

5,6,6a,7,8,13-Hexahydroquinoxalino[2,1-c][1,4]benzodiazepine

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The intramolecular cyclization of 1-(2-aminobenzoyl)-2-carbethoxy-3-oxo-1,2,3,4-tetrahydroquinoxaline, followed by lithium aluminum hydride reduction, gave the title compound.

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Our previous papers (1) report the preparation of some pyrrolo[1,4]benzodiazepines, structurally related to the antitumor antibiotics anthramycin, tomaymycin and neotramycin, starting from 2-nitrobenzoylaminomalonates. As an extension of this research, we have incorporated the aminomalonate group into the quinoxaline ring with the purpose to synthesize an unusual heterocyclic system, *viz.*, quinoxalino[2,1-c][1,4]benzodiazepine (1).

As far as we are aware, only one product 11 is postulated to possess this structure; it has been obtained by rear-

rangement of an imidazo[1,5-a]quinoxaline derivative (2) in acidic medium.

The synthesis we propose is linear and allows for the preparation of the title compound VII in a few steps (see Scheme); attempts to obtain less saturated derivatives by catalytic dehydrogenation failed.

Using 2-carbethoxy-3-oxo-1,2,3,4-tetrahydroquinoxaline (III) (3) as starting material, the reaction with 2-nitrobenzoyl chloride was carried out by heating a mixture of the two products directly; 2-carbethoxy-1-(2-nitrobenzoyl)-3-oxo-1,2,3,4-tetrahydroquinoxaline (IV) was obtained, which was then reduced by catalytic hydrogenation to the corresponding amino derivative V. Cyclization of this compound to 5,6,6a,7,8,13-hexahydro-6,7,13-trioxoquinoxalino[2,1-c][1,4]benzodiazepine (VI) was accomplished by heating V under reduced pressure. Finally, lithium aluminum hydride reduction of VI gave 5,6,6a,7,8,13-hexahydroquinoxalino[2,1-c][1,4]benzodiazepine.

The structures of new compounds were confirmed by ir, nmr and mass spectra.

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EXPERIMENTAL

All melting points were taken on a Fisher-Johns apparatus and are uncorrected.

2-Carbethoxy-1-(2-nitrobenzoyl)-3-oxo-1,2,3,4-tetrahydroquinoxaline (IV).

Equimolecular amounts of the quinoxaline III and 2-nitrobenzoyl chloride were heated at 90° for thirty minutes (the best results were obtained when the mixture of III and the acid chloride was prepared by first dissolving them in acetonitrile and then evaporating the solution). The product thus obtained was crystallized directly from a small amount of ethanol (60%; m.p. 224-226°).

Anal. Calcd. for C₁₈H₁₅N₃O₆: C, 58.53; H, 4.09; N, 11.38. Found: C, 58.79; H, 4.19; N, 11.41.

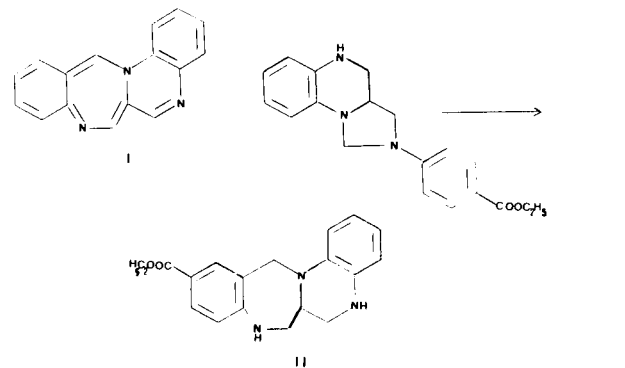
1-(2-Aminobenzoyl)-2-carbethoxy-3-oxo-1,2,3,4-tetrahydroquinoxaline (V).

A solution of the nitro derivative IV (2.4 g.) in ethanol was hydrogenated in Parr apparatus at 60 psi using palladium on charcoal as a catalyst.

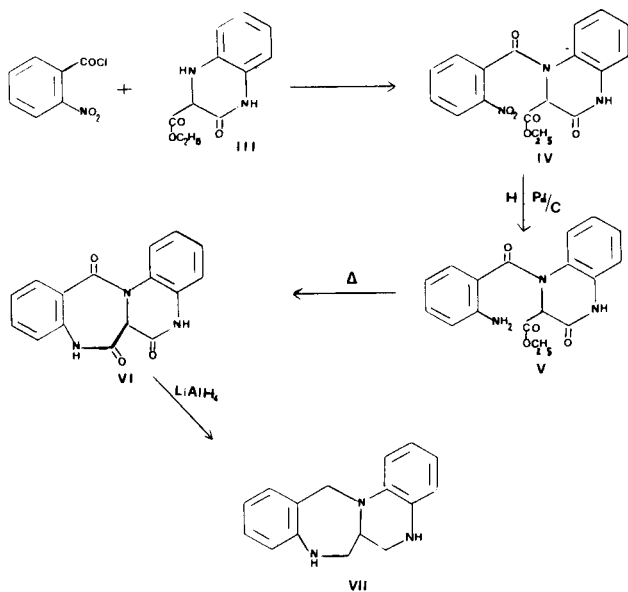
The corresponding amino derivative V was obtained as a white solid after crystallization from ethanol (1.5 g.; m.p. 171-172°).

Anal. Calcd. for C₁₈H₁₇N₃O₄: C, 63.71; H, 5.05; N, 12.38. Found: C, 63.91; H, 5.17; N, 12.45.

5,6,6a,7,8,13-Hexahydro-6,7,13-trioxoquinoxalino[2,1-c][1,4]benzodiazepine (VI).



Scheme



Tricyclic compound VI was formed by heating 1-(2-aminobenzoyl)-2-carbethoxy-3-oxo-1,2,3,4-tetrahydroquinoxaline (V) under reduced pressure at 200° for thirty minutes. The residue was triturated in ethanol, filtered off and then crystallized from *N,N*-dimethylformamide (60%; m.p. > 290°).

Anal. Calcd. for $C_{16}H_{11}N_3O_3$: C, 65.52; H, 3.78; N, 14.33. Found: C, 65.30; H, 3.81; N, 14.25.

5,6,6a,7,8,13-Hexahydro-quinoxalino[2,1-*c*][1,4]benzodiazepine (VII).

A mixture of the trioxo derivative VI (0.9 g.), lithium aluminum hydride (0.9 g.) and anhydrous tetrahydrofuran (250 ml.) was stirred and heated under reflux for twenty four hours. After cooling, ice was carefully added, the suspension was filtered and the filtrate was evaporated to dryness. The residue was first purified by passing it on an alumina col-

umn (benzene as eluent) and then was crystallized from cyclohexane (0.3 g.; m.p. 125-126°).

Anal. Calcd. for $C_{16}H_{11}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: C, 76.62; H, 6.78; N, 16.56.

REFERENCES AND NOTES

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- (3) Y. Ahmad, M. S. Habib, M. Iqbal and M. Ikram Qureshi, *J. Chem. Soc.*, 4053 (1964).