Reaction of guaianolide achillin with chlorine in methanol

O. V. Alebastrov,[a] V. A. Raldugin,[b] M. M. Shakirov,[b] I. Yu. Bagryanskaya,[b] Yu. V. Gatilov,[b]*
A. T. Kulyjasov,[a] S. M. Adekenov,[a] and G. A. Tolstikov[b]

[a]*Institute of Phytochemistry, Ministry of Sciences and Higher Education of Kazakhstan Republic,*
P.O. Box 19, ul. Erzhanova, 470032 Karaganda, Kazakhstan Republic.
Fax: +7 (321 2) 43 3773. E-mail: arglabin@phyto.karaganda.su
[b]*N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences,*
9 prosp. Akad. Lavrent'eva, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 4752. E-mail: raldugin@nioch.nsc.ru

The reaction of sesquiterpene lactone achillin with chlorine in methanol afforded four products, *viz.*, two monochlorides and two dichlorides. One of these monochlorides is an intermediate in the formation of both dichlorides. The structures of the reaction products were established by two-dimensional NMR spectroscopy. The structure of one of the products was also established by X-ray diffraction analysis.

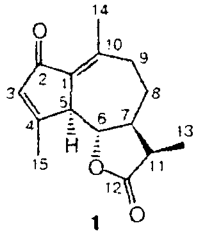
Key words: sesquiterpenoids, guaianolides, achillin; chlorination; two-dimensional NMR spectroscopy; X-ray diffraction analysis.

Sesquiterpene lactone achillin (**1**) was isolated for the first time from the plant *Achillea lanulosa* in 1963.[1] The stereochemistry of molecule **1** was established based on the results of chemical synthesis.[2] This lactone is a readily accessible compound.[3] Its natural 8α-hydroxy derivative (grossmisin),[1] C(11)-epimer (desacetoxymatricarin or leucomisin),[4] and 11-epi-8α-acetoxy derivative (matricarin)[5] were described. These compounds contain the same conjugated diene system and the guaiane carbon skeleton.

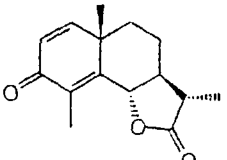
Chloro derivatives of sesquiterpene lactones have attracted interest over many years.[6] Among these derivatives, more than 30 natural compounds[7] were described, many of which exhibit pronounced physiological activity.[8,9] In connection with this interest, we performed for the first time the reaction of lactone **1** with chlorine in methanol at room temperature and isolated the reaction products. Previously, it has been demonstrated[10,11] that selinane-type dienone lactone, *viz.*, α-santonin (**2**), readily enters into the reaction under analogous conditions to form methoxychloride **3**. The molecular structure of **3** was established by X-ray diffraction analysis of the corresponding des-*O*-methyl derivative.

It appeared that achillin (**1**) reacted completely with chlorine to form four products **4**—**7** (TLC data) in 28, 11, 20, and 14% yields, respectively (after chromatographic separation on SiO_2).

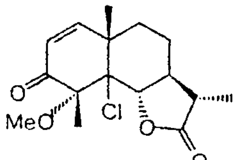
The mass spectra of methoxydichlorides **4** and **5** do not have molecular ion peaks, but the results of elemental analysis taking into account the data of ^{13}C NMR spectroscopy demonstrated that these compounds are isomers of the general formula $C_{16}H_{20}Cl_2O_4$. The molecular structures of these compounds were established by ^{13}C and ^1H NMR spectroscopy (Tables 1 and 2,



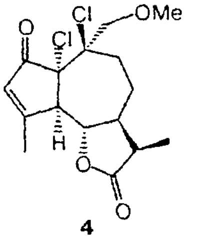
1



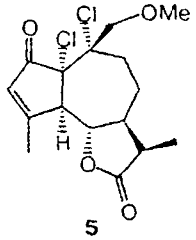
2



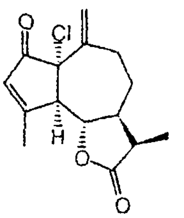
3



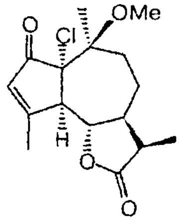
4



5



6



7

Published in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 1635—1639, September, 2000.

1066-5285/00/4909-1624 $25.00 © 2000 Kluwer Academic/Plenum Publishers

Table 1. Parameters of the ^{13}C NMR spectra ($CDCl_3$, δ) of compounds **4—7**

Atom	**4**	**5**	**6**	**7**
C(1)	75.04 (s)	77.34 (s)	72.62 (s)	75.17 (s)
C(2)	197.88 (s)	195.70 (s)	199.80 (s)	200.28 (s)
C(3)	129.93 (d)	127.87 (d)	130.01 (d)	129.65 (d)
C(4)	176.73 (s)	173.84 (s)	175.51 (s)	176.14 (s)
C(5)	65.65 (d)	63.38 (d)	65.08 (d)	64.23 (d)
C(6)	80.59 (d)	81.63 (d)	82.85 (d)	82.51 (d)
C(7)	42.46 (d)	40.37 (d)	44.30 (d)	41.71 (d)
C(8)	22.82 (t)	24.01 (t)	29.23 (t)	22.41 (t)
C(9)	30.43 (t)	39.03 (t)	32.23 (t)	32.55 (t)
C(10)	76.22 (s)	76.14 (s)	143.77 (s)	82.39 (s)
C(11)	38.92 (d)	38.97 (d)	38.35 (d)	38.99 (d)
C(12)	178.54 (s)	178.59 (s)	178.24 (s)	179.09 (s)
C(13)	10.52 (q)	10.38 (q)	11.24 (q)	10.73 (q)
C(14)	75.64 (t)	77.27 (t)	118.82 (t)	21.31 (q)
C(15)	19.02 (q)	17.96 (q)	19.98 (q)	19.03 (q)
C(16)	59.38 (q)	59.14 (q)	—	50.50 (q)

respectively). The assignment of the signals was made using two-dimensional ^{1}H—^{1}H (COSY) and ^{13}C—^{1}H (COSY, COLOC) NMR spectra. We used the known procedure for the analysis of ^{13}C and ^{1}H NMR spectra,[12] which we have successfully applied previously in the case of more complex subjects, *viz.*, triterpenic ethers containing the spirane fragment in the carbon skeleton[13] and lanostane-type lactones.[14]

The question concerning the configurations of the asymmetric C(1) and C(10) centers in the molecules of the chlorides under study was solved as follows. Monochloride **6** is an intermediate in the formation of dichlorides **4** and **5** (this fact was confirmed by the model experiment). X-ray diffraction study demonstrated that the Cl atom in this monochloride is in the α-orientation, which is in agreement with evidence that the α-side is sterically more favorable for the addition at the $\Delta^{10(1)}$-double bond in the molecule of guaiane dienone of type **1**.[15] The structure and the absolute configuration of molecule **6** are shown in Fig. 1. The bond lengths in the molecule are close to the standard values.[16] The seven-membered ring in **6** adopts a slightly distorted chair conformation. The lactone ring assumes an envelope conformation with the C(7) atom deviating from the plane through the remaining four atoms (the average deviation from the plane is 0.019 Å) by −0.425(7) Å. The cyclopentene fragment is planar to within ±0.05 Å. The closest analog of compound **6** available in the Cambridge Structural Database is 10-epi-8-desoxycumambrin B.[17] On the whole, the seven-membered rings in these molecules have similar geometric parameters and conformations. However, it should be noted that the cyclopentene fragment in the molecule of the above-mentioned lactone,[17] unlike that in molecule **6**, adopts a flattened envelope conformation, and the twist conformation of the lactone ring in the former molecule is more pronounced.

The stereochemistry of the environment at the C(10) atom in epimeric methoxydichlorides **4** and **5** was not established by X-ray diffraction analysis because we failed to obtain crystals of these compounds suitable for X-ray studies. Hence, we proceeded from the facts that the long-range spin-spin coupling between the H(14B) and H(9A) protons is manifested in the ^{1}H NMR spectrum of the minor methoxydichloride (^4J = 1.1 Hz, see Table 2), whereas this coupling is not observed in the ^{1}H NMR spectrum of the major methoxychloride. It is known that the cycloheptane ring can adopt a chair, boat, twist-chair, or twist-boat conformation.[18] The flexibility of this ring is decreased because it is fused with two five-membered rings. Dreiding models demonstrated

Table 2. Parameters of the ^{1}H NMR spectra of compounds **4—7** ($CDCl_3$, Me_4Si, δ, J/Hz)

Proton	**4**	**5**	**6**	**7**
H(3)	6.14 (dq, J = 2; 1.5)	6.12 (dq, J = 2.4; 1.4)	6.18 (quint, J = 1.5; 1.5)	6.05 (quint, J = 1.5)
H(5)	3.49 (ddq, J = 9.6; 2.0; 1.5)	3.66 (ddq, J = 9.0; 2.4; 1.4)	3.36 (ddq, J = 10.5; 2.3; 1.5)	3.44 (ddq, J = 10.5; 2; 1)
H(6)	4.85 (t, J = 9.5)	4.62 (dd, J = 11.0; 9.0)	4.06 (t, J = 10.5; 10.5)	4.60 (t, J = 9.0)
H(7)	2.72 (m)*	2.92 (m)	2.73 (m)	2.68 (m)*
H(8A)	1.83 (dm, J = 14)	1.78 (m)	1.97 (dm, J = 13)	1.65 (dm, J = 14)
H(8B)	1.76 (m)	1.65 (m)	1.43 (m)	1.47 (m)
H(9A)	2.63 (dt, J = 15.5; 4.0)	2.77 (dddd, J = 15.2; 13.0; 4.5; 1.1)	2.85 (br.ddd, J = 13.5; 13.5; 4.5)	2.34 (ddd, J = 15.0; 13.0; 4.5)
H(9B)	2.33 (ddd, J = 15.5; 12.5; 3.8)	2.29 (dt, J = 15.2; 7.4)	2.45 (dddd, J = 13.5; 4.3; 3.6; 0.7)	1.85 (dt, J = 15.0; 3.8)
H(11)	2.72 (m)*	2.73 (quint, J = 7.8)	2.73 (m)	2.70 (m)*
3 H(13)	1.22 (d, J = 7.5)	1.18 (d, J = 7.8)	1.16 (d, J = 7.8)	1.20 (d, J = 7.8)
H(14A)	3.86 (d, J = 11.0)	3.50 (d, J = 10.6)	5.17 (br.s)	1.42 (s, 3 H(14))
H(14B)	3.99 (d, J = 11.0)	3.41 (dd, J = 10.6; 1.1)	4.90 (br.d, J = 1.0)	
3 H(15)	2.25 (t, J = 1.4)	2.22 (t, J = 1.4)	2.28 (t, J = 1.5; 1.5)	2.20 (t, J = 1.4)
H_3CO	3.38 (s)	3.25 (s)		3.11 (s)

* Signals overlap with each other.

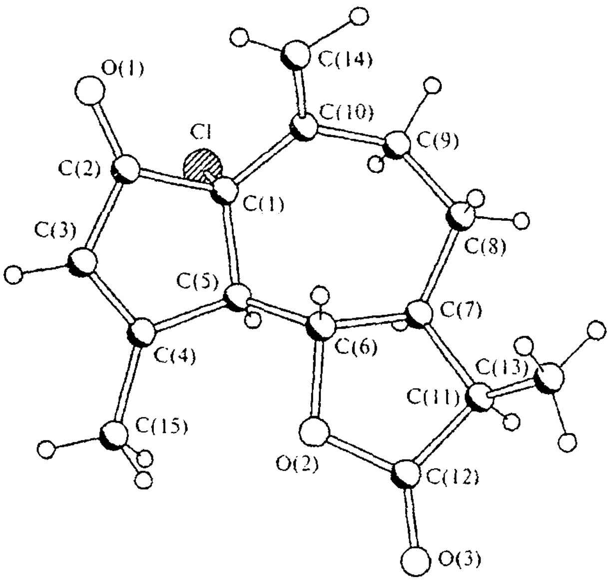


Fig. 1. Molecular structure of chloride **6**.

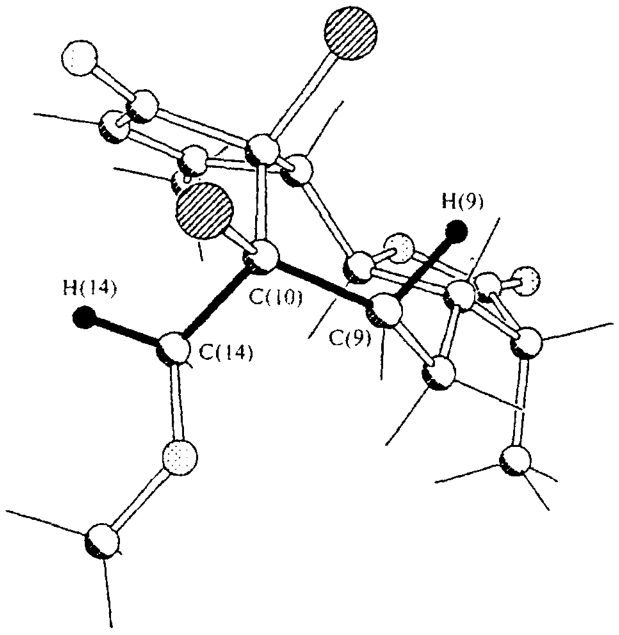


Fig. 2. Conformation of the molecule of methoxychloride **5** (the H(14)—C(14)—C(10)—C(9)—H(9) chain adopting the W-type configuration is marked).

that the cycloheptane fragment in molecules **4** and **5** can adopt either one of two distorted chair conformations or a distorted twist-boat conformation. Then, we performed calculations using the Chem3D program[19] and demonstrated that the conformations of the carbon skeletons in molecules **4** and **5** corresponding to the energy minima are virtually identical. The seven-membered carbon ring in these compounds has one of two distorted chair conformations, which is very similar to that observed in the molecule of methoxychloride **6** in the crystal. For this conformation, the W-type configuration of the H(14)—C(14)—C(10)—C(9)—H(9) chain, which is necessary for the manifestation of long-range spin-spin coupling through four σ-bonds,[20] is realized only if the $-CH_2OMe$ fragment adopts the β-configuration (Fig. 2). In the case of the α-configuration of this fragment, long-range spin-spin coupling can also occur, but only if the seven-membered ring has the second type of distorted chair conformation, which is, however, more strained (according to the results of calculations by the MM2 and PM3 methods, ΔE = 18.8 and 5.9 kJ mol^{-1}, respectively) and is energetically less favorable. Therefore, the configuration at the C(10) atom in the major epimer corresponds to formula **4**, whereas this configuration in the minor epimer, in which long-range spin-spin coupling between the H(14B) and H(9A) protons is observed, corresponds to formula **5**.

In the mass spectrum of methoxymonochloride **7**, the highest-mass ion peak belongs to $[M - Cl]^+$ ($C_{16}H_{21}O_4$). The presence of one chlorine atom in the molecule of this reaction product was confirmed by the results of elemental analysis, and the structure of this product was established based on the data of two-dimensional $^1H-^1H$ (COSY) and $^{13}C-^1H$ (COSY, COLOC) NMR spectroscopy. The configurations of the C(1) and C(10) centers in this molecule were proposed as the most probable. These configurations correspond to the "normal" product of *trans*-antiparallel addition of Cl^+ and MeO^- ions as a result of the initial attack of the Cl^+ cation on the achillin molecule from the sterically more favorable α-side.

For the methoxymonochloride under consideration, the structure of 1,10-diepi-**7** is also not ruled out. This product can be formed through analogous successive addition of the Cl^+ and MeO^- ions, but the initial attack of the Cl^+ ion on the molecule of lactone **1** should occur from the sterically more shielded β-side. The fact that under the conditions of electrophilic addition, the halogenonium ion can give minor products corresponding to its attack from the sterically more shielded side has been noted previously, in particular, in the reaction of macrocyclic diterpenoid cembrene with *N*-bromosuccinimide in aqueous acetone.[21] However, the ^{13}C NMR spectrum does not confirm the possibility of this situation occurring and demonstrates that chloride **7** corresponds stereochemically to dichloride **4** (see Table 1, the signals for the C(1)—C(5), C(8), and C(9) atoms).

The signals for the C(14) and C(15) atoms in the ^{13}C NMR spectrum of lactone **1** have not been unambiguously assigned in the study.[22] This problem can be readily solved with the use of two-dimensional $^{13}C-^1H$ NMR (COSY) spectroscopy after the assignment of the low-field signal of the methyl group (at δ 2.38; d, J = 1.0 Hz) and the signal of the second methyl group (at δ 2.31; dd, $^4J_{H(15),H(3)}$ = 1.4 Hz and $^4J_{H(15),H(5)}$ = 0.8 Hz) to $H_3C(14)$ and $H_3C(15)$, respectively. The data of $^{13}C-^1H$ correlation demonstrate that the ^{13}C signals with the smaller and larger chemical shifts belong to the C(15) and C(14) atoms, respectively.

Experimental

The melting points were determined on a Boetius instrument. The IR spectra were recorded on a Vector 22 instrument. The NMR spectra were measured on a Bruker DRX-500 spectrometer (500.13 and 125.76 MHz for ^1H and ^{13}C, respectively) with the use of standard programs (Bruker) for recording two-dimensional COSY and COLOC (7 Hz) NMR spectra.

The high-resolution mass spectra (EI, 70 eV) were recorded on a Finnigan MAT 8200 instrument. The optical rotation was measured (at 580 nm) on a Polamat A polarimeter.

Column flash chromatography was carried out on SiO_2 (Chemapol 40/100) with the use of a light petroleum—ethyl acetate mixture as the eluent, the content of the latter component being increased (from 0 to 60%). TLC was performed on Silufol plates; spots were visualized by spraying with a 1% vanillin solution in H_2SO_4.

The starting achillin (**1**) (m.p. 145.5—146.5 °C) was isolated from the above-ground part of *Achillea micrantha* according to a procedure reported previously.[3]

Chlorination of lactone 1 and separation of the reaction products. A flow of dry gaseous Cl_2 was passed through a solution of lactone **1** (0.227 g) in MeOH (15 mL) at 20 °C until the starting compound was completely converted into the reaction products (~30 min). The solvent was removed *in vacuo* with the use of a water aspirator pump. Dichloride **4**, chloride **7**, chloride **6**, and dichloride **5** were successively isolated by chromatography of the residue and crystallization of the resulting fractions from a light petroleum—ethyl acetate mixture in yields of 0.09 g (28%), 0.04 g (14%), 0.052 g (20%), and 0.035 g (11%), respectively; R_f were 0.67, 0.55, 0.47, and 0.22, respectively (Silufol, a 3 : 1 light petroleum—acetone mixture as the eluent).

1α,10β-Dichloro-1,10-dihydro-14-methoxyachillin (4). Crystals, m.p. 160—162 °C, $[\alpha]_{580}^{25}$ +207° (*c* 0.511, $CHCl_3$). Found (%): C, 55.55; H, 5.78; Cl, 20.20. $C_{16}H_{20}Cl_2O_4$. Calculated (%): C, 55.34, H, 5.80, Cl. 20.42. IR (KBr), ν/cm⁻¹: 1780 (γ-lactone); 1710 (C=O); 1625 (C=C); 1220, 1125, 1027, 985, 840 (C—O); 712 (C—Cl). UV (EtOH), λ_{max}/nm: 241 (ε 9500). MS, *m/z* (I_{rel} (%)): 309 $[M - H - HCl]^+$ (13), 275 $[M - Cl - HCl]$ (100), 149 (34), 57 (21), 45 (22). Found, *m/z*: 309.08565; calculated for $C_{16}H_{18}ClO_4$: *M* = 309.08935. The parameters of the ^{13}C and ^1H NMR spectra are given in Tables 1 and 2, respectively. Selected cross-peaks in the two-dimensional $^{13}C-^1H$ NMR spectrum (COLOC): C(1)/H(9A), H(5), H(3); C(10)/H(8A), H(9A), H(14A); C(14)/OMe.

1α,10α-Dichloro-1,10-dihydro-14-methoxyachillin (5). Crystals, m.p. 184—185 °C, $[\alpha]_{580}^{25}$ +182° (*c* 0.511, $CHCl_3$). Found (%): C, 55.61; H, 5.89; Cl, 20.06. $C_{16}H_{20}Cl_2O_4$. Calculated (%): C, 55.34, H. 5.80, Cl, 20.42. IR (KBr), ν/cm⁻¹: 1780 (γ-lactone); 1710 (C=O); 1625 (C=C); 1220, 1200, 1125, 1030, 985, 850 (C—O); 715 (C—Cl). UV (EtOH), λ_{max}/nm: 238 (ε 9300). MS, *m/z* (I_{rel} (%)): 311 $[M - Cl]$ (1.5), 275 $[M - Cl - HCl]$ (100), 55 (8), 45 (11). Found, *m/z*: 311.10646; calculated for $C_{16}H_{20}ClO_4$: *M* = 311.10500. The parameters of the ^{13}C and ^1H NMR spectra are given in Tables 1 and 2, respectively. Selected cross-peaks in the two-dimensional $^{13}C-^1H$ NMR spectrum (COLOC): C(1)/H(9B), H(3), H(14A); C(10)/H(8A); C(14)/OMe, H(9A).

1α-Chloro-1,10-dihydro-10,14-dehydroachillin (6). Crystals, m.p. 171—172 °C, $[\alpha]_{580}^{20}$ +261° (*c* 1.34, $CHCl_3$). IR (KBr), ν/cm⁻¹: 3080, 1000 ($C=CH_2$); 1780 (γ-lactone); 1710 (C=O); 1625 (C=C); 1205, 1030, 850 (C—O); 715 (C—Cl). UV (EtOH), λ_{max}/nm: 236 (ε 10900). MS, *m/z* (I_{rel} (%)): 280 $[M]^+$ (1.5), 245 $[M - Cl]^+$ (100), 171 (6), 105 (4), 91(6), 55(7). Found, *m/z*: 280.08614; calculated for $C_{15}H_{17}ClO_3$: *M* = 280.08661; found, *m/z*: 245.11855; calculated for $C_{15}H_{17}O_3$: *M* = 245.11776. The parameters of the ^{13}C and ^1H NMR spectra are given in Tables 1 and 2, respectively.

1α-Chloro-1,10-dihydro-10β-methoxyachillin (7). Crystals, m.p. 169—171 °C, $[\alpha]_{580}^{16}$ +116° (*c* 0.86, $CHCl_3$). Found (%): Cl, 11.50. $C_{16}H_{21}ClO_4$. Calculated (%): Cl, 11.33. IR (KBr), ν/cm⁻¹: 1780 (γ-lactone); 1710 (C=O); 1630 (C=C); 1216, 1190, 1033, 987, 840 (C—O); 715 (C—Cl). UV (EtOH), λ_{max}/nm: 237 (ε 11000). MS, *m/z* (I_{rel} (%)): 277 $[M - Cl]^+$ (93), 276 $[M - HCl]^+$ (48), 245 (15), 204 (35), 183 (16), 109 (21), 85 (100), 55 (33). Found, *m/z*: 277.14070; calculated for $C_{16}H_{21}O_4$: *M* = 277.14397. The parameters of the ^{13}C and ^1H NMR spectra are given in Tables 1 and 2, respectively. Selected cross-peaks in the two-dimensional $^{13}C-^1H$ NMR spectrum (COLOC): C(1)/3H(14), H(5), H(9B); C(10)/3H(14), OMe, H(8A).

Reaction of compound 6 with chlorine in MeOH. Dry gaseous Cl_2 was passed through a solution of monochloride **6** (10 mg) in MeOH (1 mL) at 20 °C until compound **6** was completely consumed (~5 min, TLC control). The reaction mixture was concentrated to dryness *in vacuo*, and the residue was obtained in a yield of 11 mg. According to the data of TLC and ^1H NMR spectroscopy, the residue consisted of two methoxydichlorides **4** and **5** (2.3 : 1.0; the ratio was determined from the relative integral intensities of the signals for the H(6) atom in the ^1H NMR spectrum).

X-ray diffraction study was carried out on a Bruker P4 diffractometer (Mo-Kα radiation, graphite monochromator, 2θ/θ scanning technique, 2θ < 50°). X-ray data were collected from a crystal of compound **6** of dimensions 1.20×0.70×0.5 mm. Crystals are orthorhombic: *a* = 10.328(1) Å, *b* = 10.832(1) Å, *c* = 12.235(2) Å, *V* = 1368.8(3) Å³, space group $P2_12_12_1$, *Z* = 4, $C_{15}H_{17}ClO_3$, d_{calc} = 1.362 g cm⁻³, μ = 0.280 mm⁻¹. A total of 1345 independent reflections were measured. The structure was solved by the direct method using the SHELXS-86 program package. The positions of the hydrogen atoms were calculated geometrically. The final refinement of the structural parameters was performed by the full-matrix least-squares method in the anisotropic-isotropic approximation (for H atoms) using the SHELXL-97 program package based on all F^2 to wR_2 = 0.1043, *S* = 1.121; 173 parameters were refined (*R* = 0.0439 based on 1192 reflections with $F > 4\sigma$). The absolute configuration of molecule **6** was determined using Flack's parameter (−0.44(19); for the inverted structure, Flack's parameter is equal to 1.28(19)). The complete tables of the bond lengths and bond angles, the atomic coordinates, and the equivalent thermal parameters of the nonhydrogen atoms for the structure of **6** were deposited with the Cambridge Structural Database.

We thank the Russian Foundation for Basic Research (Project No. 96-07-89187) for paying for the license for the Cambridge Structural Database. This work was financially supported by the Foundation for Basic Research of the Ministry of Sciences and Higher Education of the Kazakhstan Republic (F0092).

References

1. E. H. White and R. E. K. Winter, *Tetrahedron Lett.*, 1963, 137.
2. J. N. Marx and E. H. White, *Tetrahedron*, 1969, **25**, 2117.
3. S. M. Adekenov, N. M. Gafurov, F. Zh. Turmukhambetov, and V. I. Ivlev, *Khim. Prirod. Soedin.*, 1987, 305 [*Chem. Nat. Comp.*, 1987 (Engl. Transl.)].
4. M. Holub and V. Herout, *Coll. Czech. Chem. Commun.*, 1962, **27**, 2980.
5. K. H. Lee, R. F. Simpson, and T. A. Geissman, *Phytochemistry*, 1969, **8**, 1515.
6. E. Wedekind and A. Koch, *Ber. Deutsch. Chem. Ges.*, 1905, **38**, 429.
7. K. C. Engvild, *Phytochemistry*, 1986, **25**, 781.
8. S. M. Kupchan, J. E. Kelsey, M. Maruyama, and J. M. Cassady, *Tetrahedron Lett.*, 1968, 3517.
9. T. Osawa, A. Suzuki, S. Tamura, Y. Ohashi, and Y. Sasada, *Tetrahedron Lett.*, 1973, 5135.
10. H. Takyanagi, H. Osaka, T. Brian, and T. B. H. McMurry, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 1259.
11. H. Takyanagi, H. Ogura, and T. B. H. McMurry, *Chem. Pharm. Bull.*, 1990, **38**, 581.
12. *Two-Dimensional NMR Spectroscopy. Applications for Chemists and Biochemists*, Eds. W. R. Croasmun and R. M. K. Carlson, VCH Publishers, Veincheim, 1987, 233.
13. V. A. Raldugin, M. M. Shakirov, T. V. Leibyuk, and S. A. Shevtsov, *Khim. Prirod. Soedin.*, 1991, 511 [*Chem. Nat. Comp.*, 1991, 444 (Engl. Transl.)]
14. V. A. Raldugin, M. M. Shakirov, and A. G. Druganov, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2790 [*Russ. Chem. Bull.*, 1996, **45**, 2649 (Engl. Transl.)].
15. M. K. Makhmudov, A. B. Plutno, I. D. Sham'yanov, and V. Tashkhodzhaev, *Khim. Prirod. Soedin.*, 1995, 257 [*Chem. Nat. Comp.*, 1995 (Engl. Transl.)]
16. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1987, S1.
17. V. E. Sosa, J. C. Oberti, R. R. Gil, E. A. Ruveda, V. L. Goedken, A. B. Guierrez, and W. Herz, *Phytochemistry*, 1989, **28**, 1925.
18. J. B. Hendrickson, R. K. Boeckman, Jr., J. D. Glickson, and E. Grunwald, *J. Am. Chem. Soc.*, 1973, **95**, 494.
19. J. P. Bays, *J. Chem. Educ.*, 1992, **69**, 209.
20. H. Gunter, *NMR Spectroscopy. An Introduction*, Wiley, New York—London, 1980.
21. V. A. Raldugin, N. I. Yaroshenko, and M. M. Shakirov, *Khim. Prirod. Soedin.*, 1983, 150 [*Chem. Nat. Comp.*, 1983 (Engl. Transl.)]
22. N. Ohno, J. Gershenzon, C. Roane, and T. Mabry, *Phytochemistry*, 1980, **19**, 103.

Received September 22, 1999;
in revised form April 18, 2000