made on the basis of on-resonance and off-resonance values.

Anal. Calcd. for $C_{19}H_{24}N_2O_8$: C, 55.88; H, 5.92; N, 6.86. Found: C, 55.69; H, 5.96; N, 6.93.

2-Ethoxycarbonyl-4-ethyl-1-(2-nitrobenzoyl)-1*H*-pyrrole (**6**).

A solution of 1.1 g (2.7 mmoles) of **5** in anhydrous benzene (40 ml) was refluxed for three hours in the presence of phosphorus pentoxide (1 g). After cooling, the benzene solution was decanted, washed with aqueous sodium hydrogen carbonate, dried on sodium sulfate, concentrated *in vacuo* up to a small volume and then chromatographed on a silica gel column eluting with diethyl ether. A first group of fractions afforded 50 mg of product **6** (yield 5.9%) as a pale yellow oil; ^{1}H nmr: δ 8.13 (splitting d, 1H), 7.67 (m, 2H) and 7.56 (splitting d, 1H) (benzenic protons), 7.06 (s, 1H, H-5), 6.88 (s, 1H, H-3), 4.04 (q, 2H, carbethoxyl CH_2), 2.44 (q, 2H, ethyl CH_2), 1.17 (t, 6H, two CH_3); ^{13}C nmr: δ 163.78 (COO), 160.07 (CO-N), 147.44 (C-NO_2), 133.02, 131.20, 129.63 and 124.44 (benzenic CH), 131.30 (benzenic 1-C), 129.38 and 126.05 (2-C and 4-C), 123.74 (3-CH and 5-CH), 60.69 (carbethoxyl CH_2), 19.52 (ethyl CH_2), 13.95 and 13.90 (two CH_3).

Anal. Calcd. for $C_{16}H_{16}N_2O_5$: C, 60.75; H, 5.10; N, 8.86. Found: C, 60.40; H, 5.25; N, 8.65.

E,Z-2,2-Diethoxycarbonyl-4-ethylidene-1-(2-nitrobenzoyl)pyrrolidine (**7**).

A second group of fractions eluted from the above mentioned column were combined, concentrated up to a small volume and chromatographed on a silica gel/silver nitrate column, eluting first with diethyl ether/*n*-hexane mixture (7:3) and then with diethyl ether alone. This procedure allowed us to separate two products, namely compound **7** (0.30 g, yield 29%) in form of an oil and compound **8** (for the latter compound see the next paragraph). Spectral data for compound **7**: ^{1}H nmr: δ 8.22 (splitting t, 1H), 7.75 (splitting t, 1H) and 7.59 (m, 2H) (benzenic protons), 5.45 and 5.34 (two splitting q, 1H altogether, ethylidene =CH-), 4.35 (q, 4H, two ethyl CH_2), 3.88 (broad s, 2H, 5-CH_2), 3.25 (broad s, 2H, 3-CH_2), 1.65 and 1.45 (two d, 3H altogether, ethylidene CH_3), 1.36 (t, 6H, two ethyl CH_3); ^{13}C nmr: δ 167.76 and 167.68 (two carbethoxyl CO), 165.21-165.10 (CO-N), 144.81 (C-NO_2), 132.76 (benzenic 1-C), 131.63-131.58 (4-C), 134.40-134.34, 130.02-129.96, 128.40 and 124.44-124.37 (benzenic CH), 119.11-118.93 (ethylidene =CH-), 72.11-71.94 (2-C), 62.19-62.06 (two ethyl CH_2), 52.92-49.69 (5-CH_2), 42.36-38.26 (3-CH_2), 14.27-14.02 (ethylidene CH_3), 13.86 (two ethyl CH_3).

Anal. Calcd. for $C_{19}H_{22}N_2O_7$: C, 58.45; H, 5.68; N, 7.18. Found: C, 58.36; H, 5.70; N, 7.17.

2,2-Diethoxycarbonyl-1-(2-nitrobenzoyl)-4-vinylpyrrolidine (**8**).

The last product obtained from the above described chromatographic procedure was **8** (oil, 0.20 g, yield 19%); ^{1}H nmr: δ 8.20 (d, 1H), 7.74 (t, 1H) and 7.58 (m, 2H) (benzenic protons), 5.65 (octet, 1H, vinylic -CH=), 5.10 and 5.06 (two d, 2H, vinylic =CH_2), 4.37 (m, 4H, two ethyl CH_2), 3.45 (dd, 1H) and 3.18 (dd, 1H) (5-CH_2 geminal protons, J_{gem} = 10 Hz), 2.96 (m, 1H, H-4), 2.80 (dd, 1H) and 2.37 (dd, 1H) (3-CH_2 geminal protons, J_{gem} = 12 Hz), 1.39 and 1.36 (two t, 6H, two ethyl CH_3), coupling constants of >CH-CH=CH_2 system, vinyl J_{trans} = 18 Hz, vinyl J_{cis} = 11 Hz, $J_{H\text{-}4,\ vinyl\ CH}$ = 8 Hz; ^{13}C nmr: δ 168.24 and 168.01 (two carbethoxyl CO), 165.50 (CO-N), 145.08 (C-NO_2), 135.87 (vinylic CH), 133.25 (benzenic 1-C), 134.32, 129.94, 128.63 and 124.49 (benzenic CH), 117.17 (vinylic CH_2), 72.29 (2-C), 62.34 (two ethyl

CH_2), 53.72 (5-CH_2), 41.97 (3-CH_2), 41.42 (4-CH), 14.04 and 13.99 (two ethyl CH_3).

Anal. Calcd. for $C_{19}H_{22}N_2O_7$: C, 58.45; H, 5.68; N, 7.18. Found: C, 58.58; H, 5.75; N, 7.20.

5,11-Dioxo-11a-ethoxycarbonyl-1,2,3,10,11,11a-hexahydro-2-vinyl-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine (**9**).

A solution of 1.15 g of ferrous sulfate in 5 ml of water and 0.4 ml of concentrated ammonia was added to a solution of 0.15 g (0.38 mmole) of **8** in 5 ml of ethanol. The mixture was refluxed for two hours, adding dropwise ammonia at intervals during the reaction. After cooling and filtering, the solution was evaporated in order to eliminate ethanol and extracted twice with chloroform. The extract was dried on sodium sulfate, filtered and concentrated; the required product was isolated by means of a silica gel plate for preparative tlc, eluting twice with dichloromethane and then once more with chloroform-methanol (99:1) to obtain 60 mg of product **9** (mp 151-153° from *n*-hexane-benzene, yield 50%); ^{1}H nmr: δ 8.38 and 8.30 (two broad s, 1H altogether, NH, exchanged with deuterium oxide), 7.96 (splitting d, 1H), 7.47 (t, 1H), 7.28 (m, 1H mixed with $CHCl_3$ peak) and 6.98 (d, 1H) (benzenic protons), 5.80 (octet, 1H, vinylic -CH=), 5.20 (m, 2H, vinylic $=CH_2$), 4.40 and 4.20 (two dd, 1H altogether) and 3.48 (m, 1H) (3-CH_2 geminal protons), 3.85 (m, 2H, ethyl CH_2), 3.32 and 3.15 (two dd, 1H altogether), 2.35 and 2.00 (two dd, 1H altogether) (1-CH_2 geminal protons), 3.05 (m, 1H, H-2), 0.87 (t, 3H, CH_3), the above assignments were confirmed by selective decoupling experiments; ^{13}C nmr: δ 168.41, 168.32, 168.23 (carbethoxyl CO and CONH); 166.12 (CO-N), 138.25-137.11 (vinylic -CH=), 134.68-134.61 (9a-C), 132.21-132.15, 131.81, 125.28 and 121.45-121.38 (benzenic CH), 126.50 (5a-C), 117.80-117.33 (vinylic $=CH_2$), 71.41-71.27 (11a-C), 62.41 (ethyl CH_2), 53.91-53.87 (3-CH_2), 41.91-41.87 (1-CH_2), 40.21-39.87 (2-CH), 13.14 (CH_3), the above assignments were based on DEPT sequence.

Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.95; H, 5.77; N, 8.91. Found: C, 64.68; H, 5.85; N, 8.95.

E- and *Z*-5,11-Dioxo-11a-ethoxycarbonyl-2-ethylidene-1,2,3,10,-11,11a-hexahydro-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine (**2**).

A solution of **7** (0.20 g, 0.51 mmole) in 5 ml of ethanol was added with a solution of ferrous sulfate (1.5 g in 10 ml of water) and 0.5 ml of concentrated ammonia and then refluxed for 2 hours; small amounts of ammonia were added at intervals during the course of the reaction. After cooling and filtering, the solution was concentrated under reduced pressure to eliminate ethanol and then extracted twice with chloroform. The extract was dried on sodium sulfate, filtered and concentrated; the concentrated solution was chromatographed on a silica gel plate for preparative tlc, eluting four times with dichloromethane and then once more with chloroform-methanol (99:1); two products were obtained by means of this procedure:

1) Compound *E*-**2** had the lower Rf, yield 0.045 g (28%), mp 155-157° (from *n*-hexane); ^{1}H nmr: δ 8.18 (broad s, 1H, NH; exchanged with deuterium oxide), 7.96 (splitting d, 1H), 7.46 (splitting t, 1H), 7.26 (m, 1H mixed with $CHCl_3$ peak) and 6.97 (d, 1H) (benzenic protons), 5.58 (splitting q, 1H, ethylidene =CH-), 4.55 and 4.39 (two d, 1H each, 3-CH_2, J_{gem} = 10 Hz), 4.05 and 2.24 (two d, 1H each, 1-CH_2, J_{gem} = 12 Hz), 3.83 (q, 2H, ethyl CH_2), 1.72 (d, 3H, ethylidene CH_3), 0.88 (t, 3H, ethyl CH_3); ^{13}C nmr: δ 169.04 (COO), 168.42 (CONH), 166.20 (CO-N), 134.02 (9a-C), 130.55 (2-C), 126.63 (5a-C), 132.68, 131.51, 125.48 and 120.60 (benzenic CH), 118.83 (ethylidene =CH-), 69.89 (11a-C), 62.43 (ethyl CH_2), 53.88 (3-CH_2), 37.05 (1-CH_2), 14.25 (ethylidene CH_3), 13.61 (ethyl CH_3).

Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.95; H, 5.77; N, 8.91. Found: C, 64.88; H, 5.91; N, 8.85.

2) Compound *Z*-**2**, had the higher Rf, yield 0.030 g (18%), mp 153-155° (from *n*-hexane); ^{1}H nmr: δ 7.64 (broad s, 1H, NH, exchanged with deuterium oxide), 7.96 (splitting d, 1H), 7.49 (splitting t, 1H), 7.28 (m, 1H mixed with $CHCl_3$ peak) and 6.93 (d, 1H) (benzenic protons), 5.56 (splitting q, 1H, ethylidene =CH-), 4.48 (broad s, 2H, 3-CH_2), 3.94 and 2.85 (two d, 1H each, 1-CH_2, J_{gem} = 12.7 Hz), 3.85 (q, 2H, ethyl CH_2), 1.70 (d, 3H, ethylidene CH_3), 0.89 (t, 3H, ethyl CH_3); ^{13}C nmr: δ 169.08 (COO), 168.70 (CONH), 165.86 (CO-N), 134.26 (9a-C), 130.69 (2-C), 126.65 (5a-C), 132.63, 131.48, 125.38 and 120.70 (benzenic CH), 118.98 (ethylidene =CH-), 69.45 (11a-C), 62.41 (ethyl CH_2), 50.57 (3-CH_2), 41.04 (1-CH_2), 14.58 (ethylidene CH_3), 13.59 (ethyl CH_3).

Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.95; H, 5.77; N, 8.91. Found: C, 65.02; H, 5.89; N, 8.70.

1-(2-Aminobenzoyl)-2,2-diethoxycarbonyl-4-(1-hydroxyethyl)-pyrrolidine (**10**).

A solution of 1.3 g (3.2 mmoles) of **5** in 30 ml of methanol was added with 300 mg of 10% palladium on activated carbon and treated with hydrogen under atmospheric pressure, stirring at room temperature. When the hydrogen uptake ceased, the catalyst was removed by filtration and the filtrate was concentrated *in vacuo* to a small volume and chromatographed on a short silica gel column eluting with diethyl ether. The solvent was evaporated to obtain product **10** as an oil (0.85 g, yield 70%); ^{1}H nmr: δ 7.18 (m, 2H) and 6.73 (m, 2H) (benzenic protons); 4.31 (two overlapping q, 4H, two ethyl CH_2), 3.75-3.30* (series of signals, 6H, 5-CH_2 geminal protons, hydroxyethyl CH, NH_2 and OH), 2.73 (dd, 1H, one proton of 3-CH_2, J_{gem} = 11 Hz), 2.34 (m, 2H, the other proton of 3-CH_2 and H-4), 1.35 and 1.33 (two t, 6H, two ethyl CH_3), 1.14 (d, 3H, hydroxyethyl CH_3, J = 6 Hz), the asterisked assignment was confirmed by treatment with deuterium oxide, after treatment, the series of peaks between δ 3.75 and 3.30 changed into the following signals, 3.65 (m, 2H, hydroxyethyl CH and one proton of 5-CH_2) and 3.40 (dd, 1H, the other proton of 5-CH_2, J_{gem} = 10 Hz); ^{13}C nmr: δ 168.80 (one carbethoxyl CO), 168.30 (the other carbethoxyl CO and CO-N), 143.70 (C-NH_2), 130.60, 127.01, 118.7 and 117.2 (benzenic CH), 125.1 (benzenic 1-C), 72.80 (2-C), 68.80 (CH-OH), 62.10 (two ethyl CH_2), 51.79 (5-CH_2), 45.60 (4-CH), 38.10 (3-CH_2), 22.01 (hydroxyethyl CH_3), 13.71 (two ethyl CH_3), the above assignments were based on DEPT sequence.

Anal. Calcd. for $C_{19}H_{26}N_2O_6$: C, 60.30; H, 6.93; N, 7.40. Found: C, 60.12; H, 7.09; N, 7.33.

5,11-Dioxo-11a-ethoxycarbonyl-1,2,3,10,11,11a-hexahydro-2-(1-hydroxyethyl)-5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine (**11**).

Product **10** (0.80 g, 2.1 mmoles) was heated at 200° *in vacuo* for three hours. The residue was dissolved in chloroform and passed through a silica gel column eluting with diethyl ether to afford 0.45 g (yield 65%) of **11**, mp 173-176° (recrystallized from benzene added with a little amount of chloroform); ^{1}H nmr: δ 7.95 (m, 2H, NH and one aromatic proton), 7.46 (splitting t, 1H), 7.27 (m, 1H) and 6.95 (splitting d, 1H) (aromatic protons), 4.08 (dd, 1H) and 3.50 (dd, 1H) (3-CH_2 geminal protons; J_{gem} = 11 Hz), 3.85 (m, 3H, ethyl CH_2 and hydroxyethyl CH), 3.38 (dd, 1H) and

2.09 (dd, 1H) (1-CH_2 geminal protons; J_{gem} = 12.2 Hz), 2.35 (m, 1H, H-2), 1.32 (d, 3H, hydroxyethyl CH_3, J_{CH,CH_3} = 6 Hz), 0.88 (t, 3H, ethyl CH_3), the above assignments were confirmed by selective decoupling experiments, coupling constants of the four methylenic protons with H-2, 7.3 Hz (H at δ 4.08), 10.5 Hz (H at δ 3.50), 6 Hz (H at δ 3.38), 10.9 Hz (H at δ 2.09); ^{13}C nmr: δ 169.98 (COO), 168.99 (CONH), 165.65 (CO-N), 133.84 (9a-C), 132.75, 131.60, 125.63 and 120.79 (benzenic CH), 126.58 (5a-C), 69.49 (11a-C), 67.69 (CHOH), 62.54 (ethyl CH_2), 51.80 (3-CH_2), 43.59 (2-CH), 37.12 (1-CH_2), 21.95 (hydroxyethyl CH_3), 13.61 (ethyl CH_3), the above assignments are based on DEPT sequence.

Anal. Calcd. for $C_{17}H_{20}N_2O_5$: C, 61.43; H, 6.07; N, 8.43. Found: C, 61.18; H, 6.15; N, 8.35.

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