The Preparation of 8,11-aminoderivatives of C₅-trishomocubane

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Abstract – The nitrogen containing derivatives of C₅–trishomocubane have been recently shown to possess pharmacological activity. The preparation of 8,11-derivatives of pentacycloundecane complicated because of transannular interaction in C₅-structure. The method of 8,11-C₅–trishomocubane derivatives preparation based on using protecting groups was developed. The structure of newly obtained 8,11-aminoderivatives of C₅–trishomocubane was proved with NMR and GC-MS spectra.

Key words – polycyclic compounds, C₅–trishomocubane, aminoderivatives, transannular interaction, antidepressants, protecting groups.

I. Introduction

Polycarbocyclic cage compounds have attracted attention of organic chemists for years, mostly because of their unique properties, e.g. high density, moderate strain energy and great stability, which are the result of their fascinating structural carbocyclic frameworks. In particular, pentacycloundecane derivatives have presented a fairly attractive goal and various synthetic strategies have been developed for their acquirement[1].

The 8,11-derivatives of pentacyclo[5.4.0.0²,6.0³,10.0⁵,9]undecane (Cookson’s diketone, 4) have proved to be exceedingly useful as an intermediate in the synthesis of complex substituted polycyclic compounds. They also can be used as ligands to chelate metal ions and for synthesis of crown-ethers [1], [2], [3]. The 8,11-aminoderivatives of pentacycloundecane have been recently shown to possess pharmacological activity that allows them to be used as antiviral agents [4], [5], antidepressants, tranquilizers, and as agents for the treatment of extrapyramidal syndromes [6]. The aim of our work is obtaining of 8,11-derivatives of C₅–trishomocubane, containing amino group. But the obtaining of 8,11-derivatives of C₅–trishomocubane is complicated because of transannular interaction in the polycyclic frame [7].

II. Results and discussions

We have proposed the new method that based on using protecting groups into the C₅–trishomocubane cage.

The Diels-Alder reaction of cyclopentadiene (1) and 1,4-benzoquinone (2) gave the well-precedented adduct 3 which underwent [2+2] photocyclization to give pentacyclo[5.4.0.0²,6.0³,10.0⁵,9]undecane-8,11-dione (Cookson’s diketone, 4).

Protection of a single ketone functionality of Cookson’s diketone (4) as its ethylene acetal gave the ketal 5 [6]. Treatment of 5 with hydroxylamine afforded ketal-oxime 6. Reduction of oxime 6 with LAH afforded exclusively endo-aminoketal 7. Structure of amine 4 was proved by X-Ray analysis of its Boc-derivative 8 (Fig 1).

Because of higher stability of acetamide group in acidic condition we obtained acetamidoketal 9. Further cleavage of ketal group in mild acidic conditions afforded to ketone 11.

Fig. 1. X-Ray diffraction analysis of Boc-derivative of C₅–trishomocubane 8
Treatment of the last one with hydroxylamine afforded acetamidooxime \textbf{12}, that structure was proved with NMR and GC-MS spectrums.

\begin{center}
\begin{tikzpicture}
\node[draw] (11) at (0,0) {\textbf{11}}; \node[draw] (12) at (1,0) {\textbf{12}}; \node[draw] (13) at (2,0) {\textbf{13}};
\draw (11) -- (12) node[midway,above] {$\text{NH}_2\text{OH}\cdot\text{HCl}$}; \draw (12) -- (13) node[midway,above] {$\text{K}_2\text{CO}_3$ \text{(76\%)}}; \draw (12) -- (13) node[midway,above] {$\text{HON}$};
\end{tikzpicture}
\end{center}

Occurrence of characteristic oxime (7.44, 7.37 ppm) and amide (6.01) peaks in NMR spectrum as well as molecular ion peak (m/z = 232) in MS-spectrum of \textbf{12} proves that acetamidooxime was formed.

The fact of oxime obtaining proves that no transannular cyclization take place.

Reduction of oxime \textbf{12} with H\textsubscript{2} on Ni/Ra afforded acetoamine \textbf{13}.

\begin{center}
\begin{tikzpicture}
\node[draw] (12) at (0,0) {\textbf{12}}; \node[draw] (13) at (1,0) {\textbf{13}};
\draw (12) -- (13) node[midway,above] {$\text{H}_2\cdot\text{NiRa}$ \text{(93\%)}}; \draw (12) -- (13) node[midway,above] {$\text{H}_2\text{NNH}_2$}; \draw (12) -- (13) node[midway,above] {$\text{NH}_2\text{NNH}_2$};
\end{tikzpicture}
\end{center}

Conclusion

In the present work, we have developed new method of obtaining of nonsymmetrical 8,11-aminoderivatives of pentacyclo[5.4.0.0\textsuperscript{2,6}.0\textsuperscript{3,10}.0\textsuperscript{5,9}]undecane. Synthesized monoprotected $C_8$-diamine can be used for obtaining of corresponding diamine.

We thank Ukrorgsyntez Ltd for support.

References