Acid Catalysis induces a Total Change from Retention to Inversion of Configuration in CO_2 Elimination from β-Lactones

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Summary With increasing acidity of the reaction medium the stereochemistry of the CO_2 elimination from cis-3-t-butyl-4-(*p*-methoxyphenyl)oxetan-2-one (**1a**) and from *cis*-3-t-butyl-4-phenyloxetan-2-one (**1b**) gradually changes from total retention to total inversion of configuration, so that sterically pure (*Z*)- and (*E*)-3,3-dimethyl-1-(*p*-methoxyphenyl)but-1-ene (**3a**) and (**7a**) and (*Z*)- and (*E*)-3,3-dimethyl-1-phenylbut-1-ene (**3b**) and (**7b**) may be obtained from (**1a**) and (**1b**), respectively.

The assumption that β-lactones (oxetan-2-ones) eliminate CO_2 with complete retention of configuration has been undisputed for more than a decade.[1] We report that, at least for our model systems (**1a**, **b**), this stereospecificity is true only for non-acidic solvents. With increasing acidity of the reaction medium the stereochemistry continuously changes from >98% retention to >98% inversion of configuration.† Simultaneously, the reaction rate is markedly increased (Tables 1 and 2).

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† Control experiments have shown that the olefins are totally stable under the reaction conditions.

TABLE 1. Influence of acid catalysis on the stereochemistry and rate constants of CO_2 elimination from (**1a**).

Reaction medium	T/°C	Proportions[a] (**3a**) : (**7a**)	k_{rel} (100°C)
1,2-Dichlorobenzene	100	>98:2	1·0
1,2-Dichlorobenzene + 1 mol% acetic acid	100	86:14	6·5
1,2-Dichlorobenzene + 10 mol% acetic acid	50	32:68	145
1,2-Dichlorobenzene + 19 mol% acetic acid	50	15:85	290
Acetic acid	50	3:97	2,900
1,2-Dichlorobenzene + 1 mol% trifluoroacetic acid	25	<2:98	15,000

[a] The total yield of [(**3a**) + (**7a**)] is >97% in all experiments.

We have provided evidence previously[2] that the elimination of CO_2 from β-lactones proceeds *via* the zwitterionic tetramethylene intermediate (**2**) (Scheme), which on account of strong through-bond and through-space-1,4-interactions shows a high barrier to 3,4-rotation.[3] Consequently, the fragmentation of (**2**) should occur with retention of configuration even in the presence of bulky *cis*-eclipsed substituents at the 3- and 4-positions.‡

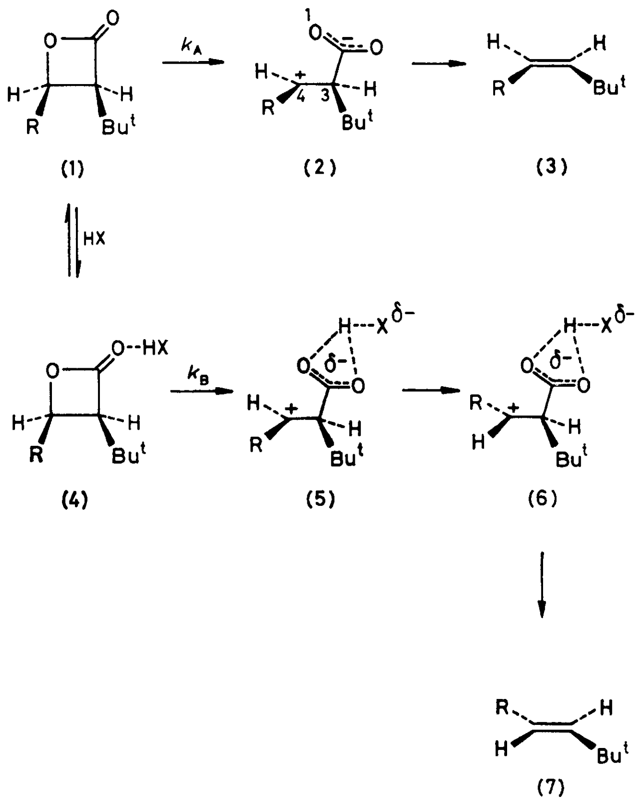
3,4-Rotation in (**2**) and, hence, inversion of configuration can only be expected if the 1,4-interaction is sufficiently reduced. In our case this is achieved by protonating the carboxylate moiety. In the presence of acid two competing reaction pathways have to be assumed (Scheme): the uncatalysed one with retention (**1**) → (**2**) → (**3**) and the acid-catalysed one with inversion (**1**) → (**4**) → (**5**) → (**6**) → (**7**), the rate-determining steps being (**1**) → (**2**) (k_A) and (**4**) → (**5**) (k_B), respectively. Intermediates (**4**), (**5**), and (**6**) may be considered as aggregates of one lactone unit and one or more molecules of HX. Owing to the superior stabilization of the negative charge in (**5**) k_B is much greater than k_A. This explains why both inversion and rate acceleration are observed with increasing acidity (Tables 1 and 2). On comparing the series **a** and **b** it can be seen that the carbenium centre in (**5a**) is much more stabilized than that in (**5b**). Therefore, to obtain effects of similar magnitude, much stronger acids are necessary in the case of (**1b**).

TABLE 2. Influence of acid catalysis on the stereochemistry and the rate constants of CO_2 elimination from (**1b**).

Reaction medium	T/°C	% Yield (**3b**) + (**7b**)	Proportions (**3b**)/(**7b**)	k_{rel} (100 °C)
1,2-Dichlorobenzene	140	98	94:6[a]	1·0
Acetic acid	100	92	82:18	140
1,2-Dichlorobenzene + 1 mol% trifluoroacetic acid	100	98	23:77	290
1,2-Dichlorobenzene + 10 mol% trifluoroacetic acid	50	67	11:89	[c]
Ether + 1 mol equiv.[b] $MgBr_2$	25	98	<2:98	[d]

[a] In mesitylene (160 °C) (**3b**) : (**7b**) >99:1. [b] Based on (**1b**). [c] Decomposition. [d] Heterogeneous reaction.

It remains an open question whether (**5**) rotates to (**6**) without undergoing any decarboxylation. However, in view of the low rotational barriers usually found in carbenium ions§ this appears quite likely, at least for (**5a**).



SCHEME

a; R = p-$MeOC_6H_4$
b; R = Ph

In conclusion, we have shown that stereoretention cannot be taken for granted in the CO_2 elimination from β-lactones, but, quite in accordance with the postulated intermediate (**2**), is rather the consequence of a non-acidic reaction medium. From the preparative point of view our findings may provide a new method for a totally stereocontrolled synthesis of both *cis*- and *trans*-olefins from a common precursor (**1**).¶

(*Received*, 18*th May*, 1981; *Com.* 585.)

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‡ *cis*-3,4-Di-t-butyloxetan-2-one eliminates CO_2 with >95% stereoretention in 1,2-dichlorobenzene.

§ About 1·5 kcal mol^{-1} for the neopentyl cation: W. A. Sanderson and H. S. Mosher, *J. Am. Chem. Soc.*, 1966, **88**, 4185. 4·184 J = 1 cal.

¶ For a different method using *threo*-3-hydroxy carboxylic acids as precursor see J. Mulzer, A. Pointner, A. Chucholouski, and G. Brüntrup, *J. Chem. Soc., Chem. Commun.*, 1979, 52.

[1] For a review see: T. Imai and S. Nishida, *J. Org. Chem.*, 1980, **45**, 2354.

[2] J. Mulzer and M. Zippel, *Tetrahedron Lett.*, 1980, **21**, 751; *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 465.

[3] G. A Segal, *J. Am. Chem. Soc.*, 1974, **96**, 7892; R. Huisgen, *Acc. Chem. Res.*, 1977, **10**, 117, 199.