High pressure mechanistic diagnosis in Baeyer–Villiger oxidation of aliphatic ketones

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Abstract—The pressure effect is examined in Baeyer–Villiger oxidation of aliphatic ketones. This effect is small, reflected in slightly negative activation volumes (-2 to -8 cm^3 mol^{-1}). These values allow the picturing of the volume profile. They refer to a late transition step and give support for a rate-determining migration step experiencing full concertedness. © 2001 Elsevier Science Ltd. All rights reserved.

In former papers, we reported on high pressure reactions involving aliphatic ketones of increasing steric complexity, e.g. Knoevenagel reactions[1] and nucleophilic additions.[2] We disclosed an important result as sterically hindered reactions are prone to increased sensitivity to pressure compared to their unhindered analogs. There are many other name reactions using ketones as main substrates. As an example, the venerable Baeyer–Villiger oxidation of ketones to esters has, to our knowledge, never been examined under pressure (Scheme 1). Our original objective was attempted generalization of the pressure versus steric hindrance relationship. To that purpose, we examined the oxidation of aliphatic ketones by *m*-chloroperbenzoic acid (MCPA) under ambient and high pressure (300 MPa) conditions (Table 1). The reaction proceeded cleanly with full chemoselectivity.

These results are indicative of a small pressure effect, as the yields are increased by a factor of 2–3 when pressure is raised to 300 MPa. There is no clear relation between pressure steric acceleration and steric bulk of R and R′ if any, at variance with our previous results.[1,2] This apparent singularity prompted us to examine kinetically the Baeyer–Villiger reaction in the pressure range 0–100 MPa in order to determine the volume of activation $\Delta V^{\neq}$.[3,4]

The alleged mechanism rests on a multi-step ionic process proposed by Criegee[5] consisting of the acid-catalyzed addition of MCPA to the protonated carbonyl bond followed by migration within the transient intermediate (A) (Scheme 2). The mechanism of the Baeyer–Villiger reaction has received extensive attention since Criegee's proposal.[6] Most authors consider the migration step as rate determining on the basis of stereochemical and isotopic labeling results, kinetic studies and theoretical calculations.[7] Interestingly, it was found that migration is synchronous with the departure of the leaving group.[8] A recent paper reported on unusual

Table 1. Effect of pressure on yields in Baeyer–Villiger oxidation of ketones[a]

R	R′	Yields (%)	
		0.1 MPa	300 MPa
CH$_3$	n-C$_4$H$_9$	12	37
CH$_3$	sec-C$_4$H$_9$	58	89
CH$_3$	$tert$-C$_4$H$_9$	37	88
CH$_3$	CH$_2$-$tert$-C$_4$H$_9$	5	16
nC$_4$H$_9$	n-C$_4$H$_9$	21	60
C$_3$H$_7$	i-C$_3$H$_7$	28	47

[a] In CHCl$_3$ at 25.0°C for 6 h.

Scheme 1.
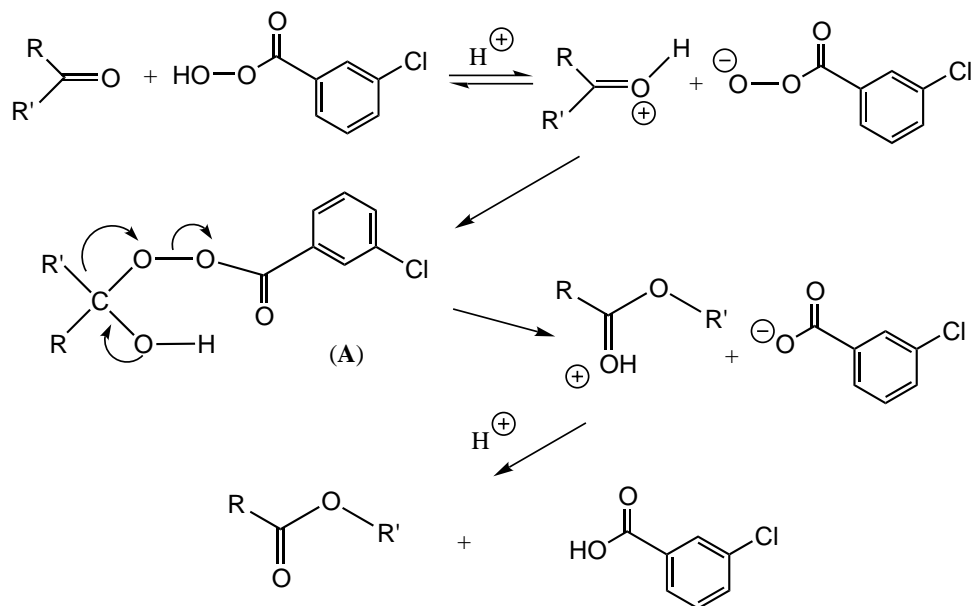
Scheme 2.

migration modes in the Baeyer–Villiger oxidation of α-fluorocyclohexanones to lactones.[9]

Considering that the addition step involves formation of a C–O bond whereas migration implies formation and cleavage of various bonds, the activation volume could be a decisive argument to determine which step is rate determining since bond making and bond breaking are clearly reflected in the volume. We therefore, followed the kinetics at different pressures of the Baeyer–Villiger oxidation of some aliphatic ketones where R and R′ have variable bulkiness.[10] All reactions satisfied clear second-order kinetics (the reaction is first-order in both ketone and peracid and is acid-catalyzed).[6,11]

If the RDS is migration it involves a major rearrangement process with several events consisting of equally matched bond-making and bond-breaking except the cleavage of the O–O bond. Intuitively, based on mere structural modifications, the RDS should feature slightly positive $\Delta V^{\neq}$-values meaning a pressure induced deceleration of the rate in B–V oxidations.

Considering the $\Delta V^{\neq}$-values listed in Table 2, this is clearly not the case although it is obvious that the first step is not rate-determining since it would require values around -20 cm^3 mol^{-1}. The results underscore the remarkable uniformity of $\Delta V^{\neq}$ values which are all less negative or around zero (from -2 to -8 cm^3 mol^{-1}).

Comparison with reaction volumes ($+9$–10 cm^3 mol^{-1}) suggests that the transition state is late but not close to products (Scheme 3). We are, therefore, inclined to consider that the slightly negative $\Delta V^{\neq}$-values reflect a perfectly concerted process involving simultaneous electron flow with concomitant migration and O–O cleavage. Interestingly, they do not reflect any steric contribution, contrasting with our preceeding results.[1,2]

These observations are in full harmony with the B–V mechanism advocated by other ways.[6–8] Particularly, it was found that with peroxidic nucleophiles a steric requirement is not important.[6] This is also corroborated by the k-values determined at ambient pressure showing only slight variations even with increasing size of R and R′. In fact, k-values are even higher when R′ is $tert$-C$_4$H$_9$ or sec-C$_4$H$_9$ than the corresponding value in the reaction involving R′$=$C$_4$H$_9$. The result is in line with earlier observations[6a] and can be accounted for by steric assistance of migration of the more bulky group.[12]

Conclusion

The present piezokinetic study nicely confirms in every aspect the mechanism of the Baeyer–Villiger reaction previously determined by a number of authors also in agreement with recent semi-empirical studies.[13] Importantly, it should be emphasized that high pressure kinetics is a complementary tool to assess mechanisms[14] supported by other lines of evidence, despite recent

Table 2. Kinetic data for Baeyer–Villiger oxidation of ketones[a]

R	R′	10^5 k (M s^{-1})	$\Delta V^{\neq}$ (± 2 cm^3 mol^{-1})
CH$_3$	n-C$_5$H$_{11}$	3.89	-8.0
CH$_3$	n-C$_4$H$_9$	3.36	-6.5
CH$_3$	sec-C$_4$H$_9$	10.93	-5.0
CH$_3$	$tert$-C$_4$H$_9$	9.34	-5.0
CH$_3$	CH$_2$-$tert$-C$_4$H$_9$	1.56	-8.0
C$_3$H$_7$	i-C$_3$H$_7$	9.03	-2.0
i-C$_4$H$_9$	i-C$_4$H$_9$	1.98	-6.0

[a] The reported k-values refer to reactions carried out in CHCl$_3$ at 49.7°C and 0.1 MPa.
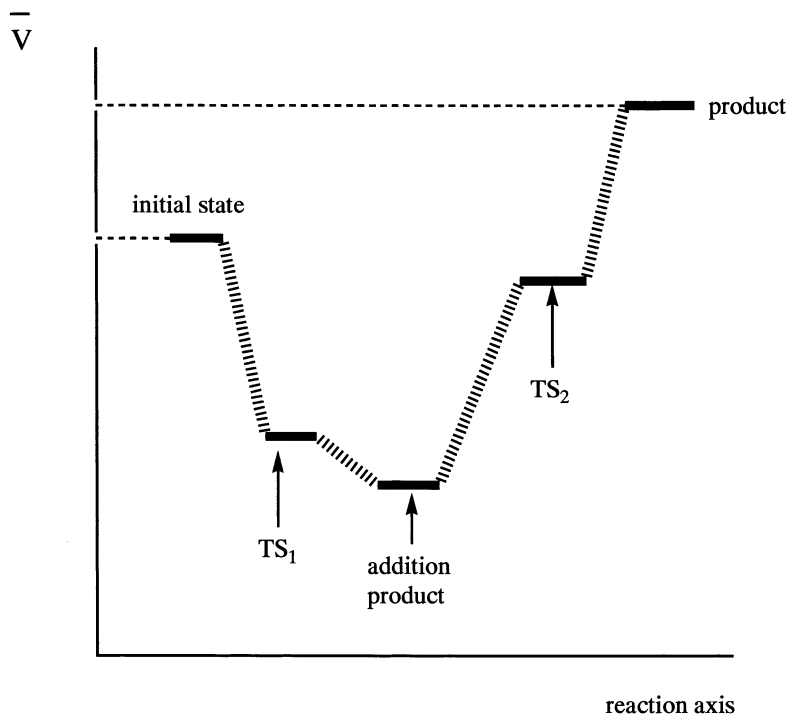
Scheme 3. A possible volume profile for the Baeyer–Villiger reaction (TS: transition state). The relative positions of the different volume levels are arbitrary.

allegations denying any value for mechanistic delineation by this method.[15]

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3. Standard runs (Table 1): In a typical run, MCPA (1.0 mmol), ketone (0.5 mmol) and bibenzyl (internal standard about 0.12 mmol) are placed in a flexible 2.5 mL PTFE tube. The volume is adjusted with $CHCl_3$. The tube is shaken and rapidly introduced into the high pressure vessel. After release of pressure, the solution is washed with an aqueous solution of $NaHCO_3$ (20%). The organic layer is extracted with ether washed first with the $NaHCO_3$ solution, then with water. The volatile compounds are removed in vacuo. The residue is directly analyzed by ^1H NMR and the yield determined from relative intensities of characteristic protons versus methylene protons of the internal standard.
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10. Kinetics. A stock chloroform solution of weighed MCPA and bibenzyl (standard) is prepared and kept at 5°C. For a kinetic run 60 μl of ketone is placed in a PTFE tube and weighed. An adjusted volume (600 μl of stock solution is added and weighed. The tube is then submitted to the desired pressure. Working up and analysis as above.
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