Additions and Corrections

1992, Volume 35

Jun Segawa, Masahiko Kitano, Kenji Kazuno, Masato Matsuoka, Ichiro Shirahase, Masakuni Ozaki, Masato Matsuda, Yoshifumi Tomii, and Masahiro Kise*: Studies on Pyridonecarboxylic Acids. 1. Synthesis and Antibacterial Evaluation of 7-Substituted-6-halo-4-oxo-4*H*-[1,3]thiazeto[3,2-*a*]quinoline-3-carboxylic Acids.

Page 4728. In Scheme I, the reaction condition used in converting **28a-j** to **29a-y** was h, not g. Also, the substituents for **28a-j** should be R^3 = Et, R^7 = cyclic amino, and for **29a-y**, R^3 = H, R^7 = cyclic amino.

Page 4730. In the second sentence of the third full paragraph of the second column, the order of in vitro activity against Gram-positive bacteria should read **29h > 29a > 29e, 29f > 29b, 29c, 29d > 29g.**

1993, Volume 36

Kristin R. Snyder, Thomas F. Murray, Gary E. DeLander, and Jane V. Aldrich*: Synthesis and Opioid Activity of Dynorphin A-(1-13)NH_2 Analogues Containing *cis*- and *trans*-4-Aminocyclohexanecarboxylic Acid.

Page 1101. The first eight lines of text were repeated from the previous page, and the last nine lines of text are missing. For clarity, the sections of text involved are reproduced below.

Results and Discussion

Design Rationale and Synthesis. Molecular modeling with the AMBER[15,16] program was used to examine possible conformational constraints for incorporation into positions 2 and 3 in Dyn A-(1-13)NH_2. These studies suggested that *trans*-4-aminocyclohexanecarboxylic acid (*trans*-ACCA) might replace Gly^2-Gly^3 in an extended conformation. The calculated nitrogen-carbonyl carbon distance was 5.70 Å for *trans*-ACCA in the diequitorial conformation vs 6.12 Å between the nitrogen of Gly^2 and the carbonyl carbon of Gly^3 when the peptide was in an extended conformation. The ACCA dipeptide replacement is equivalent to constraining ψ_2 and ϕ_3 while still allowing free rotation around ϕ_2 and ψ_3.

Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-R

Dyn A-(1-13)NH_2

[*trans*-ACCA$^{2-3}$]Dyn A-(1-13)NH_2

R = -Pro-Lys-Leu-LysNH_2

ACCA was synthesized by hydrogenation of *p*-aminobenzoic acid with PtO_2 as a catalyst[17] (Scheme I), which yielded a mixture of cis and trans isomers (approx ratio of 2.5/1 cis/trans). Separation by fractional recrystallization[18] from EtOH yielded the cis isomer, which was pure by ^1H NMR. Subsequent recrystallization from EtOH/ether yielded the trans isomer, but ^1H NMR indicated that the trans isomer contained from 10-15% up to 35% of the cis isomer, depending on the batch. Following fractional recrystallization, each isomer was converted separately to its Fmoc (9-fluorenylmethoxycarbonyl) derivative. Fmoc protection of these branched amino acids proved to be difficult, and literature procedures[19] had to be modified[20] to obtain the desired product (see Experimental Section). HPLC verified that Fmoc-*cis*-ACCA contained only the cis isomer. In the case of Fmoc-*trans*-ACCA, the contaminating cis isomer (t_R = 29.3 min) was not well resolved from the desired Fmoc-*trans*-ACCA (t_R = 29.7 min) by HPLC, so this mixture was used in the synthesis of the *trans*-ACCA analogue of Dyn A-(1-13)-NH_2.

Both the cis and trans isomers were incorporated separately into Dyn A-(1-13)NH_2 (Scheme I). The peptides were prepared as amides because of the enhanced metabolic stability of Dyn A-(1-13) amide vs its corresponding acid.[21] The peptides were synthesized on a PAL resin[22] using Fmoc-protected amino acids by procedures described previously.[23] The peptides were deprotected and cleaved from the PAL resin using trifluoroacetic acid (TFA) and purified by preparative reverse-phase HPLC. The purification of [*cis*-ACCA$^{2-3}$]Dyn A-(1-13)NH_2 was straightforward, while the purification of the trans analogue proved difficult due to the necessity of separating

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