DETERMINATION OF α,α-DIMETHYL-β-HYDROXYPROPIONALDEHYDE CYANOHYDRIN IN REACTION SOLUTIONS BY GAS—LIQUID CHROMATOGRAPHY

E. I. Byalaya, O. V. Tsvetkova, V. I. Gunar,
L. A. Yakobson, and M. Ts. Yanotovskii

UDC 547.491.06:543.544.45

α,α-Dimethyl-β-hydroxypropionaldehyde cyanohydrin (I) is an intermediate in pantolactone synthesis. It is formed by cyanohydrin formation from α,α-dimethyl-β-hydroxypropionaldehyde (II) with acetone cyanohydrin [1].

To achieve a check on the process of cyanohydrin formation in the manufacture of pantolactone it is necessary to determine I in the presence of the initial II and of acetone cyanohydrin. This problem was resolved by us with the aid of gas—liquid chromatography (GLC).

It is known that aldehyde cyanohydrins are unstable and on heating are cleaved into the initial aldehyde and hydrogen cyanide [2]. Decomposition of cyanohydrin (I) goes completely at 70°C. As a result, to analyze I in the presence of starting II by GLC is impossible.

To analyze thermally unstable compounds containing hydroxy groups by GLC use is made of their trimethylsilyl derivatives [3] which are readily formed in pyridine with trimethylchlorosilane and hexamethyldisilazane. Polar phases are used for chromatography of the trimethylsilyloxy derivatives [3]. Thus it seemed expedient to analyze the products (II) of cyanohydrin formation as their trimethylsilyloxy derivatives on a stationary phase of the polyethyleneglycol type.

Development of a method of analysis was carried out on a GCH7 18.3 instrument (GDR) with a thermal conductivity detector. As stationary phase 15% polyethyleneglycol-20000 on Chromaton N-AW-HMDS (particle size 0.16-0.20 mm) was used. For determining changes of content of reaction products it was necessary to show their absolute content in the reaction mixture. With this aim tridecane was used as internal standard.

To obtain optimal amounts of trimethylsilyloxy derivatives of cyanohydrin reaction products viz., α,γ-di(trimethylsilyloxy)-β,β-dimethylbutyronitrile (III) and α,α-dimethyl-β-trimethylsilyloxypropionaldehyde (IV) the effect of different amounts of trimethylchlorosilane and of hexamethyldisilazane on the completeness of silylation was investigated. To I (1.0 mg/mole) in pyridine (3 ml) was added hexamethyldisilazane and trimethylchlorosilane in amounts from 1.1 to 3.7 mg/mole each. A sample was put into the chromatograph after 5-30 min. It was established chromatographically that the silylation process went completely in 5-7 minutes in pyridine on interacting I, hexamethyldisilazane, and trimethylchlorosilane in molar ratios of 1.00:1.32:1.32. For the silylation of II the molar ratio of reacting substances was 1.00:0.66:0.66. Silylation of the hydroxy groups of I and II under the optimal conditions indicated above permitted the preparation of IV in 96% yield and III in 95% yield.

Chromatography of trimethylsiloxy derivatives using a GCHF 18.1 (GDR) instrument was carried out under the following optimal conditions: column temperature 115°, evaporator 200°, carrier gas (helium) flow rate 40 ml/min, detector current 190 mA. Retention time of the column, with 519 theoretical plates for III, was 3 min 30 sec for tridecane, 5 min 5 sec for III, and 9 min 15 sec for IV (see Fig. 1).

All-Union Scientific-Research Institute of Vitamins, Moscow. Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 10, No. 11, pp. 141-142, November, 1976. Original article submitted April 16, 1976.

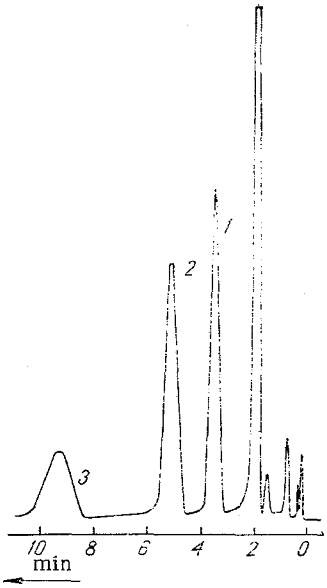

Fig. 1. Chromatogram of a mixture of III and IV with added tridecane. 1) Tridecane; 2) III; 3) IV.

Calibration curves with coordinates g_2/g_1 (abscissa) and S_2/S_1 (ordinate) and with coordinates g_3/g_1 and S_3/S_1* were constructed from data of the chromatography of eight synthetic mixtures of standard specimens of III, IV, and tridecane. The parameters of the calibration curves, viz., the slopes and intercepts on the ordinate axis, were found by the method of least squares. The mean square deviation of the calibration plot was 7.3 relative % for III and 6.6 relative % for IV.

Samples of manufactured solutions of the products of cyanohydrin formation from II were analyzed after adding tridecane to a weighed portion of reaction solution previously having removed moisture in vacuum at a temperature not exceeding 50° and having carried out silylation with hexamethyldisilazane and trimethylchlorosilane in pyridine solution.

EXPERIMENTAL

Cyanohydrin Formation from α,α-Dimethyl-β-hydroxypropionaldehyde (I). A mixture of II (1.0 g) acetone cyanohydrin (0.9 g), water (0.6 ml), and 3% alcoholic potash solution (0.2 ml) was mixed for 30 min. The obtained solution was diluted with water (8 ml) and stirred with KU-2 cation exchange resin (H^+ form) to pH 3.0. The resin was filtered off and washed with water. The filtrate and washings were evaporated and dried at 40-46° and 10-12 mm. Compound I (1.24 g: 97.6%) was obtained. Found, %: C 55.57; H 8.58; N 10.90. $C_6H_{11}NO_2$. Calculated, %: C 55.79; H 8.58; N 10.85.

α,γ-Di(trimethylsiloxy)-β,β-dimethylbutyronitrile (III). To a solution of I (4.7 g) in dry pyridine (20 ml) was added hexamethyldisilazane (7.9 g, 10.9 ml) and trimethylchlorosilane (5.4 g, 6.2 ml). The reaction mixture was stirred for 7 min then evaporated. The residue was distilled in vacuum. Compound III (9.5 g: 95.2%) was obtained, bp 74.0-74.6° (2 mm). Found, %: C 52.62; H 9.89; N 5.12; Si 20.43. $C_{12}H_{27}NO_2Si_2$. Calculated, %: C 52.69; H 9.95; N 5.12; Si 20.54.

α,α-Dimethyl-β-trimethylsilyloxypropionaldehyde (IV). To a solution of II (3.8 g) in dry pyridine (15 ml) was added hexamethyldisilazane (4.0 g, 5.5 ml) and trimethylchlorosilane (2.7 g, 3.2 ml). The reaction mixture was stirred for 7 min and then evaporated. The residue was distilled in vacuum. Compound IV (6.3 g: 95.2%) was obtained, bp 96-98° (3 mm). Found, %: C 55.07; H 10.57; Si 16.31. $C_8H_{18}O_2Si$. Calculated, %: C 55.11; H 10.42; Si 16.31.

---

*g_1, g_2, and g_3 are known weights of tridecane, III, and IV. S_1, S_2, and S_3 are peak areas on a chromatogram of tridecane, III, and IV.

LITERATURE CITED

1. E. S. Zhdanovich, E. I. Byalaya, V. N. Krylova, et al., Inventor's Certificate No. 150525: Byull. Izobret., No. 19, 22 (1962).
2. E. N. Zil'berman, Reactions of Nitriles [in Russian], (1972), p. 31.
3. C. C. Swelly, R. Bantley, M. Makita, et al., J. Am. Chem. Soc., 85, 2497 (1963).