The Enantiomers of 7a*H*-Cyclopenta[*b*]pyran-7-ones and Their Thermal Racemization

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Abstract. The separation of the enantiomers of 7a*H*-cyclopenta[*b*]pyran-7-ones **1** was performed by enantioselective liquid chromatography with the sorbent/solvent systems triacetylcellulose/methanol, tribenzoylcellulose/methanol, and (+)-poly(trityl methacrylate)/silica gel/*n*-heptane/isopropanol. Barriers to ring opening were determined for two 7a-methyl and two 7a-phenyl substituted 2,4,5-triaryl derivatives by thermal racemization of the enantiomers. Substituted cyclopentadienones **2** are discussed as intermediates in the thermal electrocyclic ring opening/ring closure reactions.

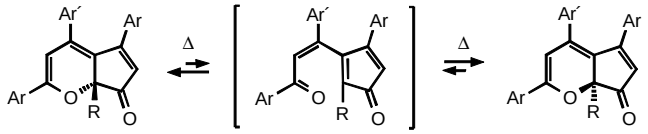
2*H*-Pyrans are known to undergo ring opening reactions to their valence isomers, the pentadienones, which are capable to recyclize forming the starting pyrans [1, 2]. These electrocyclic interconversions can be induced photochemically or by heat. In some cases an equilibrium between both isomers is observed. The favoured type of compound at given conditions strongly depends on the substitution pattern. Electron donating groups at position 5 of the pentadienone usually stabilize it by conjugation with the carbonyl group at C-1 whereas substituents at C-3 on the 2H-pyrans lead to a decrease of the tendency of electrocyclic ring opening [1, 2].

A possibility for the determination of kinetic data such as rate constants k or free enthalpies of activation $\Delta G^{\neq}$ for the electrocyclic ring opening/ring closure consists in the determination of the concentration of 2*H*-pyrans or pentadienones as a function of time. However, this method fails if one of the valence isomers is too stable that no formation of the other one by electrocyclic conversion can be detected.

Investigations on spiro[indoline-chromenes], spiro[indoline-benzoxazines] [3] and spiro[cyclohexadiene-indolines] [4] have shown that kinetic data for ring opening reactions can also be determined by liquid chromatographic separation of the enantiomers on non-racemic stationary phases followed by thermal enantiomerization, *i.e.* measuring the time-dependent loss of optical activity with a polarimeter.

Racemic 7a*H*-cyclopenta[*b*]pyran-7-ones **1**, the products of ring transformation of 2,4,6-triarylpyrylium salts with acyclic 1,2-diketones (butan-2,3-dione, 1-phenyl-propan-1,2-dione) [5] represent a novel type of 2*H*-pyran derivatives in which the pyran system is 2,3-anellated with a carbocyclic five-membered ring. At room temperature the isomeric cyclopentadienones **2** cannot be observed. Nevertheless, kinetic data for this interconversion should be obtained as in the case of spiro[indoline-chromenes], spiro[indoline-benzoxazines] [3] and spiro[cyclohexadiene-indolines] [4] by separation of the enantiomers (*R*)-**1** and (*S*)-**1** of the 7a*H*-cyclopenta[*b*]pyran-7-ones followed by thermal racemization. In this paper, we report such investigations and compare the data obtained with those of structurally related systems.

According to the substitution pattern of the chiral center at C-7a, the 7a*H*-cyclopenta[*b*]pyran-7-ones studied can be divided into the 7a-methyl derivatives **1a**–**g** and the compounds **1h**–**o** bearing a phenyl group at C-7a. The separation of the enantiomers (*R*)-**1** and (*S*)-**1** of both types of pyrans by liquid chromatography on triacetylcellulose using methanol as eluent failed with the exception of the derivatives **1a**, **1l**, **1n** and **1o** (cf. Table 1). When the sorbent was changed to tribenzoylcellulose, an improved separation of the 7a-methyl substituted pyrans **1a**–**g** could be observed whereas this system was inactive for the 7a-phenyl compounds **1h**–**o**. The latter ones were successfully separated on (+)-poly(trityl methacr-



(*R*)-**1** **2** (*S*)-**1**

1,**2**	Ar	Ar'	R
a	Ph	Ph	Me
b	Ph	4-Me-C_6H_4	Me
c	Ph	4-Cl-C_6H_4	Me
d	Ph	4-Br-C_6H_4	Me
e	4-Me-C_6H_4	Ph	Me
f	4-Cl-C_6H_4	Ph	Me
g	4-Br-C_6H_4	Ph	Me
h	Ph	Ph	Ph
i	Ph	4-Me-C_6H_4	Ph
j	Ph	4-MeO-C_6H_4	Ph
k	Ph	4-Cl-C_6H_4	Ph
l	Ph	4-O_2N-C_6H_4	Ph
m	4-MeO-C_6H_4	Ph	Ph
n	4-Cl-C_6H_4	Ph	Ph
o	4-Br-C_6H_4	Ph	Ph

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Table 1 Chromatographic parameters for the separation of enantiomers of 7a*H*-cyclopenta[*b*]pyran-7-ones **1** by liquid chromatography on different sorbents at 15–25 °C; k_1', k_2': retention factors of enantiomers [6]; Z: sign of rotation at 365 nm or 546 nm of the first eluted enantiomer; $\bar{k}'$: mean retention factors [6]

Compd.	Sorbent Triacetylcellulose [a]			Sorbent Tribenzoylcellulose [a]			Sorbent (+)-Poly(trityl methacrylate) [b] on silcagel		
1	k_1'(Z)	k_2'	$\bar{k}'$	k_1'(Z)	k_2'	$\bar{k}'$	k_1'(Z)	k_2'	$\bar{k}'$
a	0.7(–)	0.9		4.1(–)	10.1				0.7
b			0.6	3.7(+)	7.5				0.8
c			1.1	6.4(+)	19.0				0.9
d			1.2	6.6(+)	26.0				1.1
e			0.5	3.6(–)	11.1				0.6
f			1.0	8.6(+)	14.7		1.6(+)	2.3	
g			1.0	7.8(–)	28.0				0.7
h			0.9			5.9	1.9(–)	3.4	
i			0.7			5.5	1.7(–)	3.4	
j			1.1			8.7	2.3(–)	4.9	
k			1.2			7.9	1.7(–)	4.7	
l	2.1(+)	3.3				[c]	2.6(–)	13.1	
m			1.2			12.1	3.2(+)	5.7	
n	0.9(–)	1.2				[c]	3.4(–) [a]	6.9 [a]	
o	1.0(–)	1.4				[c]			2.0

[a]) Eluent: methanol; [b]) Eluent: *n*-heptane/isopropanol (v:v = 9:1); [c]) Not determined

ylate)/silica gel using a 9:1-mixture of *n*-heptane/isopropanol as eluent. Representative examples for the separation of both types of pyrans are shown in Fig 1.

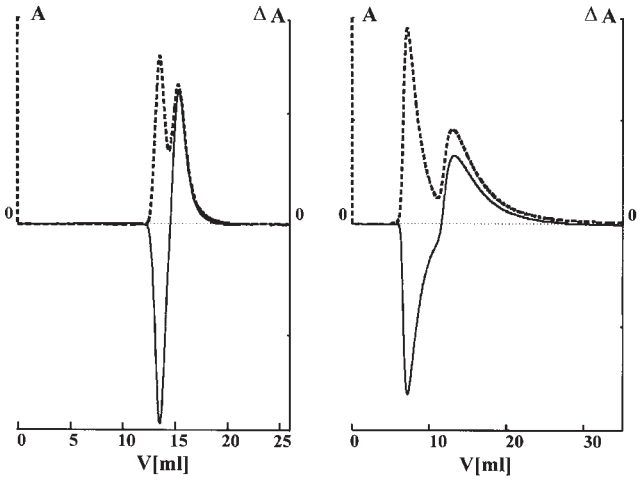

Fig. 1 Chromatograms of the 7a*H*-cyclopenta[*b*]pyran-7-ones **1a** (left, in methanol on triacetylcellulose) and **1h** (right, in *n*-heptane/isopropanol, v:v = 9:1, on (+)-poly(trityl methacrylate)/silica gel); A and ΔA: absorbance and differential absorbance at 260 nm using the Jasco CD-995 detector, V: volume of eluate (V = 0 upon injection)

For a study of the thermal racemization (details see experimental part), the derivatives **1a**, **1f**, **1h**, and **1n** with comparable substitution pattern were chosen. Table 2 contains the half life times $t_{0.5}$ of the thermal racemization determined at 73.7 °C in toluene together with the corresponding calculated figures of the free enthalpy of activation $\Delta G^{\neq}$ for ring opening [3].

Table 2 Results of thermal racemization of 7a*H*-cyclopenta[*b*]pyran-7-ones **1** in toluene at 73.7 ± 0.5 °C, monitored by polarimetry at 546 nm; $t_{0.5}$: half-life time, $\Delta G^{\neq}$: free enthalpy of activation for the ring opening

Compd.	$t_{0.5}$ (min)	$\Delta G^{\neq}$, ± 0.2 (kJ·mol^{-1})
1a	223.8	113.9
1f	142.9	112.6
1h	98.2	111.5
1n	86.4	111.1

The interconversion of the enantiomers (*R*)-**1** and (*S*)-**1** should proceed by electrocyclic ring opening/ring closure *via* the valence isomers, the cyclopentadienones **2** [1]) [7]. Although these species cannot be detected at room temperature, some other cyclopentadienones with an acyl or vinylogous acyl group in position 3 are known as stable compounds [8] supporting this hypothesis. In contrast to the 7a-methyl substituted pyrans **1a**–**g**, in the derivatives **1h**–**o** the more bulky phenyl residue is bonded at the asymmetric carbon atom C-7a. Hence, the release of steric strain in the electrocyclic ring opening **1** → **2** should be more important for **1h**–**o**, which explains the somewhat shorter half life times and lower free enthalpies of activation for these pyrans.

The strong influence of the kind of 2,3-anellation in 2*H*-pyrans on the tendency of an electrocyclic ring opening reaction is shown by a comparison with the known 2,5,5,8a-tetramethyl-6,7,8,8a-tetrahydro-5*H*-chromene [9]. An equilibrium between the two isomers can be observed, since in this case the resulting acyclic valence isomer contains the

[1]) The same type of compounds was postulated as intermediates in the formation of the 7a*H*-cyclopenta[*b*]pyran-7-ones by ring transformation of pyrylium salts with acyclic 1,2-diketones [5]

more stable cyclohexene ring instead of the cyclopentadienone system.

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Experimental

The synthesis as well as the absorption spectra (λ_{max}, lg ε) of the 7a*H*-cyclopenta[*b*]-pyran-7-ones **1a**–**o** have been reported in a previous paper [5].

High-pressure liquid chromatography was performed on triacetylcellulose (Merck, 10 μm; column 250×8 mm; eluent methanol, flow rate 10 ml·min^{-1}, pressure 60 bar), on tribenzoylcellulose (Riedel-de Haën, 10–15 μm; column 250×8 mm; eluent methanol, flow rate 15 ml·min^{-1}, pressure 60 bar), and on (+)-poly(trityl methacrylate)/silica gel (Daicel; column 250×4 mm; eluent *n*-heptane/isopropanol, v:v = 9:1, flow rate 1 ml·min^{-1}, pressure 170 bar). The injected quantities of racemates were in the range of 0.04–0.3 mg in 1 ml of eluent.

For the photometric detection the UV spectrometers ERC 7210 and ERC 7215 (Erma Optical Works, Ltd.) and for polarimetric detection the polarimeter Perkin-Elmer 241 were used. Detailed description of the injection and detector systems along with the chromatographic equipment have been given previously [3, 10]. The chromatograms shown in Fig. 1 were obtained using the Jasco CD-995 detector [11, 12].

Racemization of **1a**, **1f**, **1h**, and **1n** was monitored in toluene by an off-line procedure, *i.e.* the compounds were enriched in preparative scale by repeated chromatography as described above and then dissolved in toluene. The polarimetric cell which contained the solution of this enriched enantiomer was thermostated to the given temperature, and the decrease of the angle of rotation was monitored. The thermal stability was checked by chromatography after thermal racemization; in all cases the chromatograms obtained were identical with those of the starting compounds indicating that no decomposition had occurred. The interconversion of the enantiomers was treated as a reversible first-order reaction as previously described [3]. A computer program [13] was used for the calculation of $\Delta G^{\neq}$ for the ring opening [3] (Table 2) from the polarimetric racemization data.

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