6. Yu. A. Vladimirov and A. I. Archakov, The Peroxide Oxidation of Lipids in Biological Membranes [in Russian], Nauka, Moscow (1972), p 252.
7. Yu. M. Lopukhin, Yu. A. Vladimirov, M. N. Molodenkov, et al., Byull. Éksp. Biol. Med., 2, 61 (1983).
8. R. Harrison and G. G. Hunt, Biological Membranes, Blackie, Glasgow (1975), p. 153.
9. E. B. Burlakova, A. V. Alekseenko, E. N. Molochkina, N. P. Pal'mina, and N. G. Khrapova, Bioantioxidants in Radiation Diseases and Malignant Growth [in Russian], Nauka, Moscow (1975), p. 214.
10. A. V. Archakov and N. M. Devichevskii, Biokhimiya, 33, 479 (1968).
11. V. A. Kostyuk and E. F. Lunets, Biokhimiya, 48, No. 9, 1491 (1983).
12. E. L. Gray and V. P. Whittaker, J. Anat., 96, No. 1, 79 (1962).
13. G. L. Ellman, K. D. Courtney, V. Anders, and R. M. Featherstone, Biochem. Pharmacol., 7, 88 (1961).
14. M. M. Bradford, Anal. Biochem., 72, No. 12, 248 (1976).
15. Yu. V. Markova, K. K. Kuz'mina, M. N. Shchukina, Zh. Obshch. Khim., 30, 1039 (1950).

TRANSFORMATIONS OF GOSSYPOL IN LOW-MOLECULAR-MASS ALCOHOLS

A. I. Glushenkova, I. P. Nazarova, N. T. Ul'chenko, and É. L. Kristallovich

UDC 547.972

It has been shown that the transformations of gossypol into anhydro derivatives on its storage in methanol, ethanol, and propanol take place the faster the lower the molecular mass of the alcohol and the higher the temperature of the process. It has been established that when alcoholic solutions of gossypol in methanol are heated it is converted completely into dianhydrogossypol, in propanol into monoanhydrogossypol, and in ethanol into a mixture of equal amounts of mono- and dianhydro derivatives.

We have established previously that, in methanol, ethanol, and propanol, gossypol undergoes degradation leading to the formation of mono- and dianhydrogossypols [1]. In the present paper we consider the influence of the molecular masses of the alcohols, the temperature, and the time of storage on the rate of transformation of gossypol. The rate of change was judged from the decrease in the concentration of aldehyde groups in the products obtained.

To determine the amount of aldehyde groups we used the capacity of alcoholic solutions of gossypol for absorbing light intensively in the UV region of the spectrum. The absorption maximum at 376-378 nm in ethanolic solution is due to the presence of aldehyde groups, and a direct relationship exists between the adsorption index at the maximum and the concentration of gossypol in solution [2], which permits the amount of aldehyde groups in a mixture to be determined in a short time with fairly high accuracy (0.1-2%) with the aid of a calibration graph.

In view of this, we have calculated the parameters of the linear calibration graph by the method of least squares. The equation of the straight line reflecting the linear dependence of the optical density on the concentration of gossypol in ethanolic solution has the form $C = 0.032\ D$.

Thus, having calculated the concentration of gossypol in solution from the value of the optical density and knowing the initial concentration taken it is possible to determine the amount of aldehyde groups in the mixture.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 712-715, September-October, 1989. Original article submitted November 22, 1988.

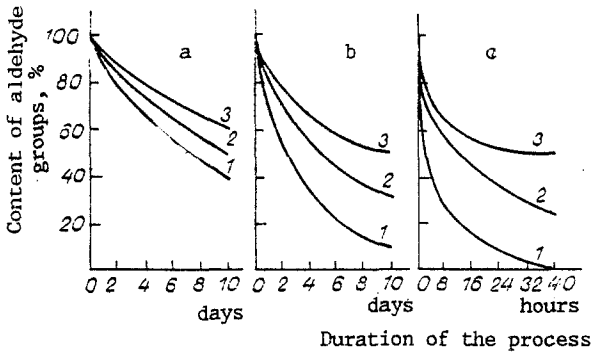

Fig. 1. Change in the concentration of gossypol aldehyde groups as a function of the molecular mass of the alcohol, the time of storage, and the temperature: a) 10°C; b) 25°C; c) 50°C; 1) methanol; 2) ethanol; 3) propanol.

The results of determinations of the amounts of gossypol aldehyde groups as a function of the factors mentioned above are shown in Fig. 1. During the storage of gossypol in the alcohols investigated the concentration of aldehyde groups decreased, and this to a greater extent the lower the molecular mass of the alcohol – i.e., more in methanol than in ethanol, and more in ethanol than in propanol.

A rise in the temperature led to a marked increase in the rate of change of gossypol. Thus, when gossypol was stored in a refrigerator (+10°C) for eight days the amount of aldehyde groups fell from 100 to 55% in ethanol and to 65% in propanol, while at room temperature (25°C) the same levels were reached in four days. In methanol, the acceleration of the process with a rise in the temperature was even more considerable. While in the refrigerator after eight days the content of aldehyde groups in the transformation products was 48.7%, at 25°C the same fall took place in 2.5 days. It must be mentioned that after storage for 10 days in the refrigerator in all the alcohols the change in the gossypol was not complete; at room temperature, however, after only eight days a constant value of the content of aldehyde groups was reached and further storage of the gossypol solutions for a month and more at this temperature led to practically no further appreciable changes.

Heating alcoholic solutions of gossypol to 50°C accelerated the process to such an extent that it was complete in only 40 h. After 24 h those changes had taken place that required eight days at room temperature. At the same time, in the final transformation products a greater fall in the amount of aldehyde groups was observed than at 25°C. Thus, at 50°C in methanol the amount of aldehyde groups was zero, in ethanol 25%, and in propanol 50%, while at 25°C the figures were 10.6, 32, and 52%, respectively.

The quantitative ratio between gossypol (G) and the products of its transformation in alcohol solutions – monoanhydrogossypol (MAG) and dianhydrogossypol (DAG) – was established by comparative TLC on Silufol. Table 1 gives the results of such a determination. The figures in this Table show that during storage the amount of gossypol decreased and that of the anhydro derivatives increased, and this the faster the higher the temperature. After two days in the refrigerator only 20-30% of the gossypol had undergone change, being converted into MAG, while at 25°C 50-70% of the gossypol had undergone change and, in this case, in methanol, DAG had been formed in addition to the MAG. After eight days in methanol the whole of the gossypol had been converted completely, mainly into DAG (80%) and also into MAG (20%). Further storage led to only a slight change in the amounts of mono- and dianhydrogossypols.

In ethanol under the same conditions after four days 30% of G, 50% of MAG, and 20% of DAG were found in the transformation products. After 6-10 days the amount of MAG remained at the same level (50-52%) the amount of gossypol had decreased and that of DAG had increased. In the final product the main components were MAG and DAG, with 6% of gossypol.

In propanol a gradual transformation of the gossypol into monoanhydrogossypol was observed with time. No dianhydrogossypol was formed either after 10 days or after a longer period.

TABLE 1. Amounts of Anhydro Derivatives of Gossypol (%) Formed as a Function of the Molecular Mass of the Alcohol and the Time and Temperature of Storage

Time of storage	Temperature, °C	Methanol			Ethanol			Propanol		
		G	MAG	DAG	G	MAG	DAG	G	MAG	DAG
2 days	10	60,5	29,5	—	75,0	25,0	—	80	20	—
	25	30,0	50,0	20,0	40,0	60,0	—	50	50	—
4 days	10	43,5	49,0	7,5	52,0	44,0	4,0	60,0	40,0	—
	25	10,0	40 0	50,0	30,0	50.0	20,0	30,0	70,0	—
6 days	10	30,0	50,0	20,0	42,0	46 0	12,0	40,0	60,0	—
	25	5,0	30,0	65,0	20,0	50,0	30.0	20,0	80,0	—
8 days	10	20,0	55,0	25,0	30,0	50,0	20,0	30.0	70,0	—
	25	—	20.0	80,0	10.0	50,0	40,0	10.0	90,0	—
10 days	10	12 0	52,0	36,0	20 0	58 0	22,0	20,0	80,0	—
	25	—	18,0	82,0	6,0	52,0	42,0	5,0	95,0	—
8 h	50	9,0	32,0	59,0	25.0	60,0	15.0	25,0	75,0	—
16 h	50	—	32 0	68,0	20,0	50,0	30,0	10,0	90,0	—
24 h	50	—	20,0	80,0	10.0	50,0	40.0	6,0	94,0	—
32 h	50	—	10,0	90,0	6,0	48,0	44,0	4,0	96,0	—
40 h	50	—	—	100	2.0	46,0	52,0	—	100	—

With a rise in the temperature to 50°C, in the final products of the methanolic solution 100% of DAG was obtained with no MAG, in propanol only MAG, and in ethanol a mixture of MAG and DAG in almost equal proportions.

It must be stated that in isopropanol, which is usually employed for the determination of gossypol [3], the latter undergoes changes similar to the changes in propanol.

In butyl and amyl alcohols, G is converted into monoanhydrogossypol but considerably more slowly than in propanol.

For comparison we obtained anhydro derivatives of gossypol by the methods of Clark [4] and of Miller [5]. The products formed in these cases were analyzed with the aid of TLC and UV spectroscopy. When using Clark's method, which includes heating gossypol to a temperature of 200°C, a mixture consisting mainly of gossypol and products of its change was formed, mono- and dianhydro derivatives being present in only slight amounts. Under the conditions of Miller's method a mixture was obtained which consisted of practically equal amounts of gossypol and MAG (content of aldehyde groups 75.3%), and no DAG whatever was formed.

Thus, heating alcohol solutions of gossypol to 50° for 40 h enables dianhydrogossypol to be obtained in ethanol, monoanhydrogossypol in propanol, and a mixture of mono- and dianhydro derivatives in equal amounts in ethanol.

EXPERIMENTAL

The amount of aldehyde groups was determined using the equation of the straight line reflecting the linear dependence of the optical density on the concentration of gossypol in solution.

To plot a calibration graph, weighed amounts of gossypol of from 4.5 to 15 mg were dissolved in 95% ethanol and the solutions were made up to the marks in previously calibrated 50-ml measuring flasks. UV spectra were recorded on a Hitachi spectrophotometer.

TLC and PTLC were performed on Silufol in the petroleum ether–ethyl acetate (3:1) solvent system. The spots were revealed with 2% $SbCl_3$.

SUMMARY

1. It has been shown that the transformation of gossypol into anhydro derivatives on its storage in low-molecular-mass alcohols takes place the faster the lower the molecular mass of the alcohol and the higher the temperature of the process.

2. When ethanolic solutions of gossypol are heated to 50°C, in the case of methanol it is converted completely into dianhydrogossypol and in propanol into monoanhydrogossypol, while in ethanol it forms a mixture of equal amounts of mono- and dianhydro derivatives.

LITERATURE CITED

1. I. P. Nazarova, N. T. Ul'chenko, I. N. Zaborskaya, and A. I. Glushenkova, Khim. Prir. Soedin., 590 (1988).
2. I. P. Nazarova, G. A. Nezhinskaya, A. I. Glushenkova, and A. A. Umarov, Khim. Prir. Soedin., 608 (1979).
3. A. L. Markman and V. P. Rzhekhin, Gossypol and Its Derivatives [in Russian], Pishchevaya Prom-St', Moscow (1965), p. 205.
4. E. R. Clark, J. Biol. Chem., 75, 725 (1927).
5. R. F. Miller and R. Adams, J. Am. Chem. Soc., 59, 1736 (1937).

INSECT PHEROMONES AND THEIR ANALOGS.

XXIII. SYNTHESIS OF (7R,8S)-(+)-cis-2-METHYL-7,8-EPOXYOCTADECANE — THE SEX PHEROMONE OF Porthetria dispar

V. N. Odinokov, V. R. Akhmetova, Kh. D. Khasanov, A. A. Abduvakhabov, A. V. Kuchin, N. I. Andreeva, and G. A. Tolstikov

UDC 632.936.2

A four-stage asymmetric synthesis of (+)-disparlure [(7R,8S)-(+)-cis-methyl-7,8-epoxyoctadecane (V)] has been effected from 8-methylnon-2Z-en-1-ol (I), obtained by the carboalumination of acetylene with tris(5-methylhexyl)aluminum using the Sharpless reaction. The asymmetric epoxidation of (I), (Ar, mol. sieve A, (+)-DET, $(iOPr)_4Ti$, t-BuOOH, −15°C, 20 h; H_2O, 1 h, NaOH, −7°C, 30 min) gave 8-methyl-2S,3R-epoxynonan-1-ol (II), which was oxidized (kieselguhr—CrO_3—Py, 0°C, 2 h; 25°C, 2 h) to 8-methyl-2S,3R-epoxynonan-1-al (III). The coupling of (III) with $n\text{-}C_8H_{17}CH{=}PPh_3$ (−78°C, 1 h; 25°C, 15 h) gave 2-methyl-7R,8S-epoxyoctadec-9Z-ene (IV), the hydrogenation (H_2/5% Pd-C, 25°C, 5 days) of which led to (V) in admixture with an isomerization product. Compound (V) was isolated by HPLC. Substance, yield, $[\alpha]_D^{25}$: (II), 73, −2.75°; (III), 80, [80.8°; (IV), 50, +37.25°; (V), 50, +0.8°. The IR and PMR spectra of (II-IV), the ^{13}C NMR spectra of (II) and (III), and the mass spectrum of (IV) are given.

Of the known methods of synthesizing (+)-disparlure [(7R,8S)-(+)-cis-2-methyl-7,8-epoxyoctadecane] [10-13], the most effective is a route based on the asymmetric epoxidation of the corresponding allyl alcohols [10-13]. The route to (+)-cis-disparlure through an unsaturated precursor — (7R,8S)-2-methyl-7,8-epoxyoctadec-5-ene, which enables a deuterium-labeled product to be obtained [14], requires the use at the stage of epoxidation of an ester of the poorly accessible (−)-D-tartaric acid.

We chose the route for the synthesis of (+)-disparlure (IV) through (7R,8S)-2-methyl-7,8-epoxyoctadec-9-ene (V), as the chiral synthon for which we used (2S,3R)-8-methyl-2,3-epoxynonan-1-ol (III) which is more readily accessible because of the use of an ester of (+)-L-tartaric acid at the stage of epoxidating 6-methylnon-2-Z-en-1-ol (II). The allyl alcohol (II) was obtained by the stereospecific carboalumination of acetylene with tris(5-methylhexyl)aluminum [15] and the subsequent interaction of the organoaluminum intermediate (I) with formaldehyde. The asymmetric epoxidation of the (Z)-allyl alcohol (II) was performed by a modified Sharpless method [16]. Oxidation of the epoxy alcohol (III) to the epoxy aldehyde (IV) and subsequent olefinization with the aid of n-nonylidenetriphenylphosphorane led to the unsaturated epoxide (V), the hydrogenation of which over 5% Pd/C gave the desired (+)-disparlure (VI) containing as impurity (~25%) the ketone (VII), obviously formed

Institute of Chemistry, Bashkir Scientific Center, Urals Branch, Academy of Sciences of the USSR, Ufa. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 715-718, September-October, 1989. Original article submitted December 19, 1988; revision submitted April 11, 1989.

 0009-3130/89/2505-0610$12.50