REACTIONS OF LYCOCTONINE ALKALOIDS WITH ACETIC ANHYDRIDE AND p-TOLUENESULFONIC ACID

A. S. Narzullaev and M. C. Yunusov

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The reactions of alkaloids having a 7,8-diol system – lycoctonine, browniine, and dihydromonticoline – with acetic anhydride and p-toluenesulfonic acid have been studied. The optimum conditions for this reaction, leading to anhydro compounds, have been found.

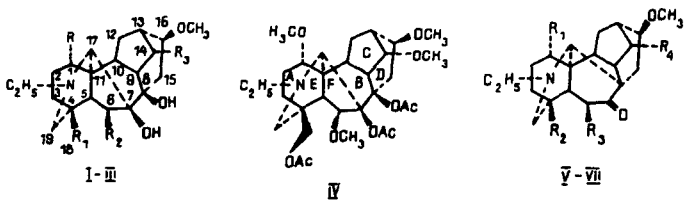
The acetylation reaction is important in establishing the number and nature of functional groups [1]. In the case of C_{19}-diterpenoid alkaloids of the lycoctonine type, which contain a vicinal diol system at C-7 and C-8, acetylation does not give the desired results since rearrangement processes take place and a complex mixture of products is formed. For this reason, acetylation of a 7,8-diol system is not usually carried out. A publication has recently appeared in which the production of winkleridine 7,8,14,18-tetraacetate is described [2].

The factors described above have induced us to study the behavior of alkaloids with a 7,8-diol system – lycoctonine (I), browniine (II), and dihydromonticoline (III) – in reactions with acetic anhydride and p toluenesulfonic acid. The reactions performed in the course of 5 and 11 days gave identical results.

The reaction of lycoctonine with acetic anhydride and p-toluenesulfonic acid gave two compounds – (IV) and (V). Decreasing the amount of p-toluenesulfonic acid led to an increase in the yield of (IV).

The IR spectrum of (VI) had the absorption band of an ester carbonyl (1710 cm^{-1}). The presence in the PMR spectrum of the signals of an aminoethyl group (3 H, triplet, J = 7 Hz, 0.8 ppm), of four methoxy groups (3 H each, singlets, 3.22, 3.24, 3.34, and 3.42 ppm), and of three acetoxy groups (6 H, singlet, 2.04 ppm; 3 H, singlet, 2.1 ppm), and also an increase in the mass (I) by 126 a.m.u. showed the formation of lycoctonine triacetate (IV). To confirm the formation of alycoctonine triacetate and the absence of any skeletal rearrangement processes whatever, we hydrolyzed (IV). The hydrolyzed product was identical with lycoctonine according to spectral characteristics, TLC, and a mixed melting point.

The presence in the IR spectrum of (V) of the absorption band of a carbonyl in a six-membered ring (1720 cm^{-1}) and in the PMR spectrum of the signals of a aminoethyl group (3 H, triplet, J =7 Hz, 0.84 ppm) and a decrease in the molecular mass of (I) by 18 a.m.u. permitted the assumption for the compound of the structure (V), which corresponds to an anhydrolycoctonine.



I-III IV V-VII

Abuali ibn Sino [Avicenna] Tadzhik State Medical Institute, Dushanbe; Institute of Chemistry, Baskir Scientific Center, Urals Branch, Academy of Sciences of the USSR, Ufa. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 545-547, July-August, 1991. Original article submitted November 22, 1990.

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I. $R=R_2=R_3=CCH_3$; $R_1=CH_2OH$

II. $R=R_2=OCH_3$; $R_1=CH_2CCH_3$; $R_3=OH$

III. $R=R_1=CH$; $R_2=H$; $R_3=OCH_3$

V. $R_1=R_3=R_4=CCH_3$; $R_2=CH_2OH$

VI. $R_1=R_3=OCH_3$; $R_2=CH_2OCH_3$; $R_4=OH$

VII. $R_1=R_2=OAc$; $R_3=H$; $R_4=OCH_3$

This types of pinacolone rearrangement is known in the literature [3, 4]. The acylation of browniine led to the initial compound and to compound (VI), which, according to its IR spectrum (1725 cm^{-1}) and its PMR spectrum – an aminoethyl group (3 H, triplet, J = 7 Hz, 0.96 ppm), four methoxy groups (3 H each, singlets, 3.26, 3.36, 3.39, 3.52 ppm) – and also its mass spectrum (M^+ 449), was an anhydrobrowniine.

The acetylation of dihydromonticoline (III) with acetic anhydride in the presence of p-toluenesulfonic acid gave compund (VII) the spectrum of which contained the signals of two methoxy groups (3 H each, singlets, 3.20, 3.22 ppm), of two acetoxy groups (3 H each, singlets, 1.94, 2.04 oom) and of an aminoethyl group (3 H, triplet, J = 7 Hz, 1.01 ppm). The increase in the molecular mass of (III) by 66 a.m.u. and the presence of two acetoxy groups permitted the assumption that (VII) was an anhydoracetate of dihydromonticoline in which the carbonyl group was located at C-7. The formation of the carbonyl group at C-8 and the expansion of ring D is excluded because of the absence of the signals of olefinic protons from the PMR spectrum [5].

EXPERIMENTAL

IR spectra were taken on a UR-20 instrument in KBr tablets, PMR spectra on a BS-567A (100 MHz) instrument in deuterochloroform with HMDS as internal standard (δ scale), and mass spectra on a MKh-1303 instrument fitted with a system for direct introduction into the ion source. Alumina "for chromatography" was used for chromatography. The homogeneity of the reaction products was checked by chromatography in a thin layer of alumina in the following systems: ether, ether–methanol (100:1), chloroform–methanol (50:1), and hexane–ether (1:4).

General Procedure. Mixtures of 1.1 g of an alkaloid, 1 g of p-TsOH, and 40 ml of freshly redistilled acetic anhydride were left for 5 and 11 days at room temperature. The acetic anhydride was evaporated off, and the residue was dissolved in 5% sulfuric acid. The acid solution was washed with ether (3 × 50 ml) and then, with cooling, was made alkaline with sodium carbonate, and the reaction product was exhaustively extracted with ether.

Acetylation of Lycoctonine. The reaction was performed with 1.1 g of lycoctonine, 1 g of p-TsOH, and 40 ml of acetic anhydride. The reaction product was separated on a column of deactivated alumina. Elution with hexane–ether (1:4) gave 0.6 g of the amorphous product (IV) and 0.4 g of the amorphous product (V).

Acetylation of Lycoctonine. The reaction was performed with 0.35 g of lycoctonine, 0.15 g of p-TsOH, and 10 ml of acetic anhydride. The reaction product was separated on a column of deactivated alumina by the procedure describe above. This gave 0.32 g of lycoctonine triacetate (IV).

Acetylation of Browniine. The reaction was performed with 0.4 g of browniine, 0.4 g of p-TsOH, and 10 ml of acetic anhydride. The reaction product was separated on a column (1.8 × 46 cm) of deactivated alumina. Eluation with ether–methanol (50:1) yielded 0.1 g of amorphous anhydrobrowniine, and ether–methanol (10:1) gave browniine (0.3 g).

Acetylation of Dihydromonticoline. The reaction was performed with 0.1 g of dihydromonticoline, 0.1 g of p-TsOH, and 4 ml of acetic anhydride. After the solvent had been distilled off, 0.04 g amorphous dihydromonticoline anhydroacetate was obtained.

Saponification of Lycoctonine Triacetate. Lycoctonine triacetate (0.1 g) was boiled in 10 ml of a 10% methanolic solution of KOH for 4 h. The solvent was evaporated off, and, after coooling, the residue was dissolved in water and extracted with ether. This gave 0.08 g of lycoctonine.

LITERATURE CITED

1. S. W. Pelletier and N. V. Mady, in: The Alkaloids R. H. F. Manske and R. G. A. Rodrigo (eds.), Academic Press, New York, Vol. XVII (1979), pp. 1-103.
2. Y.-Z. Chen and A. Wu, Phytochemistry, 29, 1016 (1990).
3. O. E. Edwards, L. Marion, and K. R. Stewart, Can. J. Chem., 34, 1315 (1956).
4. R. G. Cookson and M. E. Trevett, J. Chem. Soc., No. 3, 3121 (1956).
5. M. S. Yunusov and S. Yu. Yunusov, Khim. Prir. Soedin., No. 3, 334 (1970).