X-RAY STRUCTURAL INVESTIGATION OF GOSSYPOL AND ITS DERIVATIVES. VI. STRUCTURE OF AN ADDUCT OF GOSSYPOL WITH DIETHYL ETHER

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We have previously [1] reported the detection of seven crystalline forms of gossypol and have given the results of the structural interpretation of two of them by X-ray structural analysis [2, 3]. Yet another form crystallizes from diethyl ether, and in the present communication we consider the features of the structure of this modification of gossypol.

In 1937, R. Adams et al. obtained acicular crystals of gossypol from ether and determined their melting point as 184°C [4]. Single crystals grown from ether are small with a tendency to twinning, which makes them unsuitable for X-ray structural investigations. Crystals of better quality were obtained froma binary solvent – a mixture of ether and

TABLE 1. Coordinates of the Atoms in the Crystal Structure of the Adduct of Gossypol with Diethyl Ether ($\cdot 10^4$; for the H atoms, $\cdot 10^3$; the standard deviations are given in parentheses).

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
C1	3572(7)	6814(4)	838(3)	C2	4138(7)	7602(4)	1138(3)
C3	5773(7)	7631(4)	1464(3)	C4	6740(7)	6876(4)	1487(3)
C5	7256(8)	5270(4)	1248(3)	C6	6649(8)	4508(4)	955(3)
C7	5016(8)	4436(4)	626(3)	C8	3916(4)	5159(4)	574(3)
C9	4529(7)	6010(4)	862(3)	C10	6190(7)	6053(4)	1201(2)
C11	2968(7)	9121(4)	743(3)	C12	2998(7)	8405(4)	1110(3)
C13	1940(7)	8442(4)	1433(3)	C14	931(7)	9184(4)	1391(3)
C15	—172(8)	10715(4)	1012(3)	C16	—200(7)	11399(4)	643(3)
C17	814(7)	11386(4)	308(3)	C18	1931(7)	10672(4)	327(2)
C19	1951(7)	9908(4)	696(2)	C20	896(7)	9938(4)	1033(2)
C21	6431(8)	8488(4)	1703(3)	C21	2262(8)	4985(4)	247(3)
C23	9020(8)	5268(4)	1614(3)	C24	9272(10)	4561 5)	2075(3)
C25	10268(9)	5164(6)	1311(3)	C26	1921(9)	7667(5)	1827(3)
C27	3015(8)	10787(4)	5(3)	C28	—1275(8)	10796(4)	1381(3)
C29	—720(10)	11578(6)	1791(3)	C30	—3083(9)	10880(5)	1085(3)
O1	1989(5)	6780(3)	500(2)	O2	1815(5)	4227(3)	21(2)
O3	4630(5)	3619(3)	377(2)	O4	7629(5)	3741(3)	975(2)
O5	3977(5)	9083(3)	422(2)	O6	2954(5)	11452(3)	—310(2)
O7	681(5)	12099(3)	—33(2)	O8	—1235(5)	12153(3)	589(3)
HO1	150	717	56	HO3	351	360	24
HO4	691	344	70	HO5	485	862	51
HO7	158	1213	14	HO8	—49	1243	65
H4	775	695	172	H14	10	916	156
H22	126	545	22	H23	926	581	179
H27	381	1032	—1	H28	—116	1025	158
$H21_1$	733	837	200	$H21_2$	582	860	214
$H21_3$	622	903	166	$H26_1$	304	770	205
$H26_3$	123	778	201	$H26_3$	186	708	164
$H24_1$	1023	467	227	$H24_2$	920	393	204
$H24_3$	852	476	233	$H25_1$	1169	526	156
H25,	1019	554	107	$H25_3$	1014	460	108
H29	36	1150	198	$H29_2$	—127	1157	209
H29	—64	1212	168	$H30_1$	—332	1139	85
H30	—362	1093	140	$H30_2$	—350	1030	87
C31	5280(19)	4553(8)	7625(5)	C32	4203(18)	4071(8)	7193 5)
C33	3759(16)	2591(10)	6627(5)	C34	3965(2)	1748(9)	6648(6)
O9	4687(8)	3149(5)	7078(3)				

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hexane. The crystallographic parameters of these crystals were determined on a Syntex $P2_1$ automatic four-circle diffractometer: a = 8.557(2) Å, b = 14.474(5) Å, c = 25.651(5) Å, β = 107.22(2)°, V = 3034.7(1,4) A^3, z = 4 sp.gr. $P2_1/c$.

A three-dimensional set of experimental integral intensities was obtained on this diffractometer by the $\theta/2\theta$-scanning method in Cu K_α radiation with monochromatic reflection from a graphite crystal. The structure was deciphered by the MULTAN program that forms part of the XTLSM group of programs for a SM-4 computer [5]. The first F-synthesis showed that the crystal included diethyl ether in a ratio of gossypol to ether of 1:1.

The refinement of the structure began with the calculation of a series of successive F-synthesis and we then proceeded to its refinement by the method of least squares (MLS) first in the isotropic approximation (R = 0.118) and then in the anisotropic approximation (R = 0.089). At this stage, difference syntheses revealed all the hydrogen atoms of the gossypol molecule but the large thermal vibration of the ether molecule did not permit its hydrogen atoms to be localized. The final value of the R factor was 0.059, and the corresponding coordinates of the atoms in the structure are given in Table 1.

In the adduct, the gossypol molecule has the aldehyde tautomeric form. The dihedral angle between the planes of the naphthalene nuclei amounts to 83.5°. The isopropyl groupings of the two halves are oriented identically with respect to their nearest hydroxy groups.

The gossypol molecules are linked into a web parallel to the ab plane. In it not all the groups active in the sense of H-bond formation actually gave hydrogen bonds. The O2 carbonyl oxygen and the oxygen of the O3 hydroxy group are present in ordinary Van der Waals contact with the atoms of the closest molecules, while the corresponding atoms of the other half of the molecule have intermolecular H-bonds (for the numbering of the atoms, see [3]). Because of this nonequivalence of the two halves, the gossypol loses its characteristic symmetry of a twofold axis. The webs consist of two layers of the hydrophilic parts of the molecule turned to one another. Between the webs there are layers consisting of ether molecules. The latter are present in special pockets formed from the hydrophobic regions of the gossypol molecule.

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