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IDENTIFICATION OF ELIMINATION REACTIONS DURING THE DEGRADATION OF 5-BROMOCAMPHOR BY P. Putida

Sujit Banerjee and Gary Dec

Life Sciences Division
Syracuse Research Corporation
Syracuse, New York 13210

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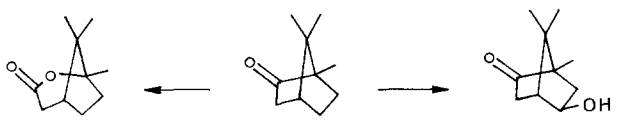
SUMMARY - (+)5-Exo-bromocamphor is degraded by camphor grown P. Putida to the corresponding 1,2-lactone and to pericyclocamphanone, a 1,3-elimination product which is subsequently lactonized.

Camphor oxidation by P. Putida initially proceeds via two parallel pathways, namely 5-exo-hydroxylation and 1,2-lactonization as shown below (1). The



effect of 5-substitution in camphor could result in (i) predominant lactone formation, (ii) recalcitrance of the substrate, or (iii) changes in the metabolic pathway. In order to distinguish between these possibilities, we have studied the degradation of (+)5-exo-bromocamphor (1), and have characterized some of the initial degradation products.

In a typical experiment, a salts medium containing the title compound (1) (2) in solution was innoculated with camphor grown P. Putida (ATCC No. 29607) (3), and the neutral metabolites in the broth were periodically analyzed by GC-chemical ionization mass spectrometry (GC-CI/MS). Controls were run to ensure that the observed products originated entirely from metabolic processes. The parent ions of some of the major observed products in order of elution from a 3 percent OV-1 on Chromosorb W column are listed in Table 1. The products

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Table 1.
Parent ions of the neutral metabolites obtained from 5-bromo-camphor and pericyclocamphanone

	M+1 (parent ion)		
Substrate:	1	2	Product
	129	129	
	151	151	2
		165	
	231,233		1
	167	167	3
	247,249		4

designated as 3 and 4 were identical to the major products obtained from peracetic acid oxidation under neutral conditions (4) of 2 and 1, respectively. This process is known to yield the 1,2-campholide (as opposed to the 2,3 isomer) for a number of similar compounds.

The bromolactone (4) was formed to a maximal extent of 60 percent after which it degraded, presumably to acidic materials. Pericyclocamphanone (2) was formed to an extent of 1-2 percent fairly early in the degradation process, and the yield of 3 approximated 15 percent. There was also some indication of 5-exo-hydroxycamphor (5), but since this material virtually co-chromatographs with the bromocamphor, a definitive mass spectrum could not be obtained.

In order to confirm the intermediacy of products 2 and 3 in the metabolism of the bromocamphor, the degadation of the tricyclic ketone (2) (5) was also studied, and the parent ions of some of the major products are included in Table 1. 5-Exo-hydroxycamphor (5) which was previously identified by us (6) in a study with strain ATCC No. 23289, was observed only as a minor product. As a point of interest, the neutral product mixture from 2 is particularly rich, and identification of the components will be the subject of a future study.

The above results lead us to believe that the initial degradation of the bromocamphor proceeds as outlined in Figure 1. The formation of the bromolactone (4) is not surprising, since 1 may be considered to be analagous to 5, and lactonization of the latter is well documented (7). The formation of pericyclo-

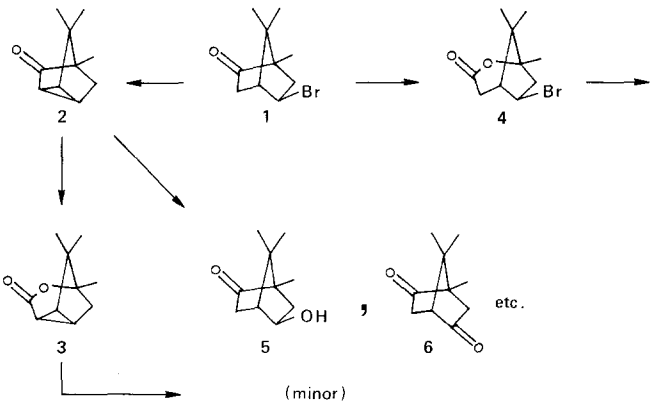

Figure 1. Initial pathway for the degradation of 5-bromo-camphor.

camphanone (2) via a microbial 1,3-elimination is interesting, since processes of this type have not been observed in the camphor series. The elimination is easily effected by base (e.g., by treatment of 1 with 1N NaOH in dioxane/water), and a similarity between chemical and microbial behavior is therefore evident.

In summary, our results demonstrate that lactonization is relatively insensitive to substituents remote to the reactive site, and that substrates bearing good leaving groups at the 5-exo-position may undergo 1,3-elimination prior to oxidation.

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