Acta Chemica Scandinavica B 28 (1974) 344—348

The Synthesis and Stereochemistry of 3-Alkyl-1,2-indandiol Diacetates

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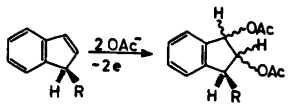
A series of alkylindenes, with the alkyl group methyl, ethyl, propyl, isopropyl, butyl, and *t*-butyl has been subjected to (a) permanganate oxidation and (b) oxidation by iodine/silver acetate under "wet" and "dry" conditions, These methods, in combination with acetylation by acetic anhydride/pyridine, give access to the four possible 3-alkyl-1,2-indandiol diacetates from each 1-alkylindene (except for the *t*-butyl compound, where the all-*trans*-isomer is not available by these methods). Structures have been assigned to all compounds by synthetic, mechanistic, and NMR spectral considerations.

Studies on the stereochemistry of the anodic side-chain acetoxylation of 2-*t*-butylindan [1] and 1-*t*-butylacenaphthene [2] have indicated that the anodic surface might exert a certain degree of steric control on the reaction. In order to extend these studies to other reaction types we have chosen to investigate the anodic addition of two acetoxy groups to 1-alkylindenes (eqn. 1). Since the steric relationships among the



(1)

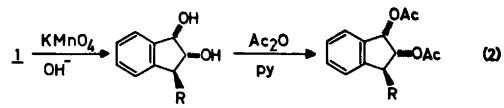
1 2

R = CH_3, C_2H_5, C_3H_7, i-C_3H_7, C_4H_9, and *t*-C_4H_9

four possible isomeric 3-alkyl-1,2-indandiol diacetates (*2*) are not known, it was first necessary to establish these by independent methods. This paper is a report of the synthesis and elucidation of the structures of all possible diacetates of the type *2* with R defined as in eqn. 1.

RESULTS AND DISCUSSION

It is known that potassium permanganate will oxidize alkenes to *cis* glycols in alkaline solution,[3] as exemplified for a 1-alkylindene in eqn. 2. It has also been shown that potassium permanganate will attack a properly substituted alkene preferentially from the sterically least hindered side and thus should give the less hindered *cis* glycol (*3*) from a 1-alkylindene [4–7] (eqn. 2). From *3*, the corresponding diacetate (*4*) should be easily available by reaction with acetic anhydride/pyridine.

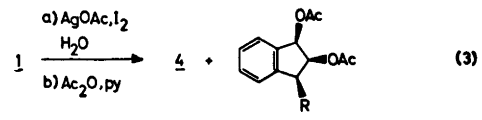


(2)

3 4

Another method of preparing *cis* glycols is the reaction between an alkene and iodine/silver acetate in "wet" acetic acid.[8] Again exemplifying with a 1-alkylindene, this reaction should give a mixture of *cis* glycol monoacetates from which the two possible *cis* diacetates *4* and *5* should be easily available (eqn. 3). The same reaction in "dry" acetic acid, [5b] known to give *trans* glycol monoacetates, should in the case of a 1-alkylindene directly give access to the two possible *trans* glycol diacetates *6* and *7* (eqn. 4).

The more often used method of preparing glycols from alkenes by peracid oxidation cannot be used here, since one usually obtains a mixture of *cis* and *trans* glycols [9,10] unless the reaction conditions are controlled very carefully.[11]



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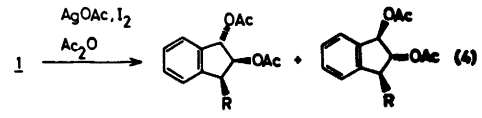

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Table 1. Yields and physical data of *4*, synthesized *via* permanganate oxidation of 3-alkylindenes (*1*) and subsequent acetylation of the product (eqn. 2).

R	Yield of *4*, %	B.p. °C at mmHg	Retention time, min[a]
CH_3	35	117–120/0.8	15.0
C_2H_5	75	130–132/1.5	20.1
C_3H_7	73	137–139/1.0	15.0
i-C_3H_7	68	127–128/0.7	13.6
C_4H_9	47	135–137/0.8	19.0
t-C_4H_9	60	125–120/1.0	17.0

[a] 2 m × 0.3 mm 5 % neopentylglycol succinate on Chromosorb W column at 180°C; carrier gas N_2, flow rate 20 ml/min.

In the oxidation of 1-alkylindenes (*1*) with potassium permanganate/water only one of the possible *cis* glycols is formed in each case. In line with the known stereochemistry of the reaction (see eqn. 2) structure *3* is assigned to these glycols. Table 1 gives overall yields of the reaction sequence (eqn. 2) and some physical data for identification of the diacetates *4*, R = CH_3, C_2H_5, C_3H_7, i-C_3H_7, C_4H_9, and *t*-C_4H_9.

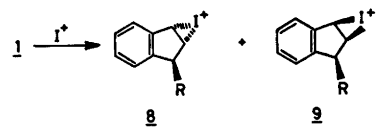
The reaction of 1-alkylindenes (*1*) with silver acetate/iodine in "wet" acetic acid, followed by acetylation of the monoacetates formed, gives a mixture of two *cis* diacetates, one of them being identical to *4* and the other one accordingly assigned structure *5*. By using GLC and/or NMR analysis it was possible to determine the relative amounts of *4* and *5* in the product mixtures (Table 2).

Table 2. Yields and retention times of products from the reaction between 1-alkylindenes (*1*) and iodine/silver acetate in "wet" acetic acid and subsequent acetylation (eqn. 3).

R	Yield of *4*+*5*, %	Relative yields, %		Retention time, min[a]	
		4	*5*	*4*	*5*
CH_3	52	69	31	15.0	17.2
C_2H_5	55	65	35	20.1	22.2
C_3H_7	72	65	35	15.0	15.5
i-C_3H_7	57	29	71	13.6	15.2
C_4H_9	49	72	28	19.0	20.1
t-C_4H_9	59	< 0.1	100	17.0	20.1

[a] 2 m × 0.3 mm 5 % neopentylglycol succinate on Chromosorb W column at 180°C; carrier gas N_2, flow rate 20 ml/min.

The reaction between an alkene and iodine/silver acetate in "wet" acetic acid is supposed [12] to follow the mechanism given in eqns. 5 – 7 for a 1-alkylindene:



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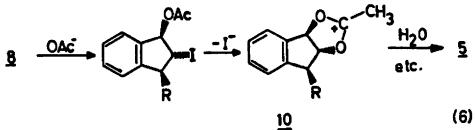

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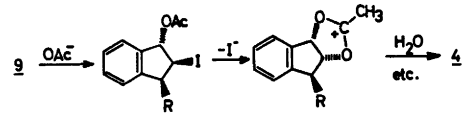

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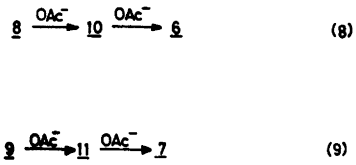
The initial step is the formation of iodonium ions *8* and *9* which then undergo S_N2 displacement by acetate ion followed by internal nucleophilic displacement of iodide ion to give acetoxonium ions *10* and *11*. These hydrolyze to give a mixture of *cis* hydroxy acetates, from which a mixture of diacetates *4* and *5* are prepared by treatment with acetic anhydride/pyridine. In the first step which controls the overall stereochemistry of the reaction sequence,

an increase in the steric demands of R should increase the percentage of iodonium ion *8* and hence the proportion of *5* in the final product. The results given for $R=C_2H_5$, i-C_3H_7 and *t*-C_4H_9 in Table 2 show this prediction to be correct.

The same reaction, run in "dry" acetic acid, gave a mixture of diacetates which by GLC and/or NMR spectral analysis were not identical with either *4* or *5*. Accordingly, the product mixture must consist of *trans* diacetates *6* and *7*. The assignment of structures to *6* and *7* is based on predictions from mechanistic considerations in the following way: Under "dry" conditions the mechanism is identical to that given in eqns. 5–7, except for the hydrolysis step which is exchanged for an S_N2 attack at the benzylic carbon of acetoxonium ions *10* and *11* by acetate ion [5b, 12] (eqns. 8 and 9). Since the first part of the reaction is performed in the same way under both "wet" and "dry" condition, *8* and *9* and hence *10* and *11* should be formed in approximately the same ratios in both cases. From this it follows that the *4*/*5* ratio should be approximately equal to the *7*/*6* ratio, and this prediction has been the basis of the structural assignments of Table 3.

The NMR spectra of compounds *4*–*7* are in good agreement with the general structure *2* but cannot be reliably used for detailed stereostructural assignments due to the irregularities of vicinal coupling constants in the indan system.[1,13,14] Table 4 illustrates these difficulties



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for two representative sets of compounds *4*–*7*, $R=CH_3$ and C_4H_9. In these cases there is no possibility of assigning *cis* or *trans* stereochemistry of H_a, H_b and H_c from the relative magnitudes of the coupling constants J_{ab} and J_{bc}.

The mass spectra of diacetates *4*–*7* are closely similar. (For an example, see Table 5). No molecular ion is detectable, the fragment with highest mass being formed by elimination of acetic acid from M^+.

Further evidence for the correctness of the structural assignments above was obtained by studying the pseudocontact shifts in the NMR

Table 3. Yields and retention times of products from the reaction between 1-alkylindenes and iodine/silver acetate in "dry" acetic acid (eqn. 4).

R	Yield of *6*+*7*, %	Relative yields, %		Retention time, min[a]	
		7	*6*	*7*	*6*
CH_3	53	68	32	13.1	15.1
C_2H_5	64	68	32	16.2	18.4
C_3H_7	61	67	33	12.0	13.8
i-C_3H_7	53	22	78	10.7	11.9
C_4H_9	51	72	28	15.6	17.7
t-C_4H_9	57	<0.1	100	14.0[b]	16.1

[a] 2 m×0.3 mm 5 % neopentylglycol succinate on Chromosorb W column at 180°; carrier gas N_2, flow rate 20 ml/min. [b] This compound was prepared by anodic oxidation of 1-*t*-butylindene.[15]

Table 4. NMR parameters of the five-ring hydrogens of 3-alkyl-1,2-indandiol diacetates (H_A on the 3-carbon; *t* denotes *trans* coupling, *c* *cis*).

R	Compound	H_a,δ	H_b,δ	H_c,δ	J_{ab},Hz	J_{bc},Hz
CH_3	*4*	3.5	5.0	6.2	7.4 (*t*)	5.2 (*c*)
	5	3.3	5.6	6.2	5.6 (*c*)	5.6 (*c*)
	6	3.2	5.5	6.2	6.6 (*c*)	4.2 (*t*)
	7	3.2	5.2	6.2	6.0 (*t*)	4.8 (*t*)
C_4H_9	*4*	3.3	5.6	6.1	5.6 (*t*)	5.6 (*c*)
	5	3.5	5.2	6.2	5.2 (*c*)	5.2 (*c*)
	6	3.1	5.5	6.2	5.0 (*c*)	6.8 (*t*)
	7	3.1	5.3	6.1	4.6 (*t*)	3.6 (*t*)

Table 5. Mass spectral data for diacetates *4*–*7*, $R=C_2H_5$.

Fragment *m/e*	Relative abundance, % *4*	*5*	*6*	*7*
202	6	9	8	8
161	12	16	12	12
160	100	100	100	100
145	36	43	40	48
132	10	12	11	11
131	33	52	33	39
115	13	15	18	20
91	8	9	7	7
43	50	74	48	57

spectrum of *4* – *7*, R = *t*-Bu, caused by the addition of tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium(III), Eu(fod)$_3$. Since Eu(fod$_3$) is sterically very demanding, one would expect it to complex at the 3-acetoxy group of the sterically most crowded diacetate, the all-*cis* isomer *5*. Hence the 3-acetoxy methyl should be more shifted than that of the 2-acetoxy group, and H_a and the methyl groups should be affected to a relatively low extent (see Table 6). The second isomer with *cis* acetoxy groups, *4*, should have nearly equivalent acetoxy groups from the steric point of view, resulting in nearly equal shifts of the acetoxy methyl signals. On the other hand, both the H_a and the R methyl signal should be relatively more shifted than in *5*.

Isomer *6*, with the 2-acetoxy group *cis* to the *t*-butyl group, again should have the 3-acetoxy group sterically more accessible for complexing with Eu(fod)$_3$. On the other hand, the all *trans* isomer *7* should have nearly equivalent acetoxy groups and hence show similar shifting of the acetoxy methyl signals.

A study of the anodic addition of two acetoxy groups across the double bond of 1-alkylindenes will be reported later.[15]

Table 6. Pseudocontact shifts in the NMR spectra of *4* – *7*, R = *t*-C_4H_9 by addition of Eu(fod)$_3$; solvent $CDCl_3$.[a]

Compound	Shift, Hz CH_3 in *t*-C_4H_9	CH_3 in 3-acetoxy	CH_3 in 2-acetoxy	H_a	[Eu(fod)$_3$]/[substrate]
4	43	166	160	143	0.39
5	38	210	143	62	0.39
6	52	134	110	100	0.42
7	68	148	137	154	0.36

[a] Recorded on a Varian T-60 NMR spectrometer.

EXPERIMENTAL

1-Alkylindenes. These compounds were prepared as described earlier.[16]

trans,cis-*3-Alkyl-1,2-indandiol diacetates* (*4*). To a cooled solution of 1-alkylindene (10.0 mmol) in acetone-water (80 + 20 ml) a solution of potassium permanganate (1.5 g) and potassium hydroxide (0.3 g) in water (30 ml) was added at a rate allowing for the purple colour caused by one drop to disappear before the next drop was added. The temperature was not allowed to exceed 0°C during the addition. After 2 h the manganase dioxide was filtered off and the solvent removed from the filtrate in a rotating-film evaporator. The residue was treated with a mixture of acetic anhydride (25 ml) and pyridine (1 ml) and refluxed for 5 min. After cooling and addition of water (100 ml) the organic material was extracted into pentane. The pentane solution was then worked up by distillation, giving the pure isomers *4* (see Table 1).

Mixtures of trans,cis- *and all*-cis-*3-alkyl-1,2-indandiol diacetates* (*4 and* 5). Iodine (6.5 g) was added all at once at room temperature to a mixture of acetic acid (125 ml), silver acetate (8.6 g, 96 %) and 1-alkylindene (25 mmol). The solution was stirred for 1 h at 20°C and water (2 ml) was added. The solution was then stirred at 80 – 90° for 2 h. From the cooled solution silver iodide was removed by filtration and acetic acid by evaporation. The residue was refluxed for 5 min with acetic anhydride (25 ml) and pyridine (1 ml). The same work-up procedure as above yielded a mixture of *4* and *5* (see Table 2; for R = *t*-Bu, only *5* is formed).

Mixtures of cis-trans- *and all*-trans-*3-alkyl-1,2-indandiol diacetates* (*6 and* 7). This reaction was carried out exactly as described in the preceding case, except that the water was replaced with acetic anhydride (5 ml) and the acetylation procedure was omitted.

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Received December 6, 1973.