

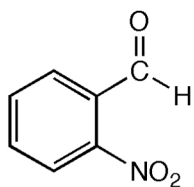
Exercise 7: Combinatorial chemistry

Pharmaceutical development is time-consuming and expensive. The initial process of finding a suitable compound may involve screening thousands of different compounds looking for the desired activity. Many of the candidate compounds will have been synthesized with nearly the same protocols, differing only in starting materials in many cases. Each compound then has to be checked individually for drug activity.

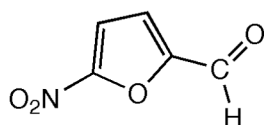
Recently, a fundamentally new approach has changed the nature of drug discovery and development. Called "combinatorial chemistry", thousands of compounds are synthesized simultaneously in a single reaction! The following protocol is based on a paper by Wolkenberg and Su (*J. Chem. Ed.* **78** (2001), 784-785).

Hydrazones are a class of compound you have seen, and some of them are effective anti-bacterial agents. Hydrazones are synthesized by combining an aldehyde with a hydrazine.

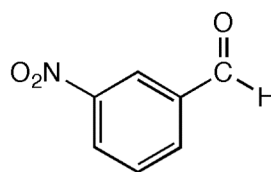
The following are the aldehydes to be used:

**A1**

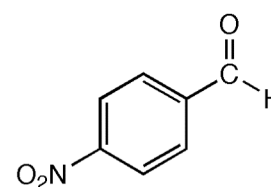
2-nitrobenzaldehyde

**A2**

5-nitro-2-furaldehyde

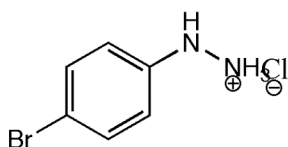
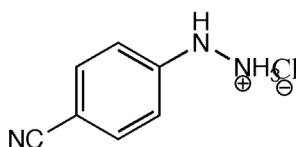
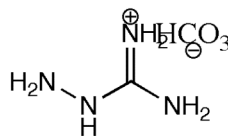
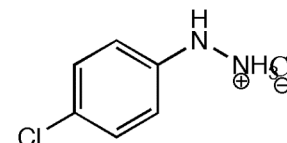
**A3**

3-nitrobenzaldehyde

**A4**

4-nitrobenzaldehyde

The following are the hydrazines they will be reacted with:

**B1**4-bromophenylhydrazine
hydrochloride**B2**4-cyanophenylhydrazine
hydrochloride**B3**aminoguanidine
bicarbonate**B4**4-chlorophenylhydrazine
hydrochloride

The protocol for the experiment is given on the following pages. Read it and answer the following questions:

1. Show the mechanism, and the product of the reaction of A1 with B1.

2. Since the mechanisms are identical, predict the product of the other combinations of A's and B's. Identify the products using the format "A#-B#" where # runs from 1 to 4. Hint: How many possible products will there be, given 4 aldehydes and 4 hydrazines?

