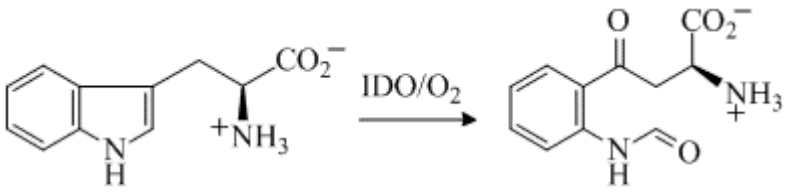
Chemical and Physical Foundations of Biological Systems

See examples from each of the four sections of the MCAT Exam. The passage in each example provides the context for the questions. The correct answer is provided as well as an explanation that refers to the Foundational Concepts and skills tested.

Passage

The heme enzyme indoleamine 2,3 dioxygenase (IDO) catalyzes Reaction 1, the first and rate-determining step of L-tryptophan (Compound **1**) metabolism, and is an important enzyme of the human immune system.

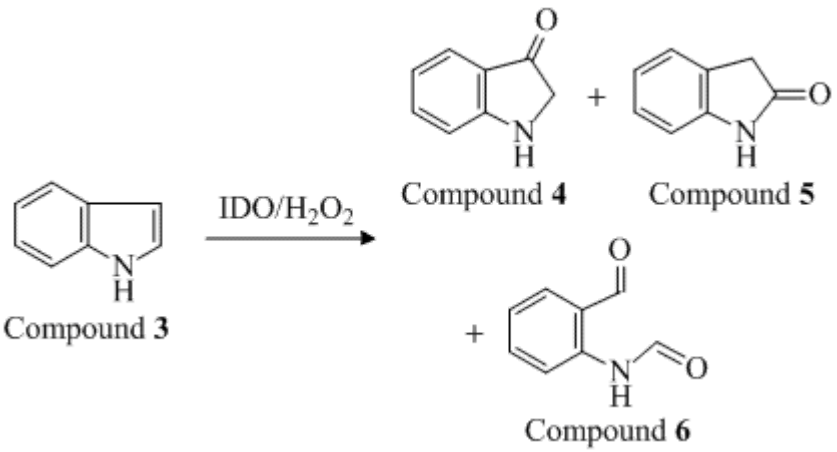


Compound **1**
L-Trp

Compound **2**
N-Formylkynurenine

Reaction 1

The IDO-catalyzed oxidation of Compound **1** by H_2O_2 does not occur. However, researchers have recently discovered that IDO-catalyzed oxidation of indole (Compound **3**) by H_2O_2 (Reaction 2) does occur.



Compound **3**

Compound **4**

Compound **5**

Compound **6**

Reaction 2

Under the conditions employed, the number of catalytic turnovers appeared to stop at roughly 100, on average. A plot of the concentration of Compound **3** that was oxidized versus the concentration of H_2O_2 employed, at two different initial concentrations of IDO, gave the results shown in Figure 1.

Aerobic oxidation of Compound **3** in the presence of ^{18}O-labeled $H_2{}^{18}O_2$ resulted in the formation of ^{18}O-labeled oxidation products (Table 1).

The formation of Compound **6** does not appear to be the result of a sequential oxidation process. Isotopically labeled Compound **4** does not exchange ^{18}O for ^{16}O in water over 3 hours, but Compound **6** completely loses its ^{18}O label in unlabeled water over the same time period.

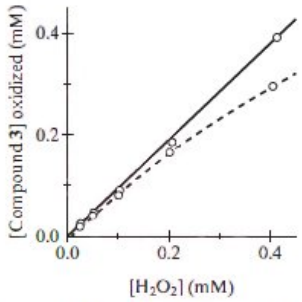


Figure 1 Stoichiometry of IDO-catalyzed oxidation of Compound **3** by H_2O_2 at 1 μM (dashed line) and 10 μM (solid line) IDO

Table 1 Isotopic Composition of Compound **3** Oxidation Products Using $H_2{}^{18}O_2$

Product	Percentage of ^{18}O incorporated (%)	
	Mono-^{18}O	Di-^{18}O
Compound **4**	100	—
Compound **5**	100	—
Compound **6**	60	40

Adapted from: Kuo HH, Mauk AG. Indole peroxygenase activity of indoleamine 2,3-dioxygenase. Proceedings of the National Academy of Sciences of the United States of America. 2012;109(35):13966–71.

Questions

1. The progress of Reaction 2 can be monitored by observing what change to the IR spectrum of the product mixture?

A) Appearance of a broad peak at 3400 cm^{-1}

B) Disappearance of a broad peak at 3400 cm^{-1}

C) Appearance of a sharp peak at 1700–1750 cm^{-1}

D) Disappearance of a sharp peak at 1700–1750 cm^{-1}

Answer

Correct Answer is C) Appearance of a sharp peak at 1700–1750 cm^{-1}

Rationale: This question requires the test taker to combine knowledge about infrared spectroscopy with reasoning about the structural differences between the products and reactants of Reaction 2. The test taker must work with the scientific model of the differences in IR absorbance of various functional groups and apply this model to the experiment described in the passage. Recognition of the presence of additional carbonyl groups in the products of the reaction should lead the test taker to conclude that appearance of a peak between 1700–1750 cm^{-1} in the IR spectrum would provide the most effective way to monitor product formation.

2. The following kinetic parameters were obtained for the IDO-catalyzed oxidation of Compound 3 by H_2O_2 in the presence of L-Trp.

[L-Trp], μM	k_{cat}, s^{-1}
0	1.3
2	0.34
5	~0

Based on this data, what effect does L-Trp have on the reaction?

A) L-Trp oxidizes Compound **3** directly.

B) L-Trp is oxidized instead of Compound **3**.

C) L-Trp does not interact with the enzyme.

D) L-Trp inhibits the enzyme.

Answer

Correct Answer is D) L-Trp inhibits the enzyme.

Rationale: This question requires the test taker to combine knowledge of enzyme kinetics with interpretation of data. The test taker must understand what the decreasing values of k_{cat} in the presence of higher concentrations of L-Trp mean with respect to the kinetics of IDO-catalyzed indole oxidation. The k_{cat} is representative of the rate of product turnover, which means that the enzyme produces less product in the presence of L-Trp. Combining this trend in the data with a knowledge of enzyme kinetics, it can be concluded that L-Trp is inhibiting the reaction.

3. Which experiment can be used to show that Compound 6 is not formed sequentially from either Compound 4 or Compound 5?

A) Conduct the reaction of Compound **4** with Compound **5**, and identify the products.

B) Oxidize Compound **4** and Compound **5** with IDO/H_2O_2, and identify the products.

C) Reduce pure Compound **6** without added catalyst, and identify the products.

D) Conduct the reaction of Compound **2** with H_2O_2 without added catalyst, and identify the products.

Answer

Correct Answer is B) Oxidize Compound **4** and Compound **5** with IDO/H_2O_2, and identify the products.

Rationale: This question requires the test taker to apply knowledge about how enzymes catalyze reactions to the design of an experiment. The question asks how researchers can be sure that Compound **6** is not formed from either Compound **4** or Compound **5** in a sequential enzyme mechanism. Enzymes are not used up during catalysis, so any experiment that includes just Compound **4** or just Compound **5** would determine if either is also a substrate for IDO-catalyzed conversion to Compound **6**. Having both compounds in solution with IDO adds unnecessary complexity to the interpretation of the experimental results. Examining the products of IDO-catalyzed reduction of Compound **6** would not give the necessary direct evidence, as Compound **6** could be sequentially reduced to Compound **3**.

AAMC Association of American Medical Colleges

655 K Street, NW, Suite 100 Washington, DC, 20001-2399