

SHORT
COMMUNICATIONS

Preparation of Adamantyl-substituted Amino Acids Lactams

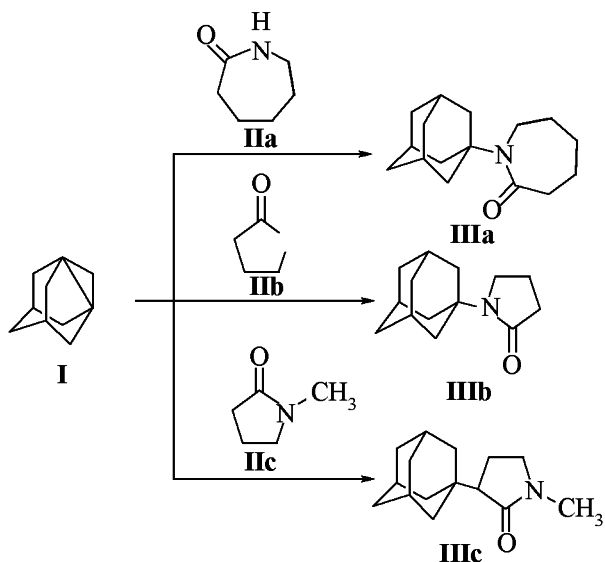
B. I. No[†], V. M. Mokhov, and E. N. Vishnevetskii

Volgograd State Technical University, Volgograd, 400131 Russia

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The known syntheses of adamantyl-containing amino acids lactams [1, 2] do not ensure easy preparation of these compounds. The introduction of adamantyl moiety into the lactam molecule requires expensive reagents, is time-consuming and results in low yield of the target products.

We are first to develop a convenient preparation procedure for adamantyl-containing lactams of various structure based on application of 1,3-dehydroadamantane as an adamantylating agent.



As substrates we used lactams of ϵ -aminocaproic acid (IIa), γ -aminobutyric acid (IIb), and also N-methylpyrrolidone (IIc). The reactions were carried out under inert atmosphere at 90–100°C within 6–8 h using lactams in 3–5-fold excess. The isolation and purification of compounds IIIa–c obtained was done by vacuum distillation followed by recrystallization from 2-propanol. Compounds IIIa–c are low-melting colorless crystalline odorless substances obtained in 70–75% yield.

The 1,3-dehydroadamantane is known to readily react both with C–H acids and with an N–H bond [3, 4]. We first established that 1,3-dehydroadamantane reacted with N-unsubstituted lactams mainly at their N–H bond affording N-adamantyl lactam derivatives IIIa, b. However with N-methyl-substituted lactam IIIc the 1,3-dehydroadamantane reacted exclusively at the C–H bond located in the α -position.

The composition and structure of compounds IIIa–c were confirmed by ¹H NMR and mass spectra. The physical properties of N-adamantyl- ϵ -caprolactam (IIIa) and N-adamantyl- α -pyrrolidone (IIIb) are consistent with the published data [2].

In the ¹H NMR spectra of compounds IIIa, b are lacking the signals of the NH groups which are present in the initial compounds indicating that adamantyl group is attached to the nitrogen and not to a carbon atom. This can be attributed to different reactivity of N–H and C–H bonds of the lactams. Besides we did not detect a product of 1,3-dehydroadamantane addition to a lactim form of lactams IIa, b. N-Methyl-substituted lactam IIIc behaves as a weak C–H acid, and the addition occurs at the α -carbon. In the mass spectrum of compound IIIc a peak of molecular ion is observed (m/z 233, I_{rel} 23%), the most abundant ion is that of adamantyl cation-radical (m/z 135, I_{rel} 100%), and the next in intensity is the ion peak of N-methylpyrrolidone (m/z 98, I_{rel} 63%).

N-Adamantylcaprolactam (IIIa). Yield 70%, mp 56°C, bp 195°C (*p*, 4 mm Hg). ¹H NMR spectrum (DMSO-*d*₆), δ , ppm: 3.4 t [2H, CH₂N], 3.2 t [2H, CH₂C(O)], 1.4–2.5 m [21H, Ad, (CH₂)₃]. Mass spectrum, m/z (I_{rel} , %): 247 (57) M^+ , 135 (100) [Ad]⁺, 112 (59) [C₆H₁₀NO]⁺, 190 (66) [AdNC₃H₆]⁺, 56 (84) [C₃H₄O]⁺. Found, %: C 77.63; H 10.31; N 5.48. M 247.29. C₁₆H₂₅NO. Calculated, %: C 77.68; H 10.19; N 5.66. M 247.38.

[†] Deceased.

N-Adamantyl- α -pyrrolidone (IIIb). Yield 75%, mp 93°C, bp 165°C (*p*, 4 mm Hg). ^1H NMR spectrum (DMSO- d_6), δ , ppm: 1.66 s, 2.00 s [15H, Ad], 2.14 t [2H, CH₂C(O)], 3.38 t [2H, CH₂N], Found, %: C 76.70; H 9.59; N 6.32. C₁₄H₂₁NO. Calculated, %: C 76.67; H 9.65; N 6.38.

N-Methyl-3-adamantyl- α -pyrrolidone (IIIc). Yield 74%, mp 84°C, bp 180°C (*p*, 4 mm Hg). Mass spectrum, *m/z* (*I*_{rel}, %): 233 (23) *M*⁺, 135 (100) [Ad]⁺, 98 (63) [C₅H₉NO]⁺. Found, %: C 77.15; H 9.81; N 6.12. *M* 233.24. C₁₅H₂₃NO. Calculated, %: C 77.21; H 9.93; N 6.00. *M* 233.36.

^1H NMR spectra were registered on spectrometer Bruker AC-200 (200 MHz), mass spectra were measured on Kratos MS-30 instrument (70 eV).

REFERENCES

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2. Dutch Patent 131489, 1971.
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