NATIONAL JUNIOR COLLEGE
SH2 PRELIMINARY EXAMINATION
Higher 3

CANDIDATE NAME			
SUBJECT CLASS		**REGISTRATION NUMBER**	

CHEMISTRY

9813/01

Paper 1
INSERT

Friday 17 September 2021

2 hours 30 minutes

INSTRUCTIONS

This insert contains information for Question 1. **Do not write your answer on the insert.**

This document consists of 3 printed pages and 1 blank page.

Information for Question 1

Domino reactions are processes where two or more consecutive reactions occur subsequently in a single reaction vessel without intermediate extraction and purification. Asymmetric domino reactions can be achieved through the use of organic catalysts (also known as organocatalysts). The following extract is one of such synthetic methodologies.

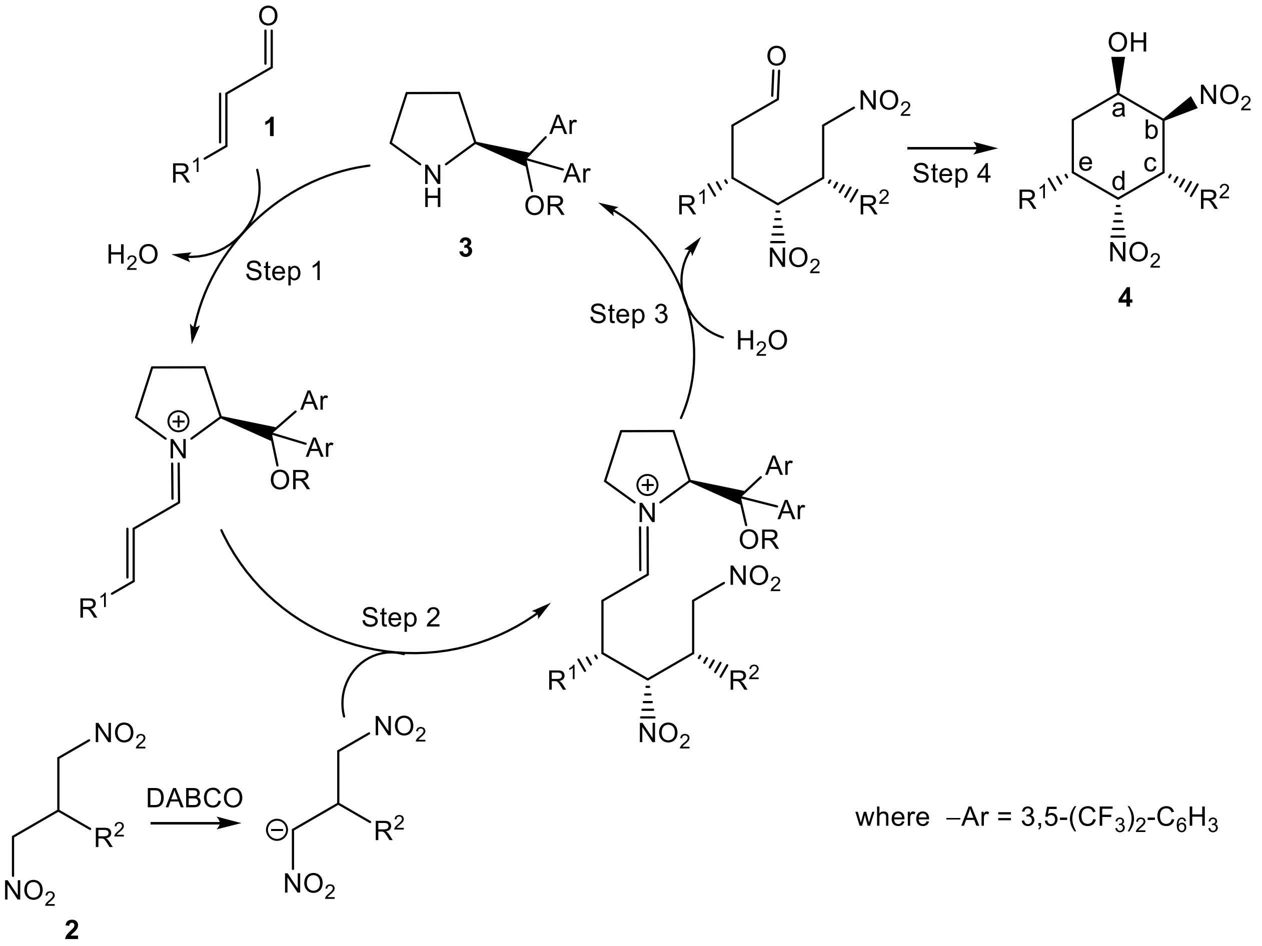
Abstract 1 (Angew. Chem., 2007, **46(48)**, 9202-5)

Asymmetric synthesis of complex molecules containing multiple stereocentres is a well-known research area used for the synthesis of a variety of natural products and other molecules of interest. One of the most important goals in this area is the generation of more than one bond in a multistep reaction concomitant with the creation of multiple stereocentres in a one-pot fashion.

In the course of our efforts to develop organocatalytic methodologies to gain rapid access to complex molecules, we recently achieved the synthesis of cyclohexenals containing three contiguous stereocentres in good yields and excellent stereoselectivities by using a multicomponent reaction. In fact, it has been demonstrated with this and other examples that organocatalysis can be a very valuable tool for controlling diverse asymmetric syntheses. Herein we describe the first one-pot asymmetric formation of five stereocentres by an intermolecular two-component reaction, which leads in this particular case to the formation of highly substituted optically active cyclohexanols under room temperature.

The optically active cyclohexanols arising from this domino process constitute valuable chiral building blocks since they contain the b-amino alcohol functional motif which is ubiquitous in biologically active compounds.

Figure 1 Proposed mechanism for the organocatalyzed asymmetric nitro-Michael/Henry domino reaction.



where $-Ar = 3,5\text{-}(CF_3)_2\text{-}C_6H_3$

Table 1 Screening of the organocatalytic nitro-Michael/Henry reaction of α,β–unsaturated aldehyde **1** with dinitro compound **2**, compound **3** and 1,4-diazabicyclo[2.2.2]octane (DABCO). These reactions are done under room temperature and pressure.

Entry	**Solvent**	**R**[a]	**R^1**	**R^2**	**Yield of isolated major stereoisomer [%]**	**%e.e.**
1	$CH_3CH(OH)CH_3$	TMS	CH_2CH_3	C_6H_5	n.d.*	80
2	$CH_3COOCH_2CH_3$	TMS	CH_2CH_3	C_6H_5	n.d.*	80
3	$HCON(CH_3)_2$	TMS	CH_2CH_3	C_6H_5	n.d.*	46
4	$CHCl_3$	TMS	CH_2CH_3	C_6H_5	n.d.*	80
5	CH_2Cl_2	TMS	CH_2CH_3	C_6H_5	45	90
6	CH_2Cl_2	H	CH_2CH_3	C_6H_5	n.d.*	–58**
7	CH_2Cl_2	TES	CH_2CH_3	C_6H_5	41	89
8	CH_2Cl_2	TBDMS	CH_2CH_3	C_6H_5	35	93

*n.d. = not determined

**Opposite enantiomer obtained

[a] TMS: $–Si(CH_3)_3$, TES = $–Si(CH_2CH_3)_3$, TBDMS = $–Si(CH_3)_2C(CH_3)_3$)

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