Preparation and spectral properties of cyclic acetals of 2,2,5,5-tetrakis(hydroxymethyl)cyclopentanone

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Dedicated to Professor Ľ. Krasnec, in honour of his 65th birthday

2,2,5,5-Tetrakis(hydroxymethyl)cyclopentanone reacts with carbonyl compounds in a 1:2 ratio to give cyclic acetals similarly as α- or β-glycols. These acetals were prepared under catalysis of acids (hydrochloric, sulfuric, and *p*-toluenesulfonic) or phosphorus pentoxide. Their structure was proved by spectral means (i.r., u.v., and ^{1}H-n.m.r. spectroscopies).

2,2,5,5-Тетракис(гидроксиметил)циклопентанон реагирует с карбонильными соединениями в отношении 1:2 с образованием циклических ацеталей аналогично α- или β-гликолям. Эти ацетали были приготовлены с использованием в качестве катализатора кислот (хлористоводородной, сернокислой и *п*-толуолсульфоновой) или P_2O_5. Их структура была подтверждена спектрофотометрическими методами (ИК, УФ и ^{1}Н-ЯМР).

Cyclic 5- or 6-membered acetals are extraordinarily easily formed from two- or morehydric alcohols containing hydroxyl groups in 1,2 or 1,3 positions. In contrast to generation of acyclic acetals, when at a 1:2 mole ratio an equilibrium is attained, cyclic acetals have their equilibrium shifted, even with a stoichiometric ratio, in favour of the acetal [1—12].

This paper concerns the preparation and spectral properties of cyclic acetals of 2,2,5,5-tetrakis(hydroxymethyl)cyclopentanone, the hydroxyl groups of which are in a β-glycol arrangement.

Experimental

Melting points were determined on a Kofler micro hot-stage. Purity of the prepared substances was checked by thin-layer chromatography on Silufol UV 254 (Kavalier, Votice) plates in the solvent system benzene—ethyl acetate 5:1. The respective spots were detected

both with iodine vapours and under an u.v. lamp. The R_f data are the mean values of three measurements. Infrared spectra were recorded with a UR-10 (Zeiss, Jena) spectrophotometer either in nujol (acetals *I*, *III—IX*, *XII—XX*, *XXII*, *XXIII*), or in KBr (*X*, *XI*, *XXI*), or in carbon tetrachloride (*VI*). The u.v. spectra were taken with a Specord UV VIS (Zeiss, Jena) apparatus in the 200—350 nm region at a 10^{-2}—10^{-5} M concentration in dioxan; cell length 0.2—2 cm. The ^{1}H-n.m.r. spectra were measured in deuteriochloroform with a Tesla BS 487 A apparatus operating at 80 MHz; internal reference hexamethyldisiloxane.

Cyclic acetals

2,2,5,5-Tetrakis(hydroxymethyl)cyclopentanone (24 mmol) prepared according to [13] was stirred with the appropriate carbonyl compound (49 mmol) a) at room temperature in 50% ethanol or methanol (10 ml) with concentrated hydrochloric acid or 40% sulfuric acid (10 ml); after 24 h the product was filtered off; b) at a given temperature in a suitable solvent with P_4O_{10} (4 g); after a convenient time the catalyst was filtered off and the filtrate was concentrated for crystallization; c) at a reflux in benzene (150 ml) with *p*-toluenesulfonic acid (5 g) using a distillation head; after neutralization with a sodium carbonate solution benzene was distilled off and the crude material crystallized from a suitable solvent.

Detailed conditions and characterization of products are listed in Table 1.

Results and discussion

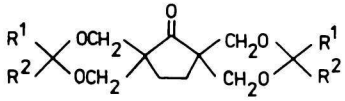
Acetals *VI* and *X* are the only two of 23 described in this paper, which were reported in the literature; they were prepared from the respective starting material and HCl as a catalyst [14]. This catalyst was also used in the synthesis of acetals *VI—XV* and *XVIII* with aliphatic and aromatic aldehydes. Sulfuric acid was found to be advantageous with *VII* and *VIII*, where hydrochloric acid furnished the products in a low yield. Further suitable catalyst for preparation of acetals, where the above-mentioned acids did not afford products in a satisfactory yield, was phosphorus pentoxide in dry benzene. The acetal from *p*-dimethylaminobenzaldehyde was prepared by an azeotropic acetalization using *p*-toluenesulfonic acid or phosphorus pentoxide, because attempts with other catalysts failed. We also examined phosphoric acid and zinc chloride, which in comparison with the preceding catalyst did not give reasonable results and therefore, we do not mention them in the following text.

Acetals mentioned in Scheme 1 are white crystals insoluble in water and soluble in organic solvents. The most part of the prepared acetals was isolated in relatively high yields even when using the stoichiometric ratio of reactants the exception being those prepared from *p*- and *o*-hydroxybenzaldehydes; here side reactions took place in a considerable measure.

The R_f values of acetals synthesized from substituted aromatic aldehydes (*o*-,

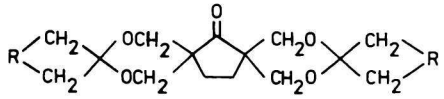
m-, *p*-Cl, *m*-, *p*-NO_2 and fluoro derivatives decrease in the order

o-isomer > *m*-isomer > *p*-isomer > unsubstituted isomer



I $R^1 = R^2 = CH_3$

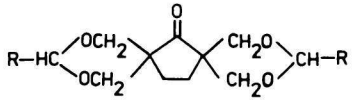
II $R^1 = CH_3$, $R^2 = C_2H_5$



III $R = CH_2CH_2$

IV $R = CH_2CH_2CH_2$

V $R = CH_2CH(CH_3)CH_2$



VI R = H

VII $R = CH_3$

VIII $R = C_2H_5$

IX $R = [(CH_3)_2CHCH_2]$

X–*XXII* R = [Ph–X]

XXIII R = [CH=CH–Ph]

Compound	*X*	*XI*	*XII*	*XIII*	*XIV*	*XV*	*XVI*
X	H	*m*-F	*p*-F	*o*-Cl	*m*-Cl	*p*-Cl	*p*-CH_3

Compound	*XVII*	*XVIII*	*XIX*	*XX*	*XXI*	*XXII*
X	*p*-OCH_3	*m*-NO_2	*p*-NO_2	*o*-OH	*p*-$N(CH_3)_2$	2-OH-3,5-diCl

Scheme 1

Cyclic acetals of 2,2,5,5-tetrakis(hydroxymethyl)cyclopentanone

Table 1

Characterization of the prepared cyclic acetals

Compound	Formula	*M*	Calculated/found			Reaction conditions			Yield %	M.p., °C Solvent	R_f
			% C	% H	% X	Solvent	Catalyst	Temperature			
I	$C_{15}H_{24}O_5$	284.36	63.36	8.51	—	Excess	P_4O_{10}	lab.	60	175	0.19
			63.26	8.72		ketone				Methanol	
II	$C_{17}H_{28}O_5$	312.41	65.36	9.03	—	Excess	P_4O_{10}	B.p.	59	136—139	0.34
			65.52	9.31		ketone				Methanol	
III	$C_{19}H_{28}O_5$	336.43	67.83	8.39	—	Excess	P_4O_{10}	lab.	95	214—215	0.35
			67.95	8.60		ketone				Acetone	
IV	$C_{21}H_{32}O_5$	364.49	69.20	8.85	—	Excess	P_4O_{10}	lab.	77	171—173	0.37
			69.26	9.00		ketone				Acetone	
V	$C_{23}H_{36}O_5$	392.54	70.37	9.25	—	Excess	P_4O_{10}	lab.	88	222—225	0.38
			70.15	9.46		ketone				Acetone	
VI	—	—	—	—	—	Ethanol	HCl	lab.	81	180—182[a]	0.17
						Methanol				Methanol	
VII	$C_{13}H_{20}O_5$	256.30	60.92	7.87	—	Ethanol	H_2SO_4	lab.	74	101—104	0.35
			60.81	7.86		Methanol				Ethanol	
VIII	$C_{15}H_{24}O_5$	284.36	63.36	8.51	—	Ethanol	H_2SO_4	lab.	76	94—95	0.35
			63.02	8.25		Methanol				Methanol	
IX	$C_{19}H_{32}O_5$	340.46	67.03	9.47	—	Ethanol	HCl	lab.	75	155—156	0.49
			67.09	9.80		Methanol					
X	—	—	—	—	—	Ethanol	HCl	lab.	90	204—206[b]	0.51
						Methanol				Methanol	
XI	$C_{23}H_{22}F_2O_5$	416.43	66.33	5.32	9.12 (F)	Ethanol	HCl	lab.	72	180—183	0.56
			66.20	5.42	9.30 (F)	Methanol				Methanol	
XII	$C_{23}H_{22}F_2O_5$	416.43	66.33	5.32	9.12 (F)	Ethanol	HCl	lab.	75	293—295	0.51
			66.03	5.10	9.20 (F)	Methanol				Methanol	

Table 1 (Continued)

Compound	Formula	*M*	Calculated/found				Reaction conditions			Yield %	M.p., °C Solvent	R_f
			% C	% H	% X		Solvent	Catalyst	Temperature			
XIII	$C_{23}H_{22}Cl_2O_5$	449.34	61.48	4.92	15.78	(Cl)	Ethanol	HCl	lab.	79	220—223	0.62
			61.29	5.10	15.65	(Cl)	Methanol				Carbon tetrachloride	
XIV	$C_{23}H_{22}Cl_2O_5$	449.34	61.38	4.94	15.78	(Cl)	Ethanol	HCl	lab.	80	174—176	0.59
			61.37	4.64	15.80	(Cl)	Methanol				Carbon tetrachloride	
XV	$C_{23}H_{22}Cl_2O_5$	449.34	61.38	4.94	15.78	(Cl)	Ethanol	HCl	lab.	78	238—239	0.55
			61.14	5.11	15.90	(Cl)	Methanol				Carbon tetrachloride	
XVI	$C_{25}H_{32}O_5$	412.53	72.80	7.82	—		Benzene	P_4O_{10}	B.p.	83	248—251	0.49
			73.00	7.66							Methanol	
XVII	$C_{25}H_{28}O_7$	440.50	68.17	6.41	—		Benzene	P_4O_{10}	lab.	69	231—234	0.40
			68.05	6.50							Methanol	
XVIII	$C_{23}H_{22}N_2O_9$	470.44	58.72	4.71	5.95	(N)	Ethanol	HCl	lab.	85	221—224	0.42
			58.90	4.76	5.60	(N)	Methanol				Acetone	
XIX	$C_{23}H_{22}N_2O_9$	470.44	58.72	4.71	5.95	(N)	Benzene	P_4O_{10}	B.p.	82	247—250	0.40
			58.60	4.61	5.60	(N)					Acetone	
XX	$C_{23}H_{24}O_7$	412.44	66.98	5.87	—		Benzene	P_4O_{10}	B.p.	15	257—259	0.14
			66.99	6.17							Chloroform	
XXI	$C_{27}H_{34}N_2O_5$	466.58	69.51	7.35	6.00	(N)	Benzene	*p*-Toluene-	B.p.	10	228—230	0.28
			69.21	7.05	5.80	(N)		sulfonic acid			Methanol	
XXII	$C_{23}H_{20}Cl_4O_7$	550.24	50.21	3.66	25.77	(Cl)	Acetonitrile	P_4O_{10}	B.p.	77	255—257	0.31
			49.95	3.71	25.90	(Cl)					Chloroform	
XXIII	$C_{27}H_{28}O_5$	432.52	74.98	6.53	—		Benzene	P_4O_{10}	lab.	80	208—210	0.53
			75.14	6.70							Acetone	

a) M.p. according to [14] 182°C; *b*) M.p. according to [14] 206.5°C.

Table 2

Ultraviolet and infrared spectra of the prepared compounds

Compound	λ_{max}/nm (ε/l mol^{-1} cm^{-1})								ν(C=O)/cm^{-1}	Bands in the region 1010—1190 cm^{-1}					
I					307 (21.0)	316 (20.0)	330 (10.5)		1720	1038	1103	1158			
II					307 (25.0)	317 (23.5)	328 (13.5)		1720	1039	1097	1148	1182		
III					306 (21.5)	317 (21.0)	328 12.0)		1727	1063	1118	1158	1188		
IV					307 (21.0)	317 (20.0)	329 (11.5)		1723	1033	1058	1078	1108	1178	1158
V					308 (26.5)	317 (25.0)	328 (14.5)		1725	1018	1038	1073	1118	1178	
VI					308 (19.0)	316 (18.5)	326 (10.5)		1735	1038	1103	1073			
VII					307 (20.9)	317 (19.1)	330 (9.8)		1720	1033	1058	1110	1150		
VIII					308 (21.5)	317 (20.5)	331 (11.5)		1725	1038	1078	1103	1123	1148	
IX					308 (23.0)	317 (22.0)	328 (13.0)		1720	1038	1073	1123	1158		
X	252 (1900)	256 (2450)	263 (2100)	267 (1350)	298 (24.0)	308 (26.0)	329 (13.5)		1720	1028	1078	1120	1178		
XI	257 (9000)		263 (12 800)	269 (15 400)	294 (29.5)	306 (30.0)	316 (26.5)	329 (14.5)	1725	1028	1078	1108	1148	1178	
XII	261 (3200)		267 (4300)	274 (3600)	298 (24.0)	307 (32.5)	317 (29.5)		1725	1028	1083	1108	1148	1178	

Table 2 (Continued)

Compound	λ_{max}/nm (ε/l mol^{-1} cm^{-1})								ν(C=O)/cm^{-1}	Bands in the region 1010—1190 cm^{-1}				
XIII	254 (1650)	262 (2650)	268 (3450)	273 (2850)	299 (23.5)	308 (25.0)	317 (23.0)	328 (13.5)	1730	1028	1058	1113		
XIV	254 (2100)	261 (3200)	267 (4300)	274 (3600)	293 (30.0)	307 (32.5)	317 (29.5)	328 (16.5)	1735	1038	1078	1118	1178	
XV	252 (1400)	257 (1900)	263 (2250)	269 (1450)	298 (20.0)	307 (24.0)	316 (23.0)	328 (12.5)	1720	1018	1038	1098	1118	1178
XVI	251 (7900)	255 (8500)	261 (7300)	267 (5100)	307 (25.5)	316 (24.5)	328 (14.5)		1720	1038	1078	1108	1178	
XVII		268 (12 800)	273 (14 800)	280 (13 200)	306 (30.0)	316 (27.0)	330 (16.0)		1725	1033	1078	1103	1183	
XVIII			259 (1700)			*a*			1680	1038	1118	1148	1178	
XIX			261 (19 000)			*a*			1729	1033	1078	1118	1143	1180
XX			276 (1200)	283 (12 200)		*a*			1725	1029	1108	1138	1158	1183
XXI			263 (3050)			302 (3600)			1725	1038	1078	1108	1178	
XXII			291 (4100)	296 (4050)		*a*			1715	1033	1068	1098	1158	
XXIII			253 (20 000)		283 (16 200)	292 (11 400)			1720	1033	1100	1139	1158	

a) Low solubility.

Acetals bearing an OH group have the R_f values far lower than acetal X without a substituent.

The structure of the prepared acetals was inferred on the basis of i.r., u.v., and ^{1}H-n.m.r. spetral data. The u.v. spectra of acetals (Table 2) reveal in the 280—340 nm range bands corresponding to $n \rightarrow \pi^*$ transitions. Aromatic acetals display additional bands ascribable to $\pi \rightarrow \pi^*$ transitions in the 240—300 nm range. Both types of bands generally form several maxima [15].

The i.r. spectra show characteristic ν(C=O) bands in the 1680—1735 cm^{-1} and ν(C—O—C—O—C) bands in the 1050—1170 cm^{-1} regions. Many authors [16—20] reported the exact differentiation of the individual bands of the latter group to ν_s and ν_{as}. Due to more complex types of acetals we listed merely the noticeable bands in this region.

The ^{1}H-n.m.r. spectra (Table 3) of aromatic acetals reveal protons in the —O—CH—O— grouping as a singlet the position of which is little substituent dependent. Acetal *VI* displays in this region protons of the —O—CH_2—O—

Table 3

Chemical shifts of protons

Compound	—CH_2— in the cyclopentane ring	—O—CH_2—C≤	—CH≤
I	2.10 (s, 4H)	3.59 (q, 8H)	—
II	2.11 (s, 4H)	3.57 (q, 8H)	—
III	2.16 (s, 4H)	3.59 (q, 8H)	—
IV	2.12 (s, 4H)	3.58 (q, 8H)	—
V	2.19 (s, 4H)	3.58 (q, 8H)	—
VI	2.19 (s, 4H)	3.57 (s, 8H)	4.70 (q, 4H)
VII	2.17 (s, 4H)	3.60 (s, 8H)	4.60 (s.t, 4H)
VIII	2.17 (s, 4H)	3.58 (s, 8H)	4.31 (t, 2H)
IX	2.11 (s, 4H)	3.50 (s, 8H)	4.35 (t, 2H)
X	2.32 (s, 4H)	3.81 (q, 8H)	5.37 (s, 2H)
XII	2.30 (s, 4H)	3.81 (s.s, 8H)	5.35 (s, 2H)
XIII	2.32 (s, 4H)	3.81 (q, 8H)	5.68 (s, 2H)
XIV	2.30 (s, 4H)	3.80 (s.s, 8H)	5.33 (s, 2H)
XV	2.30 (s, 4H)	3.81 (s.s, 8H)	5.35 (s, 2H)
XVI	2.31 (s, 4H)	3.80 (s.s, 8H)	5.32 (s, 2H)
XVII	2.30 (s, 4H)	3.72 (s.s, 8H)	5.30 (s, 2H)
XIX	2.27 (s, 4H)	3.82 (s.s, 8H)	5.41 (s, 2H)
XXI	2.25 (s, 4H)	3.70 (s.s, 8H)	5.20 (s, 2H)
XXIII	2.22 (s, 4H)	3.65 (s, 8H)	4.93 (d, 2H)

s — singlet; d — doublet; t — triplet; q — quartet; s.s — split singlet; s.t — split triplet.

grouping as a quadruplet due to a mutual interaction of the axial and equatorial protons. Proton signals of —O—CH—O— grouping in *VII* are seen as a quadruplet because of splitting caused by the neighbouring —CH_3 group, those in *VIII* and *IX* as a triplet. Protons in the —O—CH_2—C⩽ grouping present in all acetals show a pattern in accordance with the kind of the acetal involved. Thus, protons of acetals *VI—IX* prepared from aliphatic aldehydes resonate as singlets, those of acetals (*X—XIII*) from aromatic ones also as singlets, which might be in many cases split, or turned to quadruplets. Signals of these protons in acetals *I—V* appear as a quadruplet or even multiplet. These changes might be due to the steric arrangement of hydrogen atoms in the —CH_2O— group associated with alterations of the chair form as influenced by the bulkiness of substituents at the neighbouring carbon atom [21, 22]. The less bulky is the substitution at the adjacent carbon, the simplest are the observed signal patterns of acetals from aliphatic aldehydes. More rigid systems (acetals of aromatic aldehydes and ketones) display signals of both axial and equatorial protons of the grouping under investigation.

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