Cubane derivatives
1. Synthesis and molecular structures of the esters of 1,4-cubanedicarboxylic acid

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An effective method of esterification of 1,4-cubanedicarboxylic acid with alkylsulfuric acids is proposed. The derivatives of alkanols with substantially different pK_a values are obtained in high yields. Molecular structures of the esters obtained are confirmed by various methods. The X-ray study showed a remarkable effect of the nature of an alkyl radical on the geometry of the cubane core.

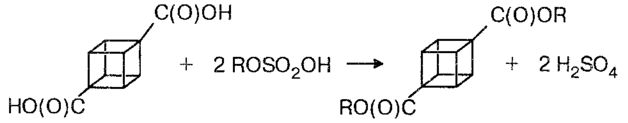
Key words: 1,4-cubanedicarboxylic acid, esterification, alkylsulfuric acids, X-ray method.

The chemistry of cubane is still poorly not well known. In recent years, only a few publications have appeared on the synthesis of compounds containing a cubane fragment. One of the key cubane derivatives is pentacyclo[4.2.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]octane-1,4-dicarboxylic acid (**1**) (the conventional name is 1,4-cubanedicarboxylic acid). Its few esters[1–3] were prepared under mild conditions in rather low yields according to individual methods.

In the present work, we have attempted to find an effective, common method of esterification of **1** and to study the effect of an alkyl radical on the geometry of the cubane core in the esters produced.

Results and Discussion

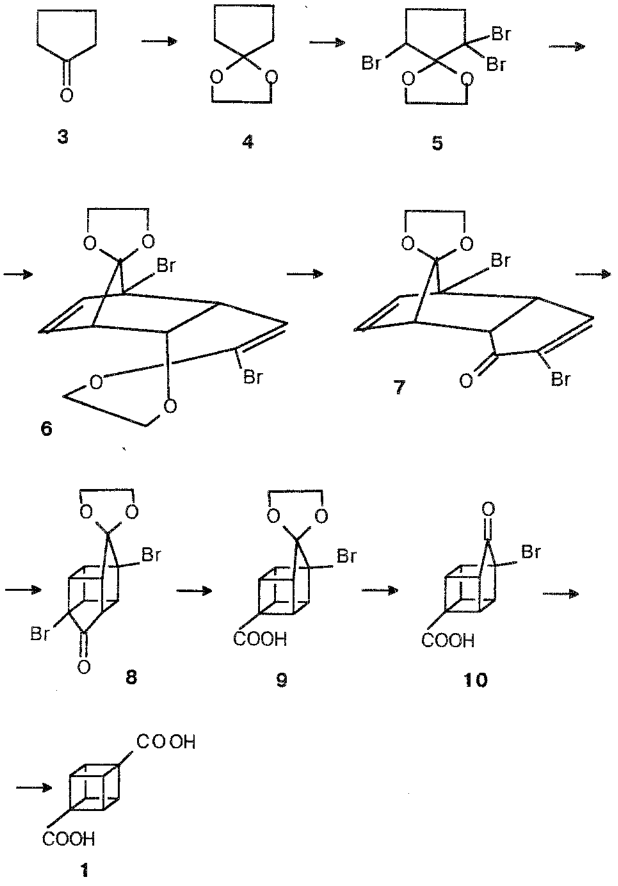
Having considered a number of known techniques of esterification of aliphatic mono- and dicarboxylic acids, we used a well-known method of preparation of esters using alkylsulfuric acids.[4]



1

2a:R = Me
2b:R = Me_2CH
2c:R = $F(NO_2)_2CCH_2$
2d:R = $(NO_2)_3CCH_2$

Scheme 1



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To test the common character of the method, we used alkanols that differ as much as possible in pK_a values: methanol, isopropyl alcohol, 2,2-dinitro-2-fluoroethanol and 2,2,2-trinitro-ethanol. The corresponding alkylsulfuric acids were obtained without isolation in a pure form from chlorosulphonic acid in an excess of alkanol. The synthesis of acid **1** was carried out according to a known scheme[1,2] starting from cyclopentanone (**3**).

A check on the reproducibility of the method of synthesis of **1** showed the necessity of improving some of its stages to optimize the yield and increase the purity of intermediate products **4—8**; necessary control was maintained using GLC.

Thus, 6-ethyleneketal-5,9-dibromopentacyclo-$[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]$decane-6,10-dione **8** was synthesized using a DRT-400 arc tube high pressure mercury lamp. This shortened the reaction time significantly (from 16—24 h[1] to 2 h) while maintaining the yield (98—99 %) at purity higher than 99 %. The reaction was monitored by UV—spectroscopy.

We managed to reduce the prolonged[2] synthesis of 1-bromopentacyclo$[4.3.0.0^{2,5}.0^{3,8}. 0^{4,7}]$-nonan-9-one-4-carboxylic acid **10** (the total time is 8 days; we failed to reproduce data of Ref. 1 in which compound **10** was prepared in a shorter time) extracting the product from the reaction medium. We reduced the time of continuous extraction of **10** with methylene chloride from 5 days to 40 h by saturating the reaction medium with Na_2SO_4. However, the yield of **10** was 86—87 %.

The acid **1** synthesized according to the method described in Ref. 1, 2 (recrystallized from glacial CH_3COOH), was unsuitable for producing esters **2** (see experimental), because it contained 2 moles of acetic acid per 1 mole of **1**. Therefore crystallosolvate **1** was heated for 6—8 h before esterification at 30—50 °C *in vacuo* (1—2 Torr) until CH_3COOH was completely removed.

The structure of the obtained esters **2a—c** was established by X-ray analysis (Figs. 1—3, Tables 1—4). The cubane fragment of molecules **2a** and **2b** is practically symmetrical, the C—C bonds are slightly lengthened (1.556(2)—1.568(2) Å in **2a** and 1.55(1)—1.57(1) Å in **2b**, Table 5) relative to standard[5,6] lengths of the $C(sp^3)$—$C(sp^3)$ bond in paraffins (1.537 Å). The $C(sp^2)$—$C(sp^3)$ exocage bonds (1.483(2) Å in **2a** and 1.49(1) Å in **2b**), on the contrary, are shortened in both cases relative to the standard value of 1.510 Å.[5,6] The same effect is also observed for the dinitrofluorosubstituted analog of **2a—2c** ($C(sp^2)$—$C(sp^3)$ 1.468(8) Å). However, the latter compound has a considerably distorted cubane fragment; the endocage C—C bonds of the cubane frame carbon atoms bounded to substituents turned out to be essentiall

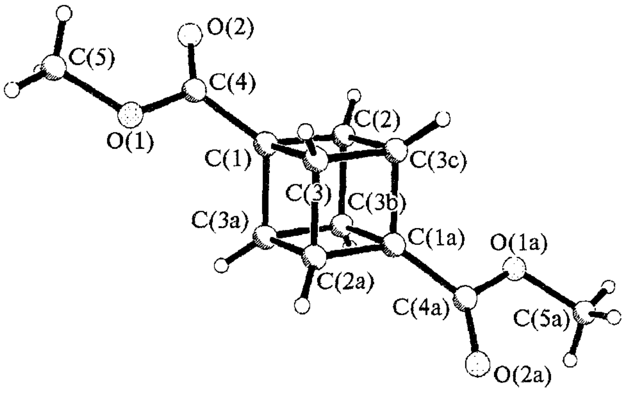

Fig. 1. Structure of molecule **2a**

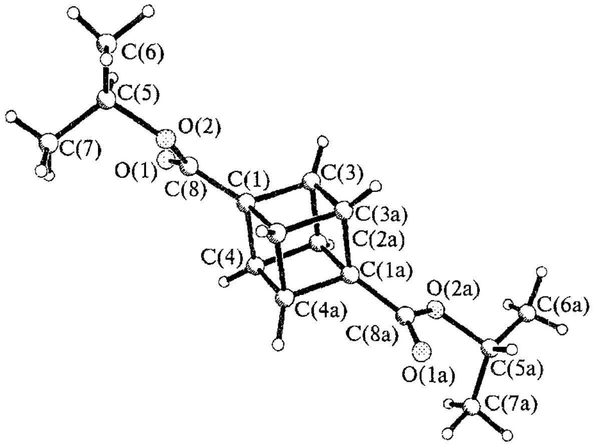

Fig. 2. Structure of molecule **2b**

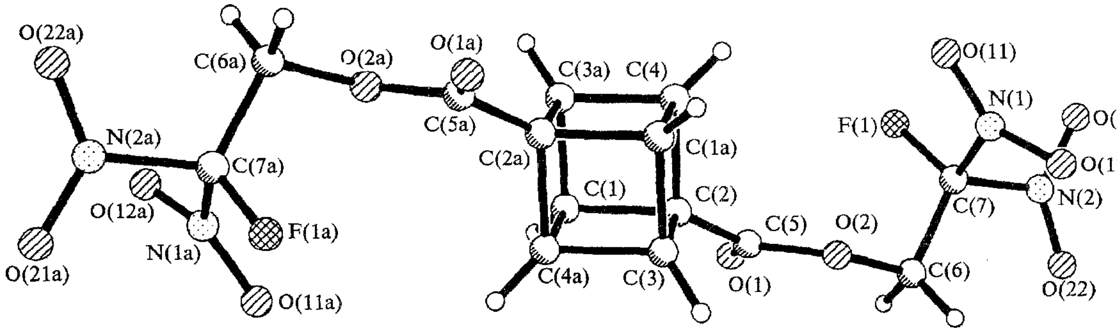

Fig. 3. Structure of molecule **2c**

Table 1. Crystal data of the studied esters of acid **1**, conditions of X-ray diffraction experiments and final *R* values

Parameter	**2a**	**2b**	**2c**
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$C2/m$	$C2/c$	$P2_1/n$
a, Å	13.569(4)	12.317(3)	15.180(7)
b, Å	6.423(2)	18.287(5)	5.812(3)
c, Å	5.859(2)	6.921(2)	20.704(9)
β/deg	92.10(1)	112.40(2)	104.30(2)
V, Å^3	513.40(5)	1441.3(1)	1770.0(2)
Z	2*	4**	4***
Number of the measured reflection	1032	1892	2193
Number of the observed reflection [$I > 4\sigma(I)$]	837	831	1794
R	0.037	0.085	0.059
R_w	0.041	0.089	0.059

* The molecule is in the special position *2/m*.

** The molecule lies on the crystallographic 2 axis.

*** Here are two independent molecules in a cell lying in the crystallographic inversion centre

nonequivalent and weak (1.559(8)—1.604(7) Å, Table 5), while all other bonds of the cubane framework remain practically undistorted (1.577(9)—1.581(7) Å, Table 5).

It should be noted that this type of cubane fragment distortion was observed for the first time and might be caused by the influence of the NO_2 acceptor groups and the fluorine atom. This assumption is confirmed by the IR spectroscopy data, according to which for **2c** the C=O valence vibration (1730 cm^{-1}) is shifted to the high frequency region compared to alkyl derivatives of **2a** and **2b** (118 and 1695 cm^{-1}, respectively). The weakening of the C=O bond and strengthening of the acceptor properties of the whole COOR group leads, in its turn, to a withdrawal of electron density from the carbon atoms in the cubane moiety and to weakening of the C—C bons. In **2a** and **2b**, which have donor alkyl groups, an opposite situation is observed. The C=O bond is strengthened, and the acceptor properties of COOR are neutralized. Therefore, the effect of the substituents on the cubane skeleton is insignificant. It is reflected in the equivalence of all the C—C bonds. A similar picture is also observed for acid **1** (Table 5), although its structure is distorted because of hydrogen bonds between the molecules.[8]

The weakening of the C—C bonds in cubanes even in the absence of 1,4-substituents (1.549(3)—1.553(3) Å)[7] is due to the fact that the C—C—C angles are close to 90°. It is markedly different from tetrahedral (109.5°). With such geometry, the overlapping of the bonding orbitals becomes considerably worse and the formal distances between the carbon atoms appear to be only projections of the real "banana" carbon—carbon bonds. Thus, a significant change in the geometric parameters

Table 2. Coordinates of non-hydrogen atoms (×10^4) of structure **2a**

Atom	x	y	z
O(1)	2172(1)	0	6955(2)
O(2)	2713(1)	0	10585(2)
C(1)	980(1)	0	9663(3)
C(2)	510(1)	0	12031(3)
C(3)	232(1)	1716(2)	8814(2)
C(4)	2046(1)	0	9193(3)
C(5)	3172(2)	0	6226(4)

Table 3. Coordinates of non-hydrogen atoms (×10^4) of structure **2b**

Atom	x	y	z
O(1)	8114(4)	3542(3)	3841(9)
O(2)	7293(4)	3894(3)	490(7)
C(1)	6063(6)	3731(4)	2348(10)
C(2)	4855(6)	3742(5)	467(12)
C(3)	5603(7)	4340(4)	3437(13)
C(4)	5599(6)	3132(4)	3446(12)
C(5)	8456(6)	3878(5)	333(13)
C(6)	8405(11)	4443(8)	−1252(21)
C(7)	8685(10)	3123(7)	−242(26)
C(8)	7271(6)	3704(4)	2346(11)

Table 4. Coordinates of non-hydrogen atoms (×10^4) of structure **2c**

Atom	x	y	z
F(1)	7745(3)	2262(7)	1395(2)
O(1)	9661(3)	4336(7)	1684(2)
O(2)	9416(3)	992(7)	1118(2)
O(11)	7407(3)	327(10)	273(2)
O(12)	7832(3)	−2994(9)	715(2)
O(21)	6760(4)	−1209(12)	1703(3)
O(22)	8062(4)	−2209(11)	2344(3)
N(1)	7722(3)	−961(11)	730(3)
N(2)	7584(5)	−1247(12)	1870(3)
C(1)	10315(4)	6514(9)	520(3)
C(2)	9867(4)	4135(11)	577(3)
C(3)	10442(4)	2926(11)	136(3)
C(4)	9091(4)	4670(11)	−87(3)
C(5)	9659(3)	3244(10)	1187(3)
C(6)	9082(4)	−43(10)	1642(3)
C(7)	8062(4)	118(11)	1422(3)
F(1')	11683(3)	2872(7)	3128(2)
O(1')	9847(3)	882(7)	3223(2)
O(2')	10420(3)	4061(7)	3825(2)
O(11')	12873(4)	5509(15)	3792(3)
O(12')	11870(4)	8029(10)	3883(2)
O(21')	11148(3)	8034(9)	2366(2)
O(22')	11779(3)	4955(10)	2089(2)
N(1')	12118(4)	6319(12)	3655(3)
N(2')	11453(3)	6105(11)	2455(2)
C(1')	9122(4)	−245(10)	5015(3)
C(2')	9582(4)	2101(11)	4926(3)
C(3')	10428(4)	1406(10)	5501(3)
C(4')	10027(4)	920(10)	4403(3)
C(5')	10095(4)	1876(10)	3752(3)
C(6')	10455(4)	5238(11)	3221(3)
C(7')	11404(4)	5031(11)	3130(3)

Table 5. The main geometric parameters of 1,4-disubstituted cubanes

Sibstituent (R)	Bond	d/Å	Bond Angle	ω/deg	References
H(7)	C_k—C_k	1.549—1.553	C_k—C_k—C_k	89.3—90.5	7
NO_2(9)[a]	C_3—C_k	1.542—1.564	C_k—C_3—C	90.2—90.7	9
	C_k—C_k	1.562—1.566	C_k—C_k—C_k	88.5—90.9	
	C_3—N	1.466			
	N—O	1.210—1.213			
I(10)[a]	C_3—C_k	1.542—1.568	C_k—C_3—C	90.1—91.3	10
	C_k—C_k	1.532—1.576	C_k—C_k—C_k	88.1—91.6	
	C_3—I	2.123			
Br,	C_3—C_k	1.532—1.576 (R = Br)	C_k—C_3—C	90.9—91.0 (R = Br)	11
C_8H_7(11)[a]	C_3—C_k	1.565—1.585 (R = C_8H_7)		88.9—89.4 (R = C_8H_7)	
	C_k—C_k	1.551—1.563	C_k—C_k—C_k	89.1—90.3	
	C_3—Br	1.938			
	C_3—C	1.474			
HOOC(8)[b]	C_3—C_k	1.560—1.585	C_k—C_3—C	89.0—90.3	8
	C_k—C_k	1.557—1.566	C_k—C_k—C_k	Нет данных	
	C_3—C	1.480	C_k—C=O	122.3, 123.2[c]	
	C_k=O	1.218, 1.224[c]	C_k—C—OH	114.2, 118.5[c]	
	C—OH	1.313, 1.319[c]	O—C=O	119.3, 122.5[c]	
H_3COOC **(2a)**	C_3—C_k	1.556(2)—1.568(2)	C_k—C_3—C	89.3(1)—90.2(1)	
	C_k—C_k	1.554(3)—1.563(2)	C_k—C_k—C_k	87.7(1)—90.5(1)	
	C_3—R	1.483(2)	C_k—C_3=O	126.1(1)	
	C=O	1.200(2)	C_3—C—OR′	110.2(1)	
	C—OR′	1.336(2)	O—C=O	123.7(1)	
	O—$C_{R'}$	1.438(2)	C—O—$C_{R'}$	116.8(1)	
$(CH_3)_2$C(H)OOC **(2b)**	C_3—C_k	1.560(8)—1.570(1)	C_k—C_3—C	89.3(5)—90.3(5)	
	C_k—C_k	1.55(1)—1.56(1)	C_k—C_k—C_k	89.5(5)—90.5(5)	
	C_3—R	1.49(1)	C_3—C=O	123.2(8)	
	C=O	1.190(8)	C_3—C—OR′	112.1(5)	
	C—OR′	1.34(1)	O—C=O	124.7(7)	
	O—$C_{R'}$	1.48(1)	C—O—$C_{R'}$	116.5(5)	
$F(NO_2)_2CCH_2$OOC **(2c)**	C_3—C_k	1.559(8)—1.604(7)	C_k—C_3—C	89.1(4)—92.1(5)	
	C_k—C_k	1.577(9)—1.581(7)	C_k—C_k—C_k	88.8(4)—90.5(4)	
	C_3—R	1.468(8)	C_3—C=O	126.2(5)	
	C=O	1.209(7)	C_3—C—OR′	111.1(5)	
	C—OR′	1.358(7)	O—C=O	122.6(5)	
	O—$C_{R'}$	1.468(7)	C—O—$C_{R'}$	117.5(4)	

Note. C_c and C_s are unsubstituted and substituted atoms of the cubane cluster, $C_{R'}$ is a substituent atom bound with the ester oxygen atom of the carboxy group.

[a] The geometric parameters are taken from the Cambridge Crystallographic Database.[13] [b] There are two independent centrosymmetric molecules in a unit cell. [c] The data are given for two conformers.

of the cubane core should be expected only for strong external electron effects (as in **2c**). Substituents having comparatively weak effects (both donors and acceptors), may change the character of the orbital overlap in the cubane skeleton, but they still change the magnitudes of the projections of the real C—C bonds only slightly. This conclusion is in agreement with the data on practically the same geometry of the cubane skeleton in its symmetric derivatives with donor or acceptor substituents, for example, 1,4-$(NO_2)C_8H_6$ (C—C 1.542—1.566 Å)[9] and 1,4-$I_2C_8H_6$(C—C 1.532—1.576 Å).[10] On the other hand, the introduction of two substituents having different electron characteristics (for example, in 1-bromo-4-cubylcubane[11]), leads to some asymmetry of the skeleton (Table 5). In addition, the enhanced sensitivity toward external influences of those C—C bonds that contain carbon atoms bound to a substituent probably indicate weak delocalization of the σ-electron density in the cubane nucleus. In this feature the carbon cubane C_8 is significantly different from, for example, metallocubanes M_4S_4 (M = V, Cr), for which a high degree of delocalization is observed.[12]

Experimental

General method of preparation of esters 2. Freshly distilled chlorosulfonic acid (3 mmol) was added dropwise to alkanol (6 mmol) at 5—10 °C; the reaction mixture was kept for 1 h at 30 °C. Then 1 mmol of acid **1** was added at the same temperature and the solution was mixted for 1 h, and the product was poured onto cut ice. The precipitate (**2**) was washed with water, with a 1 % solution of $NaHCO_3$, and once more with

Table 6. Yields and some physical properties of esters of **2**

Compound	Molecular formula	Yield (%)	M.p./°C (solvent)*	d_4^{20} exp.	^{1}H NMR, δ ($CDCl_3$,TMC)	IR ν/cm^{-1}
2a	$C_{12}H_{12}O_4$	80.5	162—163 (heptane)	1.42	3.686 c (3H,OCH_3) 4.209 c(3H,CH)	480 w, 615 m, 730 s, 786 s, 820 m, 842 m, 910 s, 1028s, 1090 s, 1225 s, 1328 s, 1435 m, 1718 s, 2843 w, 2950 m, 2990 s
2b	$C_{16}H_{20}O_4$	85.5	108—110 (heptane)	1.27		610 w, 720 m, 765 m, 815 m, 830 m, 895 m, 940 m, 955 m, 1075 s, 1105 m, 1140 w, 1190 m, 1230 s, 1308 s, 1355 s, 1370 m, 1380 m, 1435 m, 1695 s, 2860 w, 2915 w, 2970 m, 2990 m
2s	$C_{14}H_{10}N_4O_{12}F_2$	67.5	149—150 (CCl_4, $CHCl_3$)	1.66	4.27 s(3H,CH) 5.18 d (2H,CH_2) J_{HF} = 16 Гц	440 w, 455 w, 555 w, 600 w, 720 w, 750 w, 770 m, 790 s, 835 s, 895 m, 935 w, 1003 m, 1065 s, 1185 s, 1200 s, 1235 m, 1260 m, 1305 s, 1320 s, 1350 w, 1385 s, 1390 m, 1425 s, 1600 s, 1730 s, 2968 w, 3012 m
2d	$C_{14}H_{10}N_6O_{18}$	69.5	152—153 (CCl_4, $CHCl_3$)		4.30 s(3H,CH) 5.40 br.s (2H,CH_2)	

* Solvent for crystallization.

water. The final purification was carried out *via* recrystallization from organic solvents. The yields and some physical characteristics of the synthesized esters are given in Table 6.

The NMR spectra were recorded on a NMR spectrometer (developed and produced at the Institute of Chemical Physics in Chernogolovka, Russian Acad. Sci.) with a superconducting magnet (294 MGTs). The IR spectra were recorded on a Specord 75 IR instrument in KBr tablets. The UV spectra were obtained on a Specord UV-VIS spectrophotometer.

GLC analysis was carried out on a Chrom-5 chromatograph with a glass column 4.0 mm × 1.0 m filled with Inerton Super containing 5 % 225-OV silicone (gas-carrier He, flame-ionization detector).

X-ray study. Single crystals of **2a**, **2b**, **2c** suitable for X-ray study were obtained in ampules (200×5mm) by the diffusion of heptane (1 ml) into a concentrated solution of the substance in CH_2Cl_2 (2 ml) at ~20 °C. The X-ray data for **2a** and **2b** were obtained on a Syntex $P2_1$ diffractometer at −55 °C and 20 °C, respectively (λMo-Kα, θ/2θ-scan technique). The study of **2c** was performed on a Siemens P3/PC diffractometer (−55 °C, λMo-Kα, θ/2θ-scan technique). The crystal data are given in Table 1. All the structures were solved by direct methods and refined in full-matrix anisotropic approximation for non-hydrogen atoms. Hydrogen atoms were found from the difference Fourier synthesis and refined in isotropic approximation. The atomic coordinates are given in Tables 2—4. All calculations were carried out using the SHELXTL package of programs.

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