Chemistry of Natural Compounds, Vol. 30, No. 1, 1994

SYNTHESIS OF NEW IMINO DERIVATIVES OF GOSSYPOL

A. Kh. Khaitbaev, Kh. A. Aslanov, S. A. Auelbekov, Kh. Kh. Khaitbaev, and S. M. Saiitkulov

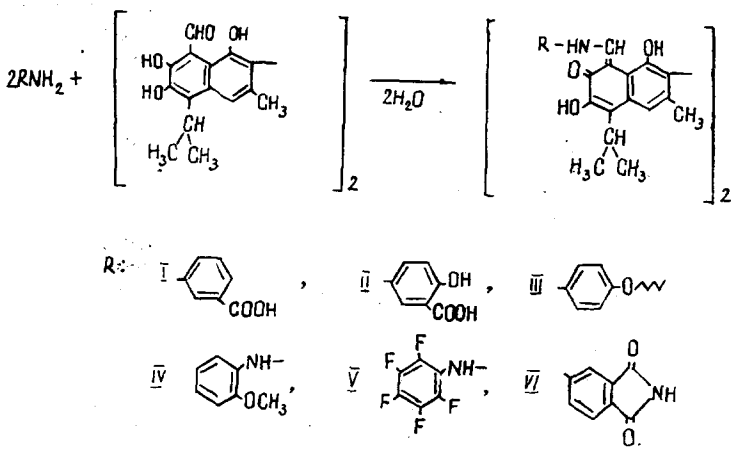
UDC 547.565+547.589

Imino derivatives of gossypol have been synthesized. The individuality of the products obtained was characterized with the aid of TLC. The compositions and structures of these substances have been shown by IR and PMR spectroscopies.

Gossypol derivatives obtained by condensation with compounds containing primary amino groups or active methylene units possess a broad spectrum of biological activity [1, 2]. Among these compounds substances have been found with antiviral, interferon-inducing, immunosuppressive, and antitumoral activities [3, 4]. The biological activity of gossypol derivatives depends on the chemical structure of the molecule [5].

Our task consisted of obtaining Schiff bases with the aim of studying their properties and features of their structure.

The gossypol derivatives were synthesized by the following scheme:



As the starting materials we used gossypol and the appropriate aromatic and heterocyclic amines. The synthesis was carried out by heating alcoholic solutions of equimolar amounts of gossypol and the amine concerned.

To demonstrate the structures of the imino derivatives of gossypol obtained, we recorded their IR and PMR spectra. The IR spectra contained absorption bands in the 1610-1630, 1500-1535, and 1100-1400 cm^{-1} region, corresponding to the stretching vibrations of a benzene ring and of C–C, C=N, and C=O bonds, and a broad band at 3200-3500 cm^{-1} characteristic for the stretching vibrations of hydroxy groups bound by intermolecular and intramolecular hydrogen bonds. In the PMR spectra taken in DMSO-d_6, a signal in the 10.10-10.72 ppm region consisted of the superposition of a doublet and a singlet with different intensities. In addition, in all the PMR spectra in DMSO-d_6 a doublet or a broadened unresolved signal was observed in the 13.80-15.80 ppm region due to the presence of a NH proton bound by a strong hydrogen bond.

The antiviral activities of the compounds synthesized were studied in a culture of L-929 cells. The best system used was an experimental viral infection of murine encephalomyocarditis of the Columbia strain. The highest antiviral activity was possessed by compound (II), which, at a concentration of 50 μg/ml, protected cell cultures from viral infection by 25%, while

Tashkent State University, fax 462472. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 48-49, January-February, 1994. Original article submitted July 13, 1993.

 0009-3130/94/3001-0040$12.50

with an increase in the dose the antiviral activity of the preparation was enhanced. The highest activity was detected at a concentration of 250 μg/ml. The number of viable cells then reached 50-75%.

The results obtained show that among the compounds synthesized there were substances promising as antiviral drugs.

EXPERIMENTAL

The individuality of the compounds synthesized was checked by TLC on Silufol UV-254 plates in the systems 1) benzene–methanol (5:1); 2) chloroform–methanol (5:1); and 3) acetone–benzene (3:2).

The structures of the compounds synthesized were shown with the aid of IR and PMR spectroscopies.

Gossypolydenebis-N-(3-carboxyaniline) (I). A solution of 0.41 g (0.003 mole) of 3-carboxyaniline in 10 ml of ethyl alcohol was added over 2 h, with heating in the water bath, to a solution of 0.8 g (0.0015 mole) of gossypol in 15 ml of ethyl alcohol. The mixture was heated at the boiling point of the solvent for 3 h and was left overnight at room temperature. The yellow precipitate that had deposited was filtered off and was washed successively with alcohol and ether. The compound was dried in vacuum drying chamber at 50-60°C. Empirical formula $C_{44}H_{40}O_{10}N_2$, yield 77.6%, mp 269-271°C, R_f 0.49 (system 1). The following were obtained analogously:

Gossypolydenebis-N-(3-carboxy-4-hydroxyaniline) (II), $C_{44}H_{40}O_{12}N_2$, yield 95. 31%, mp 237-239°C, R_f 0.53 (system 2).

Gossypolydenebis-N-(4-pentyloxyaniline) (III), $C_{52}H_{60}O_8O_2$, yield 55. 63%, mp 211-213°C, R_f 0.51 (system 1).

Gossypolydenebis-N-(2-methoxyphenylhydrazone) (IV), $C_{44}H_{46}O_8N_4$, yield 78. 21%, mp 243-245°C, R_f 0.73 (system 3).

Gossypolydenebis-N-(pentafluorophenylhydrazone) (V), $C_{42}H_{32}O_6N_4F_{10}$, yield 54. 89%, mp 232-234°C, R_f 0.74 (system 1).

Gossypolydenebis-N-(3-iminophthalimide) (VI), $C_{46}H_{38}O_{10}N_4$, yield 90. 17%, mp 259-262°C, R_f 0.50 (system 2).

REFERENCES

1. S. A. Auelbekov and Kh. A. Aslanov, Abstracts of Lectures at the Vth All-Union Symposium on Phenolic Compounds [in Russian], Tallinn (1987), p. 7.
2. E. M. Vermel' and S. A. Kruglyak, Vopr. Onkol., **9**, 39 (1963).
3. N. I. Baram, L. B. Biktimirov, Kh. L. Ziyaev, R. Z. Paizieva, V. I. Ananchenkov, and A. I. Ismailov, in: Abstracts of Lectures at the Vth All-Union Symposium on Phenolic Compounds [in Russian], Tallinn (1968).
4. S. A. Vichkanova and L. V. Goryunova, Antibiotiki, **13**, No. 9, 828 (1968).
5. N. I. Baram, Kh. L. Ziyaev, G. A. Ismailov, L. B. Biktimirov, A. I. Ismailov, and K. G. Urazmetov, Khim. Prir. Soedin., No. 5, 647 (1988).