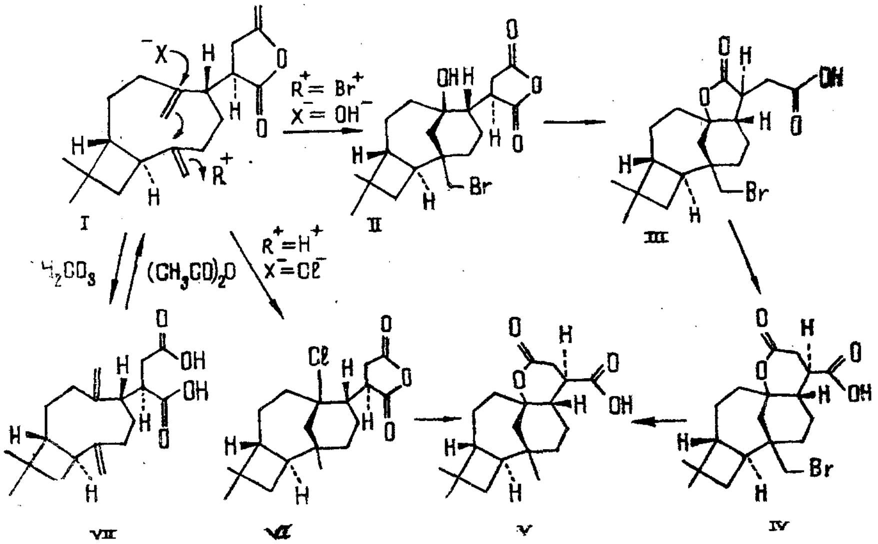
STRUCTURE OF THE "ADDUCT" OF CARYOPHYLLENE WITH MALEIC ANHYDRIDE AND ITS TRICYCLIC DERIVATIVE

Yu. V. Gatilov, A. V. Tkachev,
T. D. Drebushchak, Zh. V. Dubovenko,
and V. A. Pentegova

UDC 539.26:547.913.2

The structure of the N-methylanilide of 3-oxo-9,12,12-trimethyl-2-oxatetracyclo-$[7,6,1,0^{1,6}0^{10,13}]$hexadecane-5-carboxylic acid, obtained from the "adduct" of caryophyllene with maleic anhydride, has been investigated by x-ray structural analysis.

The reaction of caryophyllene with maleic anhydride has been discussed in a number of publications [1, 2]. After the elucidation of the structure of caryophyllene and the products of its cyclization, A. Nickon returned to the investigation of the structure of the "adduct" of caryophyllene with maleic anhydride [2]. For the "adduct" he proposed structure (I); the configuration at C5 was deduced by analogy with the reactions of caryophyllene with peracids. The adduct readily underwent a cyclization reaction of a new type with electrophilic reagents (scheme). The structure and stereochemistry of the tricyclic derivatives obtained (only the carbocyclic skeleton is considered) were proposed without sufficiently strict proofs [2]. Examples of such a direction of the cyclization of caryophyllene derivatives were given in later papers [3, 4].

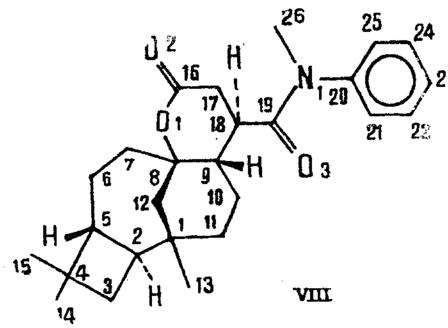


The adduct and its derivatives are of interest as the starting materials in the synthesis of various biologically active substances, and we therefore decided to establish the precise structure of some one derivative of this group of compounds by x-ray structural analysis.

We have repeated some of the reactions described by Nickon [2] and obtained identical results. In addition, we have recorded the PMR spectra of compounds (I-III, V, and VII). This spectral information does not contradict the structures given in the scheme, but not one of the compounds mentioned gave single crystals suitable for x-ray structural analysis.

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. I. G. Kutateladze Institute of Pharmacochemistry, Academy of Sciences of the Georgian SSR, Tbilisi. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 433-437, July-August, 1984. Original article submitted June 10, 1983.

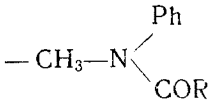
0009-3130/84/2004-0410$08.50



VIII

Fig. 1

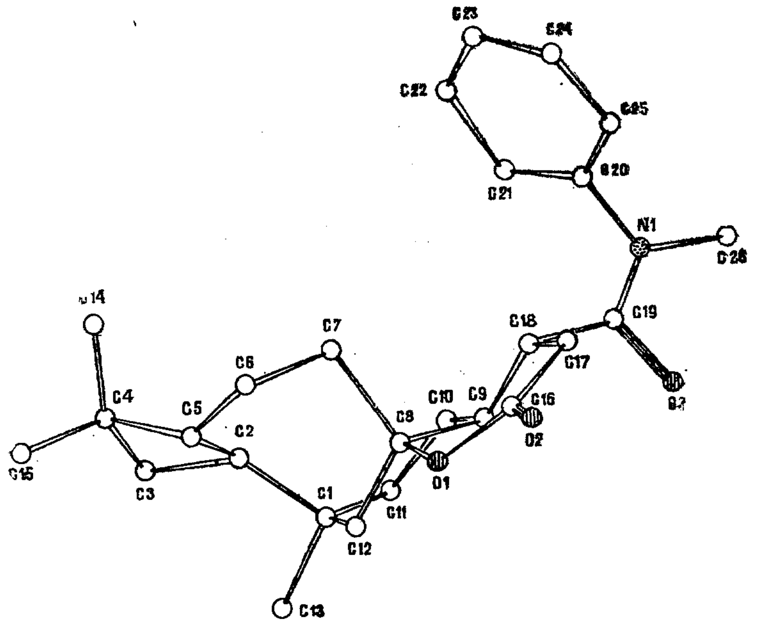
When 3-oxo-9,12,12-trimethyl-2-oxatetracyclo[7,6,1,$0^{1,6}0^{10,13}$]hexadecane-5-carboxylic acid (V) was treated with thionyl chloride, the corresponding chloride was readily obtained, and on the addition of N-methylaniline this was converted into the amide (VIII). This amide is a crystalline substance with mp 171-173°C which retains the δ-lactone ring (IR: 1730 cm^{-1}). The PMR spectrum of the amide contains the signals of a N-methylaniline residue: 3.24 ppm



$$-CH_3-N\begin{matrix}\diagup Ph\\ \diagdown COR\end{matrix}$$

and 7.06-7.63 ppm ($C_6H_5NR'R''$). The structure of this amide was also studied by x-ray structural analysis.

The structure of the molecules of (VIII) is shown in Fig. 1.* The geometry of the caryolane fragment is very close to that of the caryolane chloride molecule [4]. Thus, the seven-membered ring has the boat form and the six-membered ring the chair conformation, while the four-membered ring is nonplanar. The intracyclic torsional angles of the molecules of (VIII) are given in Table 1.



Configuration of the molecule of N-methylanilide, VIII

The δ-lactone ring is trans-linked with the six-membered ring of the carbon skeleton of the amide. The conformation of the lactone ring is close to the half-boat form in which the C9 atom deviates from the plane of the C8, O1, C16, C17, and C18 atoms. The amide fragment C18, C19, N1, O3, C26 is planar to within 0.05 Å and is arranged quasi-equatorially with respect to the lactone ring. The phenyl ring is also planar with an accuracy of ±0.02 Å and is rotated by an angle of 101° relative to the plane of the amide fragment. The intermolecular contacts are the usual ones.

---

*The numbering of the carbon atoms of the caryolane skeleton is used in Fig. 1.

TABLE 1. Some Torsion Angles of the Molecule (VIII)

Angle	Value, degrees	Angle	Value, degrees
C5C2C3C4	22	C12C1C11C10	—50
C2C3C4C5	—22	C11C1C12C8	53
C3C4C5C2	22	C1C12C8C9	—63
C4C5C2C3	—23	O1C8C9C18	—60
C12C1C2C5	—25	C8C9C18C17	56
C1C2C5C6	73	C9C18C17C16	—26
C2C5C6C7	—5	C18C17C16O1	1
C5C6C7C8	—62	C17C16O1C8	—7
C6C7C8C12	29	C9C8O1C16	35
C7C8C12C1	63	C9C18C19N1	133
C8C12C1C2	—65	C17C18C19N1	—102
C12C8C9C10	56	C18C19N1C20	2
C8C9C10C11	—51	C19N1C20C21	—85
C9C10C11C1	50	C19N1C20C25	98

TABLE 2. Coordinates of the Atoms ($\times 10^4$) of the Molecule of (VIII)

Atom	x	y	z	$\frac{1}{3}\sum_i B_{ii}$ (Å²)
C1	2552 (13)	4073 (12)	6604 (9)	3,8
C2	3425 (11)	4079 (12)	5928 (8)	3,4
C3	3316 (15)	4603 (13)	5089 (8)	5,3
C4	4088 (17)	3625 (13)	4766 (9)	4,6
C5	3688 (13)	3012 (11)	5504 (9)	3,7
C6	4428 (14)	2174 (13)	5945 (9)	4,7
C7	4729 (13)	2504 (12)	6826 (8)	3,7
C8	3604 (13)	2631 (11)	7369 (9)	3.8
C9	3879 (13)	3402 (12)	8090 (8)	3,1
C10	3921 (12)	4553 (12)	7771 (8)	3,7
C11	2859 (12)	4881 (11)	7273 (9)	4,1
C12	2503 (13)	2953 (12)	6981 (8)	3,7
C13	1269 (14)	4331 (13)	6270 (9)	5.2
C14	5290 (13)	3915 (14)	4699 (10)	7,1
C15	3621 (17)	3141 (16)	3974 (10)	7,3
C16	3961 (14)	1181 (15)	8366 (9)	3,7
C17	4746 (15)	1881 (14)	8836 (9)	4,7
C18	4908 (12)	3047 (14)	8547 (9)	4,0
C19	5249 (20)	3732 (14)	9285 (10)	5,4
C20	7223 (14)	3755 (14)	8967 (9)	4.4
C21	7446 (15)	4352 (13)	8306 (10)	5,3
C22	8498 (19)	4075 (18)	7869 (11)	7,9
C23	9169 (15)	3211 (19)	8073 (11)	5,9
C24	8894 (17)	2621 (15)	8731 (13)	6,4
C25	7889 (16)	2904 (16)	9205 (10)	5.5
C26	6445 (15)	4597 (13)	10232 (9)	6,6
N1	6271 (11)	4058 (12)	9463 (8)	4,8
O1	3383 (8)	1560 (8)	7707 (6)	4.4
O2	3800 (10)	0265 (9)	8543 (7)	5,9
O3	4346 (10)	3994 (9)	9685 (6)	6,0

The results that we have obtained completely confirm the structure and stereochemistry of the adduct of caryophyllene with maleic anhydride and its tricyclic derivatives proposed by A. Nickon.

EXPERIMENTAL

Compounds (I-III, V, and VII) were obtained as described by Nickon [2].

Preparation of the N-Methylanilide (VIII). The acid (V) (2.5 g) was dissolved in 20 ml of a mixture of benzene, chloroform, and CCl_4 (1:1:1). The solution was cooled to 0°C, and, with stirring and cooling 0.62 g of pyridine and 0.93 g of $SOCl_2$ were added to it. The reaction mixture was kept at 0°C for 2 h and then, with stirring, 0.62 g of pyridine and 2 g of N-methylanilide were added dropwise. The mixture was left at room temperature for 1 h. After elimination of the solvent, the residue was treated with 20 ml of ether and 20 ml of water, and the ether layer was separated off and washed with hydrochloric acid, with water, with aqueous $NaHCO_3$, and with water again and was dried over anhydrous Na_2CO_3. The residue after the elimination of the solvent was recrystallized from methanol, giving 3.1 g of the N-methylanilide (VIII) with mp 171-173°C and $[\alpha]_D$ −17.2° (c 4.11; $CHCl_3$).

^{1}H NMR spectrum (CCl_4) (ppm): 0.82 (3 H, s), 0.89 (3 H, s), 0.96 (3 H, s); 3.24 (3 H, s), 7.06-7.63 (5 H, m).

IR (KBr) (cm^{-1}): 3063, 3040, 1766, 1730, 1661, 1599, 1500, 1463, 1425, 1392, 1368, 1250, 1220, 1184, 1148, 1125, 1037, 1003, 779, 706, 667, 561.

The x-ray structural experiment was performed on a Syntex-$P2_1$ diffractometer using Mo radiation with a graphite monochromator. The crystals of the amide (VIII) belong to the rhombic system: a = 11.504 (5), b = 12.505 (5), c = 16.753 (7) Å, z = 4, space group $P2_12_12_1$, d_{calc} = 1.13 g/cm^3, $C_{26}H_{35}O_3$. The intensities of 1953 independent reflections with $2\theta < 50°$ were measured by the standard $2\theta/\theta$ scanning method. The calculations were performed with 1008 reflections having $I > 3\sigma$. The structure was interpretated by the direct method of least squares in the full-matrix anisotropic approximation to R = 0.085 and R_W = 0.096, where $w^{-1} = \sigma_f + (0.01\ F)^2$. No attempts to localize the hydrogen atoms were undertaken in view of the low quality of the single crystal. The values of the coordinates of the atoms of the (VIII) molecule obtained are given in Table 2.

SUMMARY

The structure of the N-methylanilide (VIII) has been studied by the method of x-ray structural analysis and the structure of the "adduct" of caryophyllene with maleic anhydride has been confirmed.

LITERATURE CITED

1. L. Ruzicka, and W. Zimmermann, Helv. Chim. Acta, 18, 219 (1935); L. Ruzicka, R. A. Plattner, and G. Balla, Helv. Chim. Acta, 24, 1219 (1941); L. Ruzicka, P. A. Plattner, and L. Werner, Helv. Chim. Acta, 26, 966 (1943).
2. A. Nickon, J. Am. Chem. Soc., 77, 1190 (1955).
3. E. Warnhoff, Can. J. Chem., 42, 1664 (1964).
4. M. ul-Haque, and D. Rogers, J. Chem. Soc., Perkin Trans. II, 228 (1974).
5. J. M. Robertson and G. Todd, J. Chem. Soc., 1254 (1955).

STEREOSELECTIVITY OF PHOTO-OXIDATION AT THE C_7 DOUBLE BOND OF ISOCEMBROL AND ITS DERIVATIVES

N. I. Yaroshenko and V. A. Raldugin

UDC 547.595.9

The products and stereochemistry of the photo-oxidation at the C_7 double bond of isocembrol and two of its derivatives have been investigated. The stereoselectivity of the transformations performed is discussed.

In connection with the detection in plants of natural terpenoid hydroperoxides [1], the investigations of the photo-oxidation of unsaturated terpenoids modeling the processes of their secondary metabolism in the green parts of plants is acquiring particular importance. In a preceding communication [2] we described the products of the photo-oxidation of isocembrol (I) at the C_{11} double bond — the diols (II-V) and the Δ^{12}-isomer of the diol (V). The photo-oxidation products were analyzed after the conversion of the hydroperoxides into the corresponding alcohols.

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 437-444, July-August, 1984. Original article submitted June 10, 1983.

0009-3130/84/2004- 0413$08.50