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RHAMNOSE ORTHOACETATES OF ACONITINE AND IMPERIALINE

N. Sh. Pal'ants, R. Sh. Shakirov, M. N. Sultankhodzhaev, and S. T. Akramova

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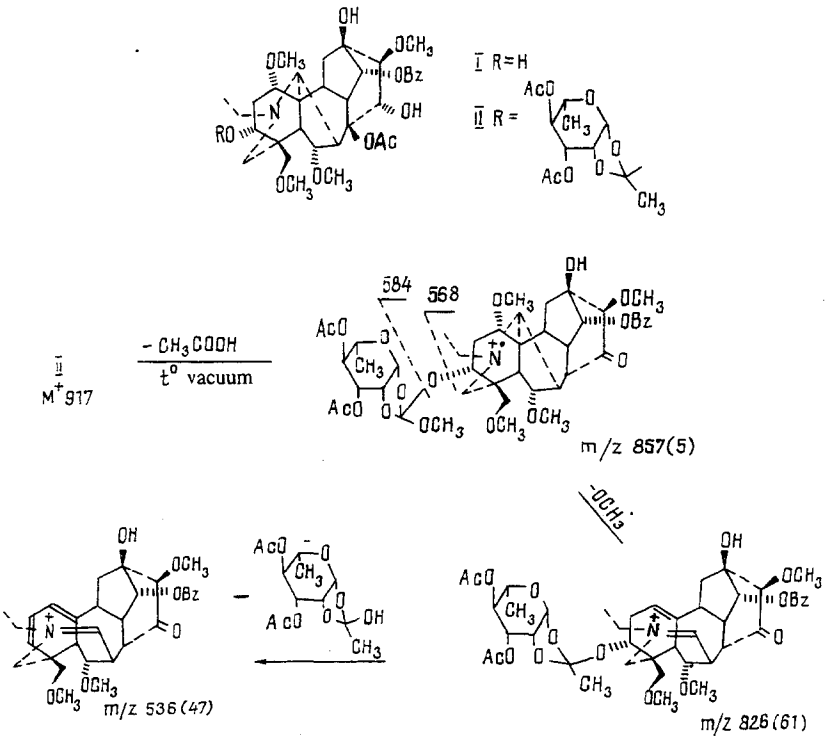
The preparation and spectral properties of rhamnose orthoacetates of aconitine and imperialine are described.

Up to the present, no glycosylated diterpene alkaloids have been found in nature, nor have they been obtained by synthesis. We have studied the reaction of the diterpene alkaloid aconitine (I) with acetobromorhamnose by the Koenigs–Knorr method [1], and have obtained substance (II) as the main product.

The PMR spectrum of substance (II) showed the signals of the N-ethyl, 8-acetoxy, benzoyl and four methoxy groups of the aconitine moiety and of the two acetoxy groups and the 5′-methyl group of the rhamnose moiety. The signals of methylene protons appeared in the 4.00-4.15 ppm region. A three-proton singlet at 1.70 ppm from the protons of a methyl group showed that the product was an orthoester with the –OR group in the exo- position [2, 3]. The signal of the anomeric proton of rhamnose appeared at 5.40 ppm in the form of a doublet with a SSCC of 3 Hz. The peak of the molecular ion was absent from the mass spectrum of (II), but the peak of a $M^+ - 60$ ion formed by the elimination of an acetic acid molecule under the conditions of mass spectrometry [4] was present. The mass-spectrometric fragmentation of (II) showed that rhamnose orthoacetate was attached to the hydroxy group at C-3. The mass spectrum of (II) had intense peaks of ions formed on the ejection of a methoxy radical from C-1 (m/z 826), of rhamnose acetate at C-3, and of a proton at C-2 (m/z 536) with the formation of a $\Delta^{2,3}$ double bond. Consequently, the product obtained was 3-O-[1′,1′-(3″,4″-di-O-acetylrhamnopyranose-1″,2″-diyloxy)-1′-ethyl]aconitine (II).



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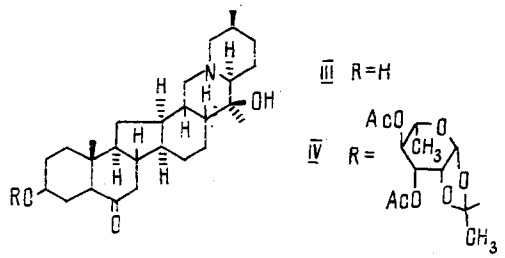
Continuing a study of the reaction of imperialine (III) [5] with acetobromosugars [6], we have reacted this steroid alkaloid with acetobromorhamnose and have obtained a product (IV) with the composition $C_{39}H_{58}NO_{10}$. The mass spectrum of compound (IV) included the peak of the molecular ion. In addition to the signals of protons belonging to the steroid part of the molecule, the PMR spectrum of (IV) showed the signals of two acetoxy groups, of the 5′-methyl group, and of the methine protons of rhamnose. A three-proton singlet of the methyl radical of the ethylidene group of the rhamnose derivative at 1.67 ppm showed that substance (IV) was an orthoester, with the −OR group in the exo- position [2, 3].



Thus, the compound obtained was 3-O-[1′,1′-(3″,4″-di-O-acetylrhamnopyranose-1″,2″-diyloxy)-1′-ethyl]imperialine (IV).

EXPERIMENTAL

Type KSK silica gel was used for chromatography.

PMR spectra were taken on a Tesla BS 567A, 100 MHz, instrument, mass spectra on a MKh-1310 spectrometer with a system for direct insertion into the ion source, and IR spectra on a UR-20 spectrophotometer in KBr tablets.

3-O-[1′,1′-(3″,4″-Di-O-acetylrhamnopyranose-1″,2″-diyloxy)-1′-ethyl]aconitine (II). Aconitine (I) (0.19 g, 0.25 mole) was dissovled in 10 ml of tetrahydrofuran, and to this solution were added 30 ml of ether, 0.5 g of 4Å mólcular sieve, 0.5 g of Ag_2O, and a solution of 0.353 g (1 mmole) of acetobromorhamnose in 10 ml of ether that had previously been kept over 4Å molecular sieve or 15 min. The mixture was stirred at room temperature for 24 h, the course of the reaction being monitored by TLC in the chloroform−methanol (9:1) system. Thus gave 0.113 g of product (II), mp 185-192°C (from methanol) $[\alpha]_D^{22}$ + 0.3° (c 0.84; chloroform).

IR spectrum: (ν_{max}^{KBr}, cm^{-1}): 720, 860, 905, 960, 1000, 1040, 1060, 1110, 1130, 1170, 1250, 1290, 1390, 1470, 1740, 1760, 2970, 3510. Mass spectrum (m/z, %): M^+ — 60, 875 (5), 842 (3), 826 (61), 798 (2), 796 (1), 628 (4), 612 (2), 596 (16), 584 (100), 568 z(60), 554 (83), 536 (47), 526 (5), 524 (3), 522 (7), 273 (35), 213 (8), 207 (10), 115 (8), 111 (35), 105 (52). PMR spectrum: ($CDCl_3$, δ, ppm, 0 — HMDS): 1.15 (3H, t, J = 7 Hz, $N-CH_2-CH_3$), 1.18 (3H, d, J = 5.5 Hz, CH_3 of rhamnose), 1.37 (3H, s, 8-$OCOCH_3$), 1.70 (3H, s, CH_3 of the rhamnose ethylidiene group), 2.00 (6H, s, 2 × $OCOCH_3$), 3.15; 3.17; 3.22; 3.68 (each 3H, s, 4 × OCH_3), 4.00-4.15 (8H, m, methine protons), 5.40 (1H, d, J = 3 Hz, H-1′), 7.75 and 7.88 (5H, m, 5-Ar−H).

3-O-[1′,1′-(3″,4″-di-O-acetylrhamnopyranose-1″,2″-diyloxy)-1′-ethyl]imperialine (IV). A solution of 2 g of imperialine (III) in 10 ml of chloroform was treated with 100 ml of toluene, 4.8 g of Ag_2CO_3 and 4 g of 4Å molecular sieve, and the mixture was heated to the boil. After the solvent had been distilled off, 5 g of acetobromorhamnose in toluene was added over 1.5 h, azeotropic distillation being continued at such a rate that the volume of the reaction mixture remained constant. The course of the reaction was monitored by TLC on silica gel in the chloroform−methanol (10:1) system. The reaction mixture was filtered, and the filtrate was evaporated in vacuum to dryness. The residue was chromatographed on a column of silica gel with elution successively by chloroform and chloroform−methanol in ratios of 10:1, 10:2, and 10:5. Elution with the chloroform−methanol (10:1) mixture yielded product (IV), mp 255-257°C (acetone−petroleum ether (9:1))

Mass spectrum of (IV), m/z: 701 (M^+), 686, 683, 658, 644, 628, 630, 471, 454, 428, 412, 393, 384, 368, 356, 340, 289, 273, 260, 171, 153, 156, 140, 124, 112 (100%), 98. PMR spectrum ($CDCl_3$, δ, ppm, 0 — HMDS): 0.65 (3H, s, H-19), 1.00 (3H, s, H-21), 1.04 (3H, d, J = 6.5 Hz, H-27), 1.15 (3H, d, J = 5.5 Hz, CH_3 of rhamnose), 1.67 (3H, s, CH_3 of the rhamnose ethylene group), 2.00, 1.95 (each 3H, 2 × $OCOCH_3$); 3.30-3.60 (2H, m, H-3 and H-5′); 4.47 (1H, m, H-2′), 5.00, 4.95 (2H, m, H-3′ and H-4′), 5.26 (1H, d, J = 2.5 Hz, H-1′).

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