SUPPLEMENTARY INFORMATION

Nucleophilic catalysis of *p*-substituted aniline derivatives in acylhydrazone formation and exchange

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1. DERIVATION OF INTEGRATED RATE LAWS

Derivation of rate laws using the initial rates method

General reaction scheme:

$$A + B \xrightarrow{k} \text{Products}$$

General rate law for this scheme:

$$\text{rate} = k \cdot [A]^{\alpha} \cdot [B]^{\beta} \qquad \text{(Eq. 1)}$$

The rate of the reaction can be defined as the rate of decrease of the concentration of either A or B, or the rate of increase of the concentration of products:

$$\text{rate} = -\frac{\Delta[A]}{\Delta t} = -\frac{\Delta[B]}{\Delta t} = \frac{\Delta[C]}{\Delta t} \qquad \text{(Eq. 2)}$$

In our case, the initial rate, defined as:

$$\text{initial rate} = k \cdot [A]_0^{\alpha} \cdot [B]_0^{\beta} \qquad \text{(Eq. 3)}$$

was calculated as the average of the instantaneous rates upon formation of 10% product:

$$\text{initial rate} = \frac{\sum_0^n \left(\frac{[C]t_n - [C]t_{n-1}}{t_n - t_{n-1}}\right)}{n} \qquad \text{(Eq. 4)}$$

In order to estimate the coefficients α and β (i.e. partial orders of each reagent), several sets of initial concentrations ($[A]_0$, $[B]_0$) were used, in which the initial concentration of either A or B was kept constant. For example, for a set of experiments in which the initial concentration of A is kept constant and using the logarithmic form of equation 3:

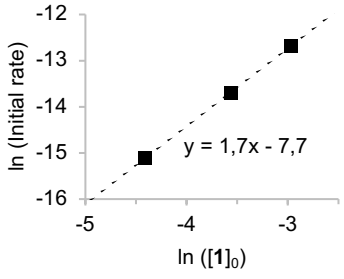
$$\ln(\text{initial rate}) = \ln(k \cdot [A]_0^{\alpha}) + \beta \cdot \ln([B]_0) \qquad \text{(Eq. 5)}$$

where $\ln(k \cdot [A]_0^{\alpha})$ is constant. Coefficient β can thus be estimated from the slope of the linear representation that better fits **ln(initial rate) vs ln($[B]_0$)**. Analogously, coefficient α can be estimated from another set of experiments in which the initial concentration of B is kept constant.

As an example, data obtained for the reaction between aldehyde **1** and 4-methoxyaniline (**4c**) are shown below:

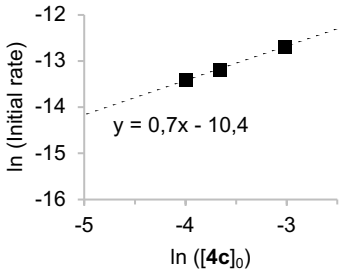
$[\mathbf{4c}]_0 = 49\text{Mm}$

$[\mathbf{1}]_0$(mM)	initialrate (M s^{-1})
12	$2.73 \cdot 10^{-7}$
28	$1.13 \cdot 10^{-6}$
51	$3.12 \cdot 10^{-6}$



$[\mathbf{1}]_0 = 51\text{mM}$

$[\mathbf{4}]_0$ (mM)	initial rate (M s^{-1})
18	$1.52 \cdot 10^{-6}$
26	$1.89 \cdot 10^{-6}$
49	$3.12 \cdot 10^{-6}$



Rounding the coefficients α and β obtained from the slopes of these linear representations, the reaction is determined to be second order in aldehyde **1** (α = 1.7 ~ 2) and first order in aniline **4c** (β = 0.7 ~ 1):

$$\text{rate} = -k \cdot [\mathbf{1}]^2 \cdot [\mathbf{4c}] \qquad \text{(Eq. 6)}$$

Derivation of integrated rate laws

Considering equation 6 and depending on the experimental conditions, two situations can be identified:

Situation 1: $[\mathbf{1}]_0 \neq [\mathbf{4c}]_0$

Let *x* be the concentration of each reagent reacted at time *t*. Let the initial concentrations of each reagents be $[\mathbf{1}]_0 = a$, and $[\mathbf{4c}]_0 = b$, then $[\mathbf{1}] = a - x$; $[\mathbf{4c}] = b - x$.

The expression for the rate law becomes:

$$rate = -\frac{dx}{dt} = -k \cdot (a-x)^2 \cdot (b-x) \qquad \text{(Eq. 7)}$$

which can be rearranged to:

$$\frac{dx}{(a-x)^2(b-x)} = k \cdot dt \qquad \text{(Eq. 8)}$$

We integrate between $t = 0$ (when $x = 0$) and *t*:

$$\int_0^x \frac{dx}{(a-x)^2(b-x)} = \int_0^t k \cdot dt \qquad \text{(Eq. 9)}$$

To solve the integral at the left side of the equation, we use the partial fractions method:

$$\int_0^x \frac{dx}{(a-x)^2(b-x)} = \frac{\ln(a-x)-\ln(b-x)}{(a-b)^2} - \frac{1}{(a-b)\cdot(a-x)} - \frac{\ln(a)-\ln(b)}{(a-b)^2} + \frac{1}{(a-b)\cdot a} \qquad \text{(Eq. 10)}$$

which can be simplified:

$$\int_0^x \frac{dx}{(a-x)^2(b-x)} = \frac{\ln\left(\frac{(a-x)\cdot b}{(b-x)\cdot a}\right)}{(a-b)^2} - \frac{1}{(a-b)\cdot(a-x)} + \frac{1}{(a-b)\cdot a} \qquad \text{(Eq. 11)}$$

and then translated back to:

$$\int_0^x \frac{dx}{(a-x)^2(b-x)} = \frac{\ln\left(\frac{[\mathbf{1}]\cdot[\mathbf{4c}]_0}{[\mathbf{4c}]\cdot[\mathbf{1}]_0}\right)}{([\mathbf{1}]_0-[\mathbf{4c}]_0)^2} - \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]} + \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]_0} \quad \text{(Eq. 12)}$$

Finally, we obtain the integrated rate law under the imposed conditions that the initial concentrations of the reactants are not equal:

$$\frac{\mathrm{Ln}\left(\frac{[\mathbf{1}]\cdot[\mathbf{4c}]_0}{[\mathbf{4c}]\cdot[\mathbf{1}]_0}\right)}{([\mathbf{1}]_0-[\mathbf{4c}]_0)^2} - \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]} + \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]_0} = kt \quad \text{(Eq. 13)}$$

which upon rearrangement becomes:

$$\boxed{\frac{\mathrm{Ln}\left(\frac{[\mathbf{1}]\cdot[\mathbf{4c}]_0}{[\mathbf{4c}]\cdot[\mathbf{1}]_0}\right)}{([\mathbf{1}]_0-[\mathbf{4c}]_0)^2} - \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]} = kt - \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]_0}} \quad \text{(Eq. 14)}$$

Hence, the third-order kinetic constant (k) can be obtained from a linear representation of the form:

$$y = ax + b$$

where $y = \frac{\mathrm{Ln}\left(\frac{[\mathbf{1}]\cdot[\mathbf{4c}]_0}{[\mathbf{4c}]\cdot[\mathbf{1}]_0}\right)}{([\mathbf{1}]_0-[\mathbf{4c}]_0)^2} - \frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]}$

$a = k$

$x = t$

$b = -\frac{1}{([\mathbf{1}]_0-[\mathbf{4c}]_0)\cdot[\mathbf{1}]_0}$

Situation 2: $[\mathbf{1}]_0 = [\mathbf{4c}]_0$

Since aldehyde **1** and aniline **4c** react in a 1:1 stoichiometry, at any time t the concentrations of the reactants will be equal, $[\mathbf{1}] = [\mathbf{4c}]$ and the rate law will be:

$$rate = -\frac{d[\mathbf{1}]}{dt} = k\cdot[\mathbf{1}]\cdot[\mathbf{1}]^2 = k\cdot[\mathbf{1}]^3 \quad \text{(Eq. 15)}$$

which can be rearranged to:

$$-\frac{d[\mathbf{1}]}{[\mathbf{1}]^3} = k\cdot dt \quad \text{(Eq. 16)}$$

We integrate between $t = 0$ and t:

$$\int_{[\mathbf{1}]_0}^{[\mathbf{1}]_t} -\frac{d[\mathbf{1}]}{[\mathbf{1}]^3} = \int_0^t k\cdot dt \quad \text{(Eq. 17)}$$

Finally, we obtain the integrated rate law under the imposed conditions that the initial concentrations of the reactants are equal:

$$\frac{1}{2[\mathbf{1}]^2} - \frac{1}{2[\mathbf{1}]_0^2} = kt \quad \text{(Eq. 18)}$$

which upon rearrangement becomes:

$$\boxed{\frac{1}{2[\mathbf{1}]^2} = kt + \frac{1}{2[\mathbf{1}]_0^2}} \qquad \text{(Eq. 19)}$$

Hence, the third-order kinetic constant (k) can be obtained from a linear representation of the form:

$$y = ax + b$$

where $y = \frac{1}{2[\mathbf{1}]^2}$

$a = k$

$x = t$

$b = \frac{1}{2[\mathbf{1}]_0^2}$

2. KINETIC STUDY BY NMR

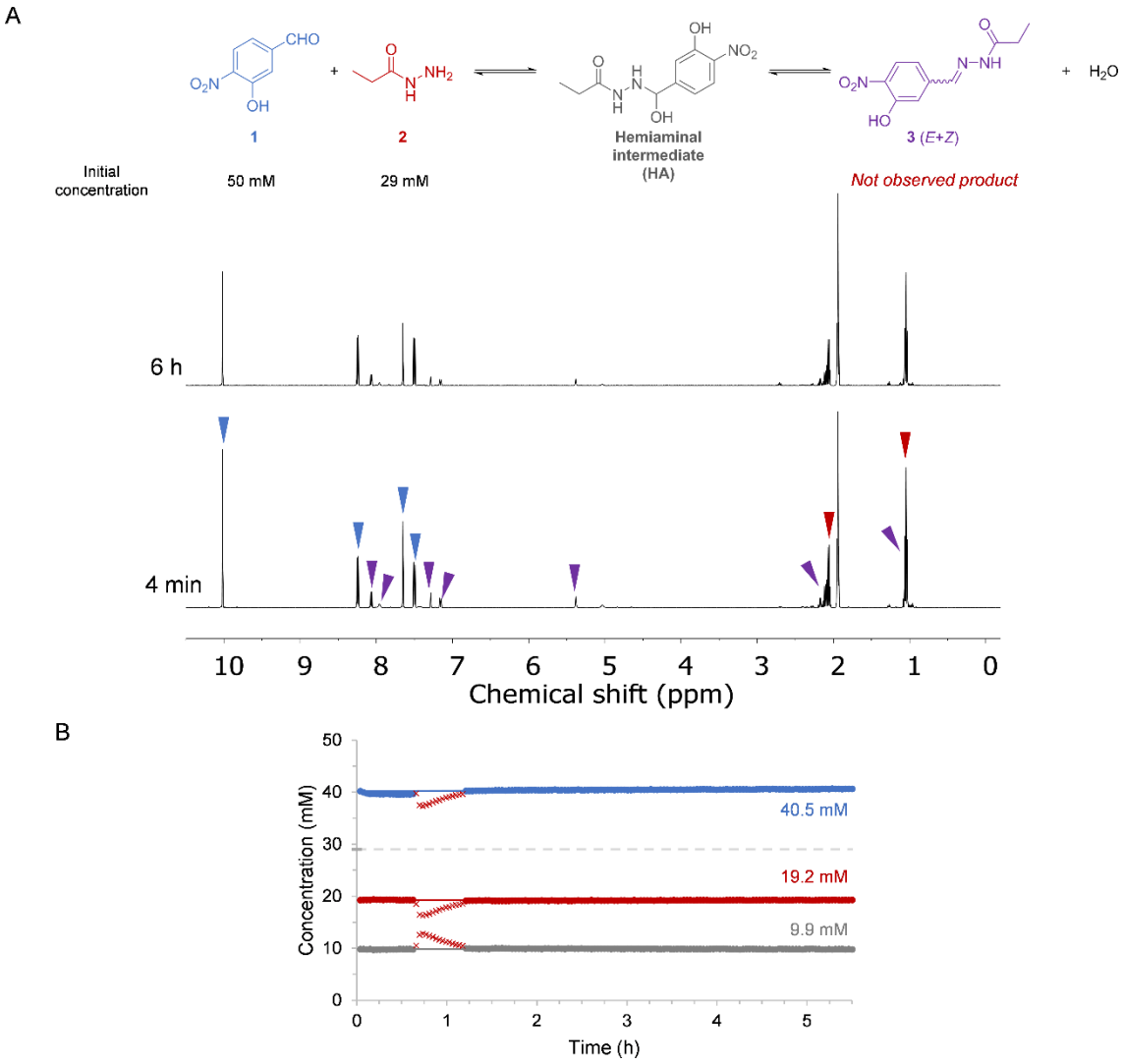


Figure S1. A) Reaction between aldehyde **1** (50 mM) and acylhydrazide **2** (29mM) in CD_3CN to form acylhydrazone **3**. B) Overlay of ^1H NMR (500 MHz, 288 K) spectra at different reaction times. Blue, red and gray arrows point to signals of compounds **1**, **2** and **HA**, respectively. C) Concentrations (mM) of compounds **1**, **2** and **HA** at different reaction times. The grey dashed line indicates the initial concentration of the limiting reagent **2** (29 mM). Red crosses indicate data points that were discarded due to a technical issue during the experiment.

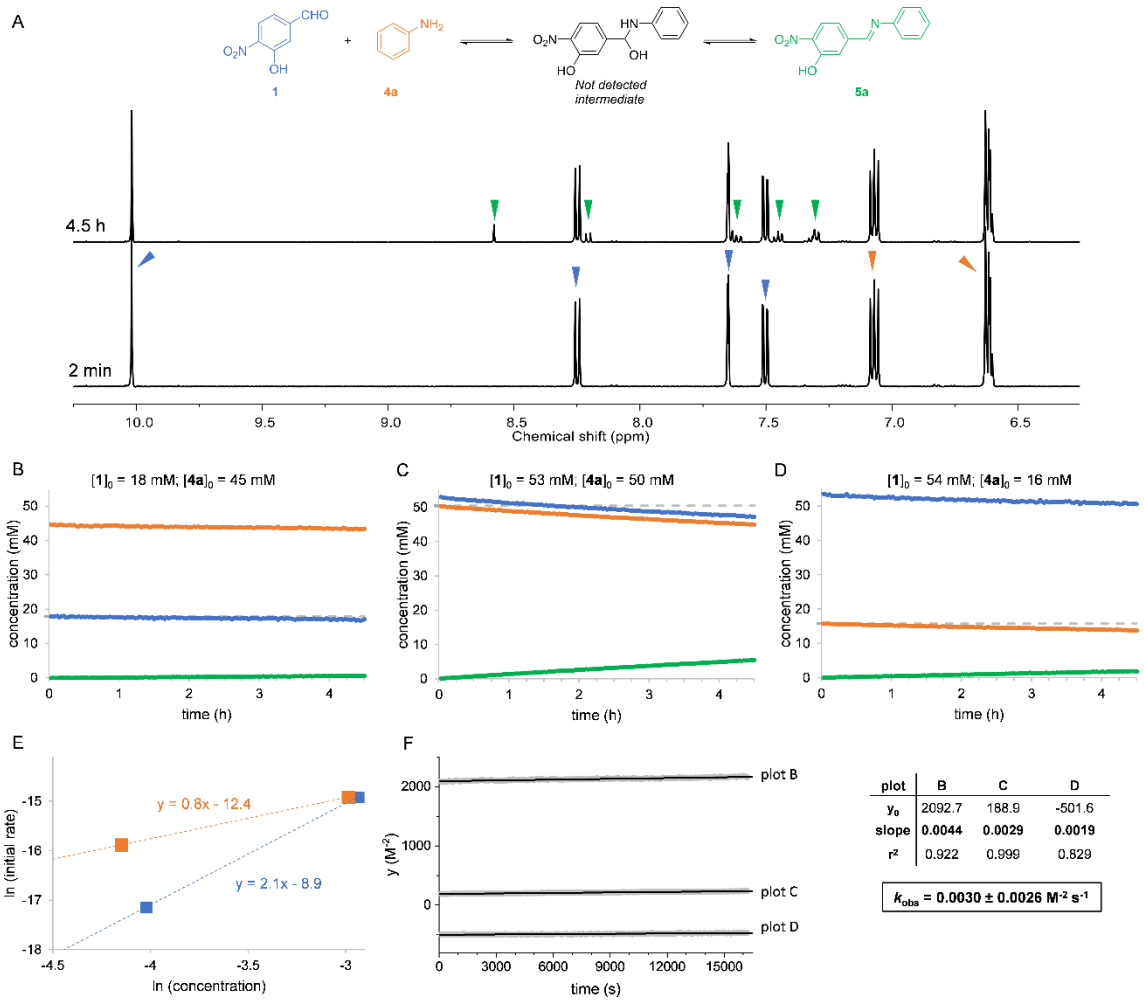


Figure S2. A) Reaction between aldehyde **1** and aniline **4a** in CD_3CN to form imine **5a** and overlay of ^1H NMR (500 MHz, 288 K) spectra at different reaction times. Blue, orange and green arrows point to signals of compounds **1**, **4a** and **5a**, respectively. B-D) Concentrations (mM) of compounds **1**, **4a** and **5a** at different reaction times, using different initial concentrations for reagents **1** and **4a**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. E) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (aldehyde **1** in blue, aniline **4a** in orange), derived from graphs B-D. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. F) Linear regression models for data in plots B-D expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of all the experimentally derived values.

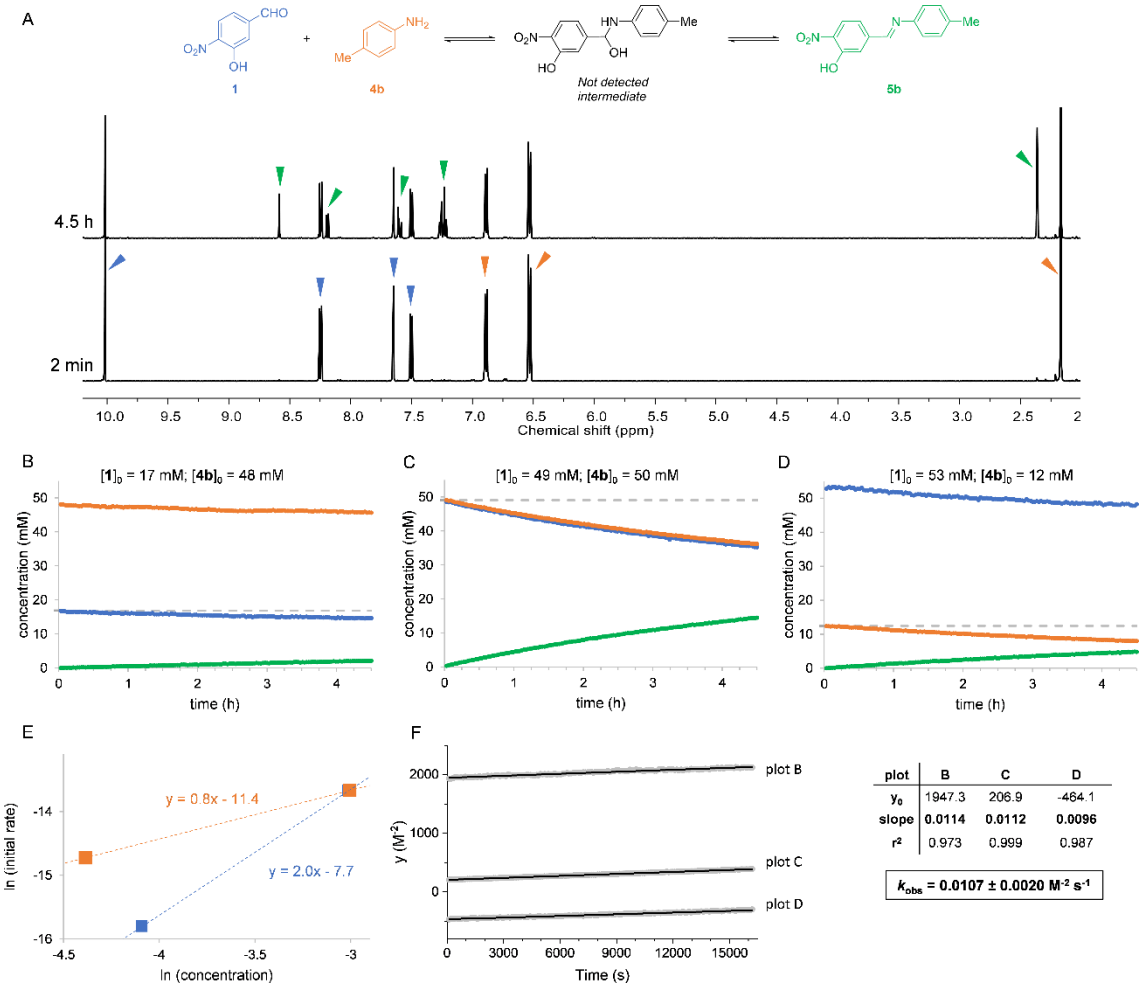


Figure S3. A) Reaction between aldehyde **1** and aniline **4b** in CD_3CN to form imine **5b** and overlay of ^{1}H NMR (500 MHz, 288 K) spectra at different reaction times. Blue, orange and green arrows point to signals of compounds **1**, **4b** and **5b**, respectively. B-D) Concentrations (mM) of compounds **1**, **4b** and **5b** at different reaction times, using different initial concentrations for reagents **1** and **4b**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. E) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (aldehyde **1** in blue, aniline **4b** in orange), derived from graphs B-D. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. F) Linear regression models for data in plots B-D expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of all the experimentally derived values.

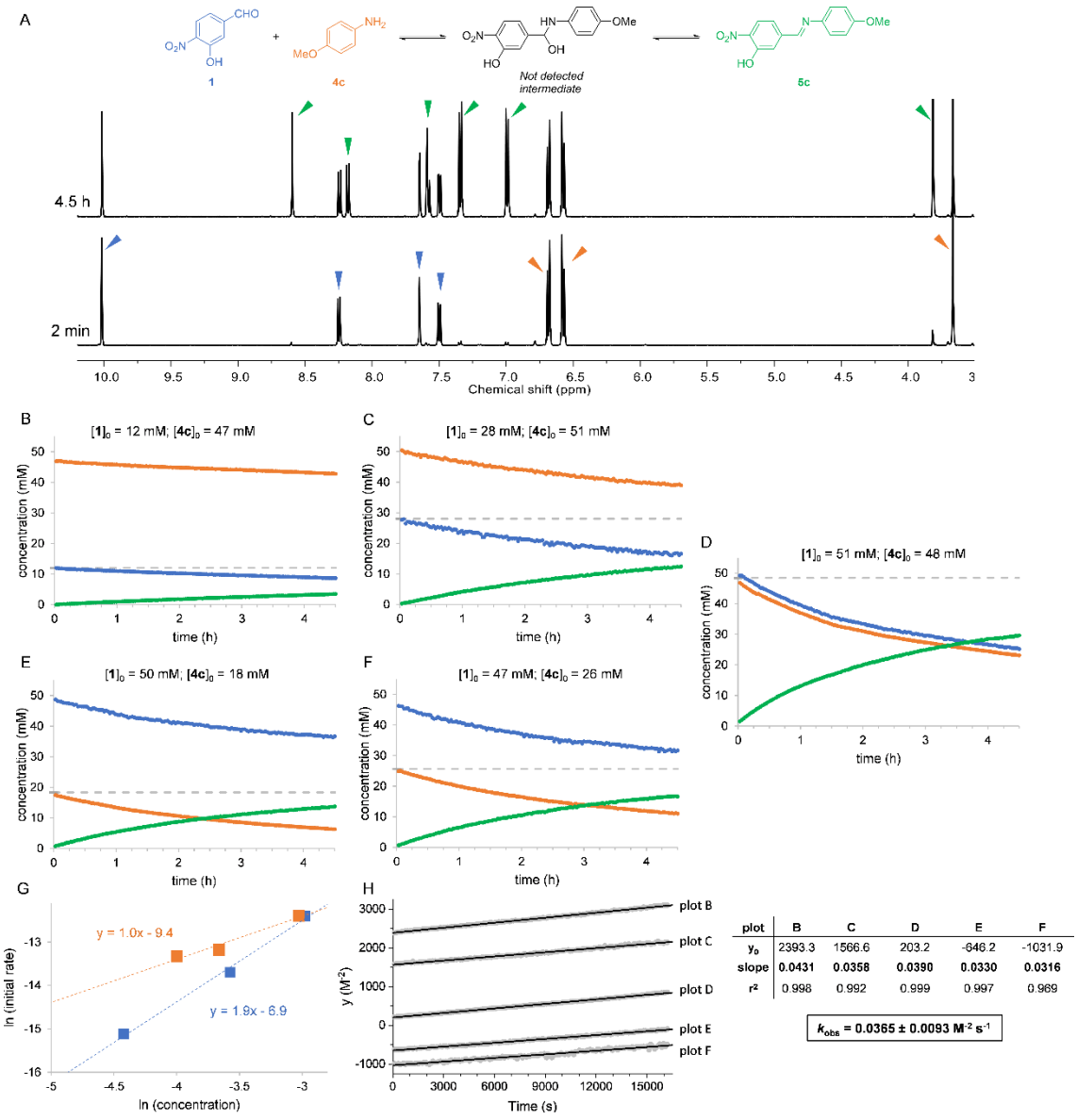


Figure S4. A) Reaction between aldehyde **1** and aniline **4c** in CD_3CN to form imine **5c** and overlay of ^1H NMR (500 MHz, 288 K) spectra at different reaction times. Blue, orange and green arrows point to signals of compounds **1**, **4c** and **5c**, respectively. B-F) Concentrations (mM) of compounds **1**, **4c** and **5c** at different reaction times, using different initial concentrations for reagents **1** and **4c**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. G) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (aldehyde **1** in blue, aniline **4c** in orange), derived from graphs B-F. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. H) Linear regression models for data in plots B-F expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of all the experimentally derived values.

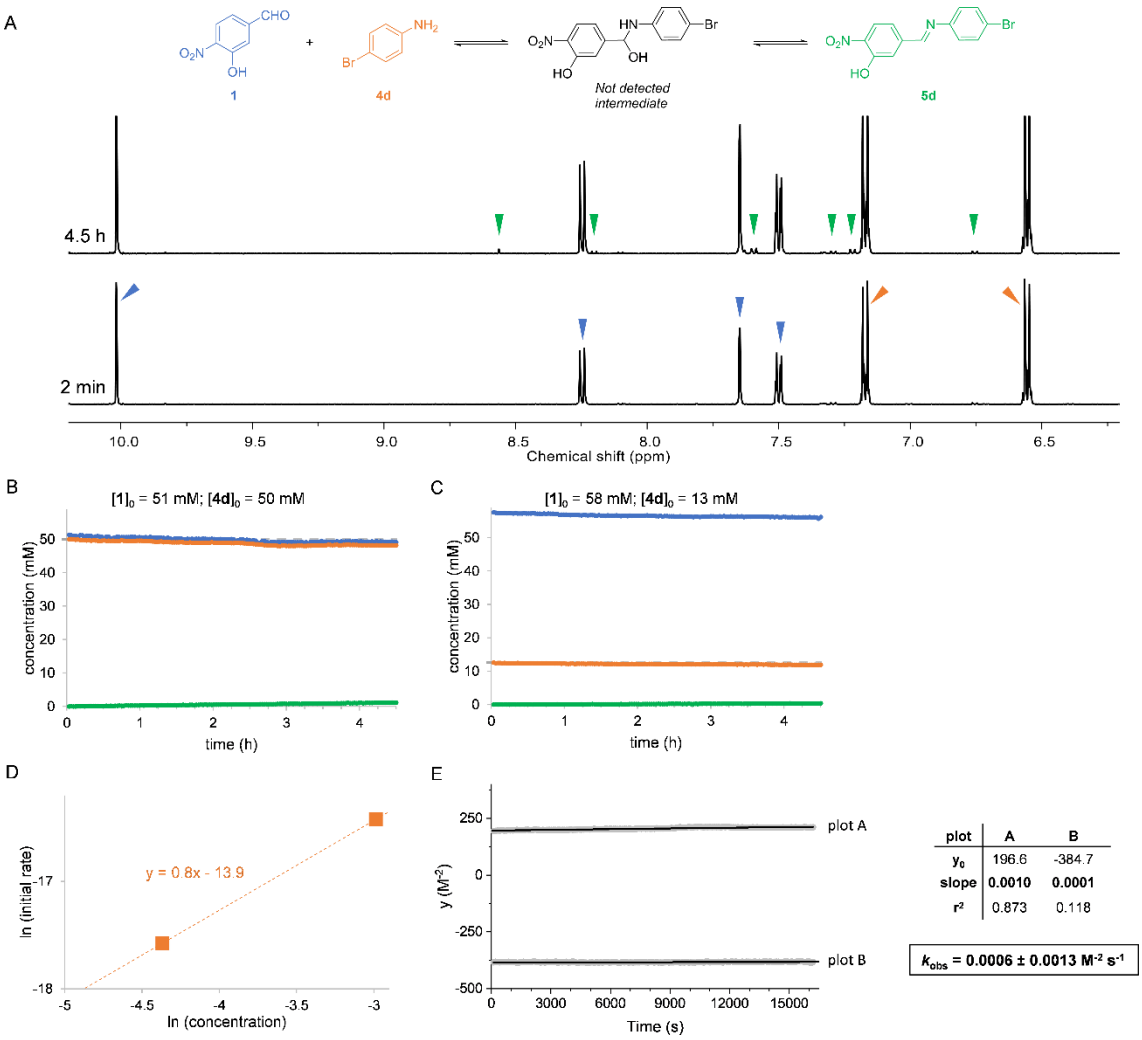


Figure S5. A) Reaction between aldehyde **1** and aniline **4d** in CD_3CN to form imine **5d** and overlay of ^1H NMR (500 MHz, 288 K) spectra at different reaction times. Blue, orange and green arrows point to signals of compounds **1**, **4d** and **5d**, respectively. B-C) Concentrations (mM) of compounds **1**, **4d** and **5d** at different reaction times, using different initial concentrations for reagents **1** and **4d**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. D) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (aldehyde **1** in blue, aniline **4d** in orange), derived from graphs B-C. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. E) Linear regression models for data in plots B-C expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of all the experimentally derived values.

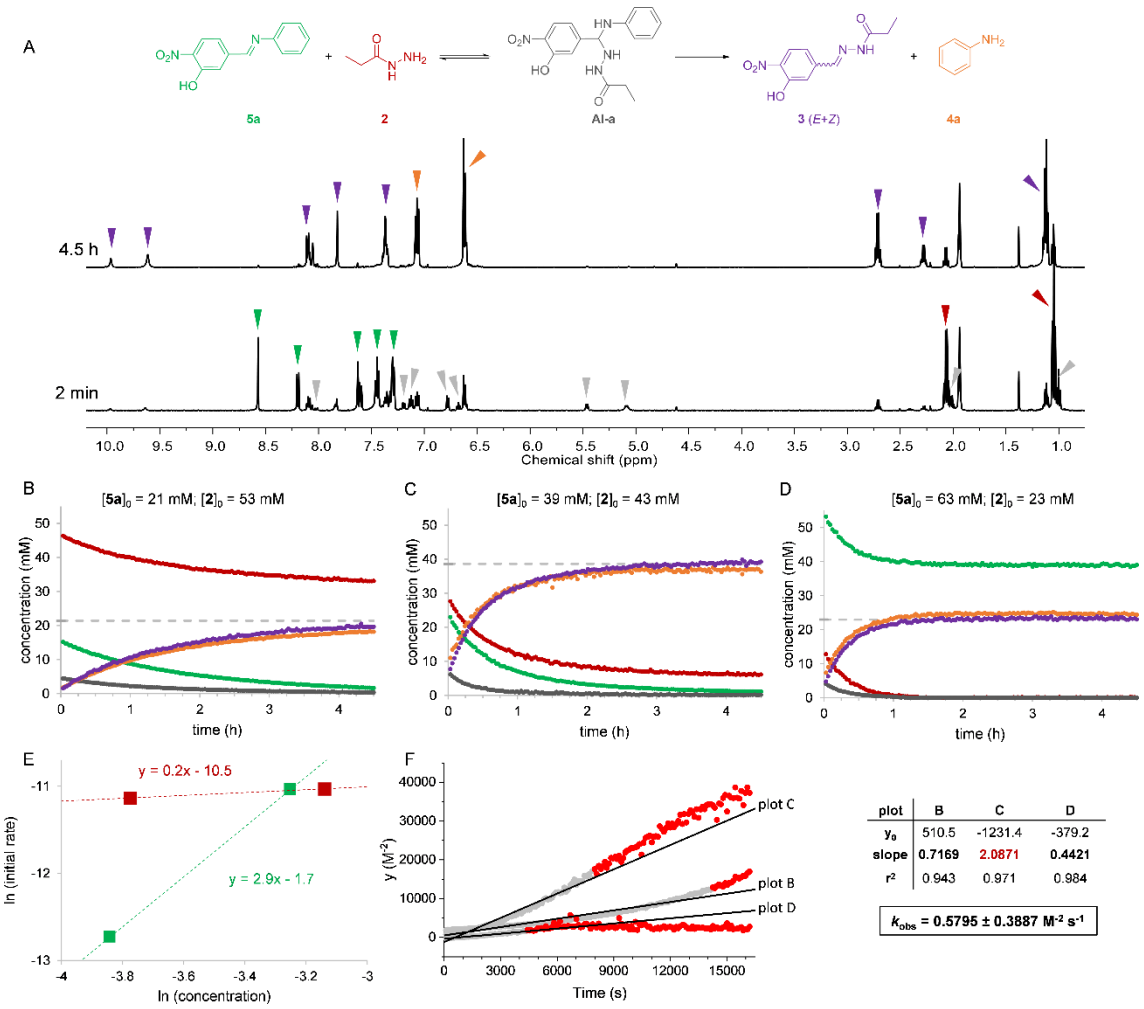


Figure S6. A) Reaction between imine **5a** and acylhydrazide **2** in CD_3CN to form acylhydrazone **3** and overlay of ^{1}H NMR (500 MHz, 288 K) spectra at different reaction times. Green, red, grey and purple arrows point to signals of compounds **5a**, **2**,**AI-a** and **3** (*E* and *Z* isomers), respectively. B-D) Concentrations (mM) of compounds **5a**, **2**,**AI-a** and **3** at different reaction times, using different initial concentrations for reagents **5a** and **2**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. E) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (imine**5a** in green, acylhydrazide**2** in red), derived from graphs B-D. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. F) Linear regression models for data in plots B-D expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). Only the data shown in grey are used for the linear regression, since data in red deviate too much from linearity. The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of the experimentally derived values (value in red was not considered since it is too different from the other two).

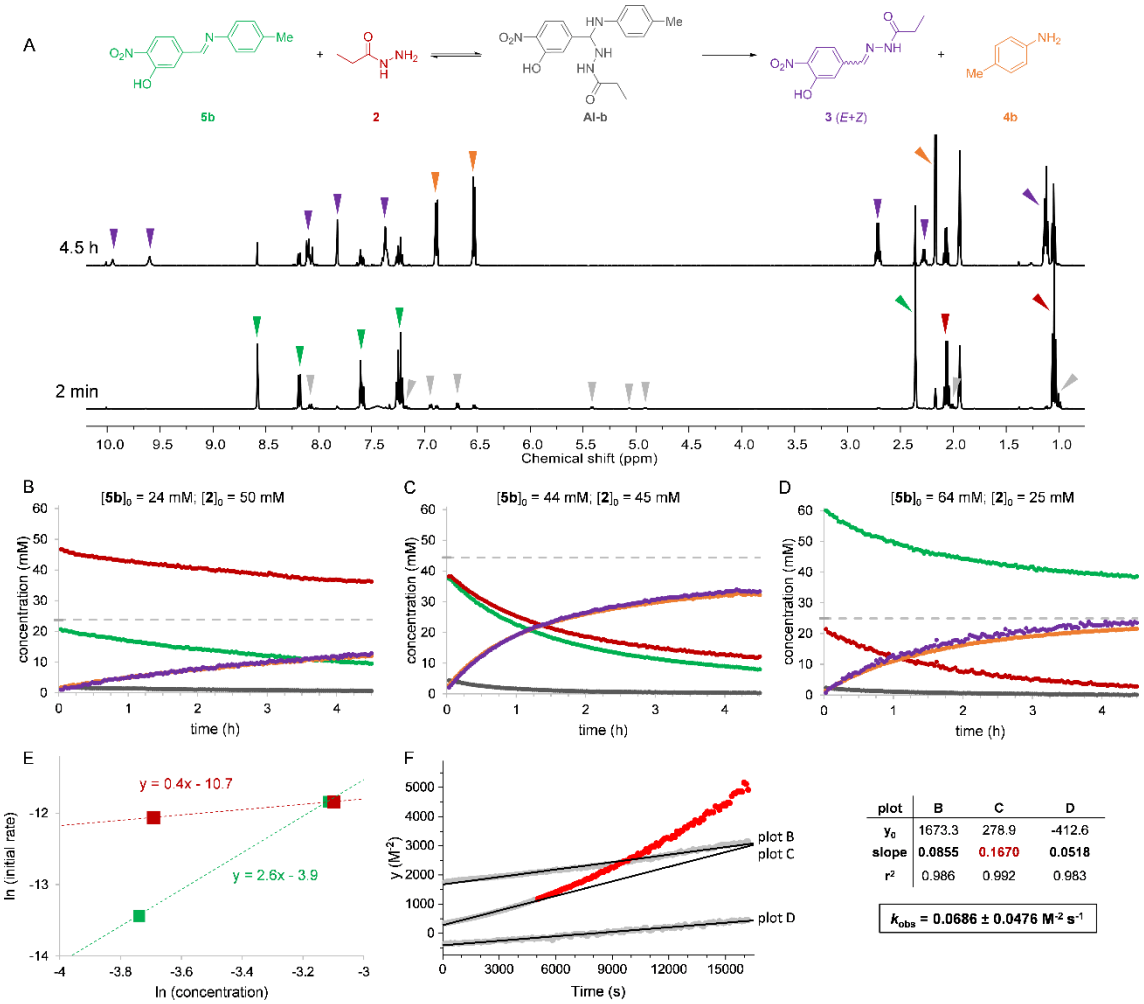


Figure S7. A) Reaction between imine **5b** and acylhydrazide **2** in CD_3CN to form acylhydrazone **3** and overlay of ^{1}H NMR (500 MHz, 288 K) spectra at different reaction times. Green, red, grey and purple arrows point to signals of compounds **5b**, **2**,**AI-a** and **3** (*E* and *Z* isomers), respectively. B-D) Concentrations (mM) of compounds **5b**, **2**,**AI-a** and **3**at different reaction times, using different initial concentrations for reagents **5b** and **2**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. E) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (imine **5b** in green, acylhydrazide**2** in red), derived from graphs B-D. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. F) Linear regression models for data in plots B-D expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). Only the data shown in grey are used for the linear regression, since data in red deviate too much from linearity. The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of the experimentally derived values (value in red was not considered since it is too different from the other two).

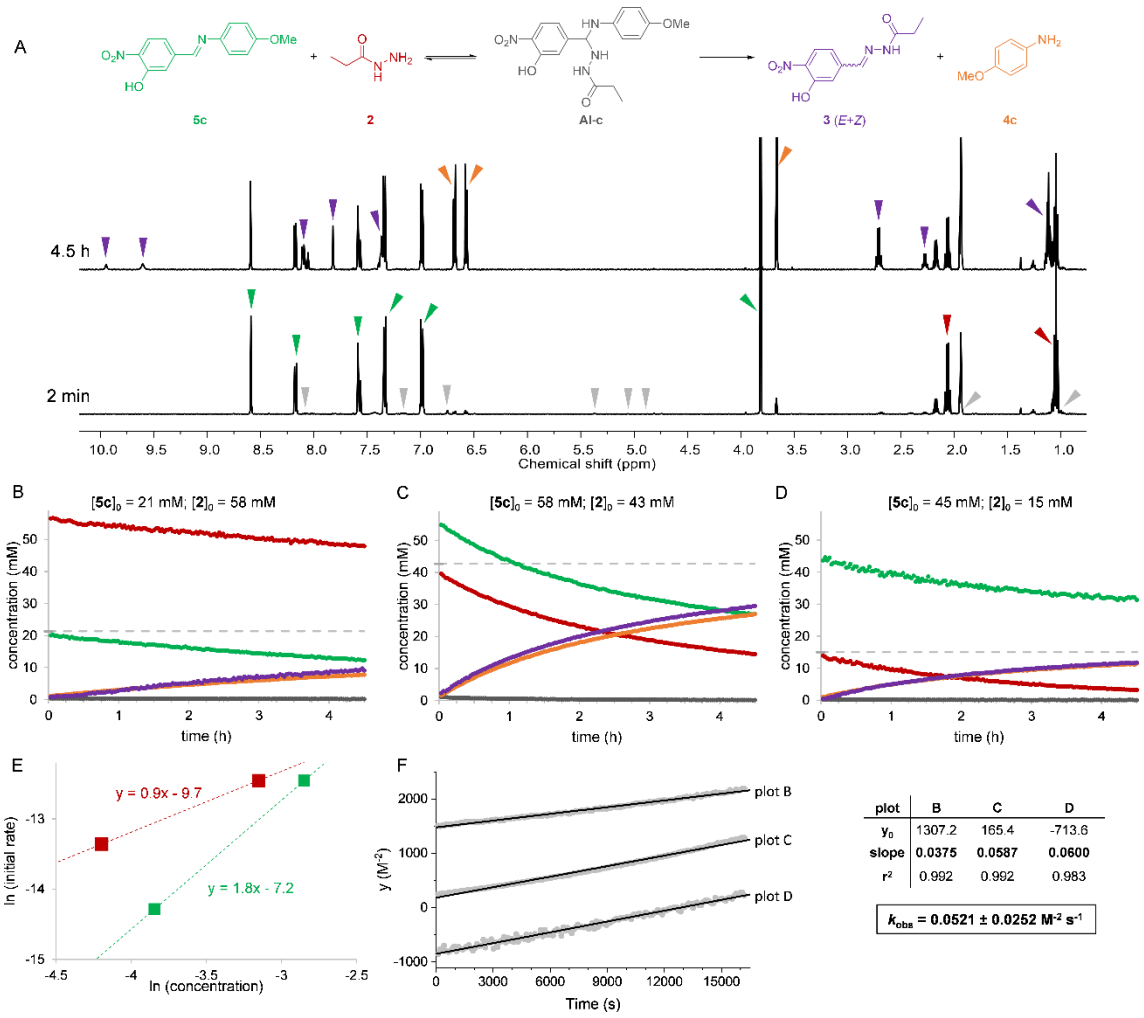


Figure S8. A) Reaction between imine **5c** and acylhydrazide **2** in CD_3CN to form acylhydrazone **3** and overlay of ^1H NMR (500 MHz, 288 K) spectra at different reaction times. Green, red, grey and purple arrows point to signals of compounds **5c**, **2**, **AI-a** and **3** (*E* and *Z* isomers), respectively. B-D) Concentrations (mM) of compounds **5c**, **2**, **AI-a** and **3** at different reaction times, using different initial concentrations for reagents **5c** and **2**. Grey dashed lines indicate the initial concentrations of the limiting reagents for each reaction. E) Logarithmic representations of *initial reaction rate vs initial concentration of reagents* (imine **5c** in green, acylhydrazide **2** in red), derived from graphs B-D. In each plot, the concentration of the other reagent is maintained constant. The slopes of the linear regression models represent the partial orders of each reagent in the reaction. F) Linear regression models for data in plots B-D expressed in the form of the integrated third-order rate laws for reactions in which the initial concentrations of reagents are different or equal (equations 14 and 19, respectively). The slopes of the linear regression models represent the observed kinetic constants (k_{obs}) for each reaction. Final values of k_{obs} are given as the average ± 2 times the standard deviation of all the experimentally derived values.

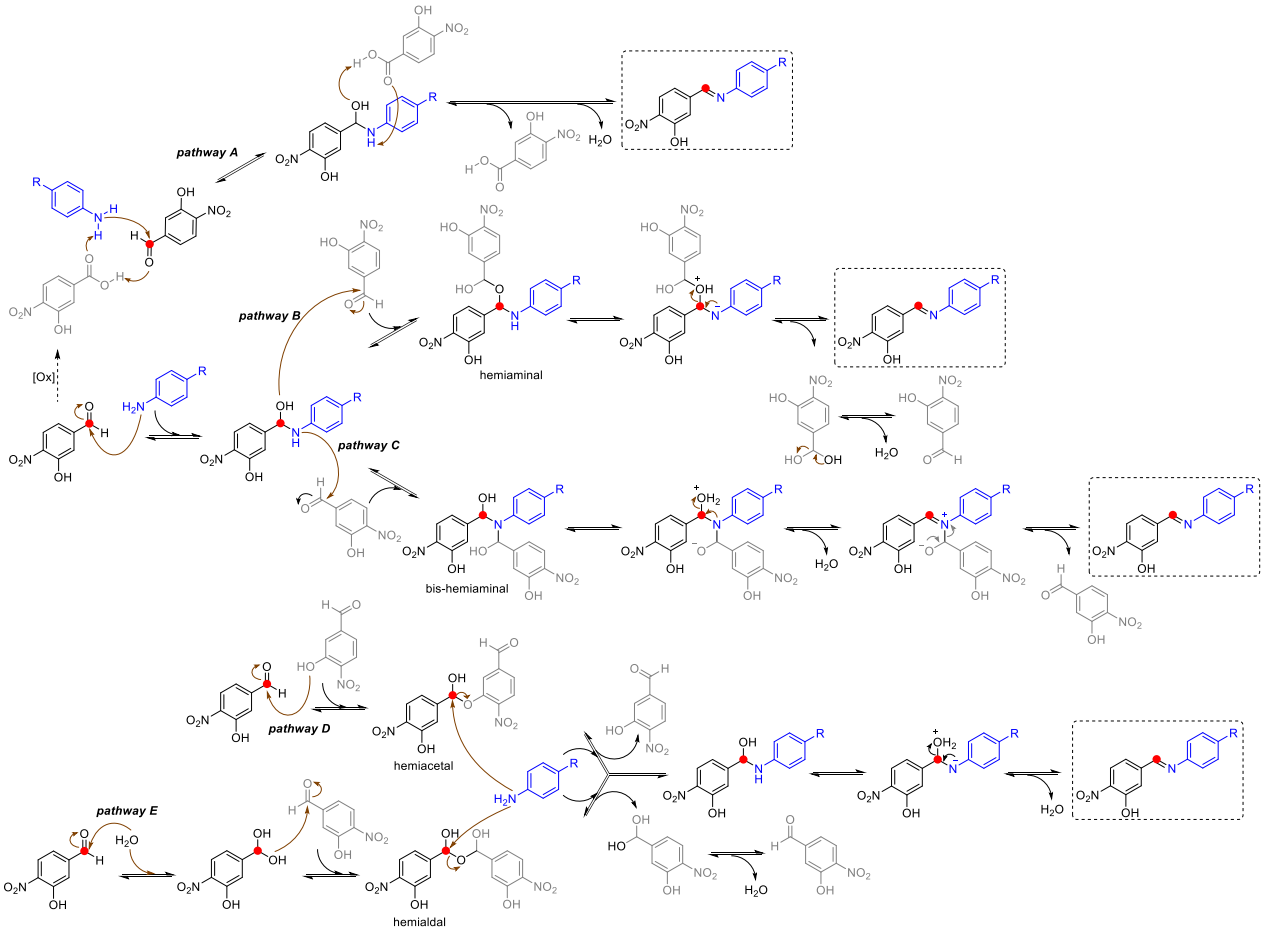
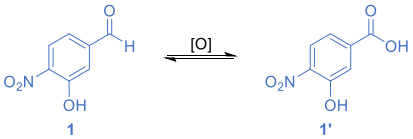


Figure S9. Possible mechanisms for imine formation explaining the experimentally determined partial order of 2 for aldehyde **1**. First, a 3-hydroxy-4-nitrobenzoic acid molecule existing as an impurity or generated by spontaneous oxidation of aldehyde **1**, catalyzes the concerted nucleophilic attack of anile and subsequent proton transfer to yield the hemiaminal intermediates, which then undergoes acid-catalyzed water elimination (*pathway A*). Alternatively, two possible reaction pathways arising from the nucleophilic attack of either the OH (*pathway B*) or NH (*pathway C*) groups of the putative hemiaminal intermediate to the carbonyl group of another molecule of **1**, are proposed. The resulting intermediates would facilitate imine formation by water or 3-hydroxy-4-nitrobenzaldehyde acetal elimination. The third possibility involves an intermolecular self-acetalization of aldehyde **1** by nucleophilic attack of its phenol group to the carbonyl of another molecule (*pathway D*); subsequent nucleophilic substitution at the resulting acetal carbon with anilines would lead to the putative hemiaminal intermediate, which in turn would yield the final imine after water elimination. Finally, the formation of an hemialdal intermediate by reaction of two molecules of aldehyde **1** with water (*pathway E*, very unlikely in anhydrous conditions) followed by nucleophilic displacement of 3-hydroxy-4-nitrobenzaldehyde acetal to yield the same putative hemiaminal intermediate, is hypothesized. None of the proposed intermediates have been detected and these proposed mechanisms remain purely speculative.

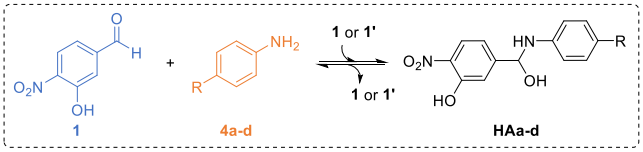
3. COMPUTATIONAL DATA

1. First reaction (imine formation)

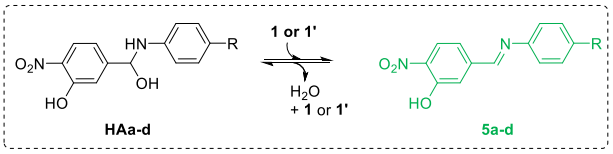
1a. Aldehyde spontaneous oxidation



1b. Aniline nucleophilic attack assisted by aldehyde **1** or carboxylic acid **1'**

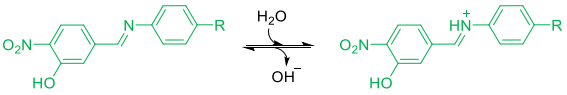


1c. Water elimination assisted by aldehyde **1** or carboxylic acid **1'**

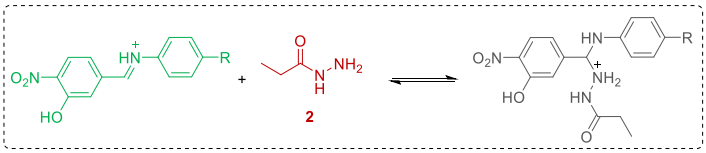


2. Second reaction (hydrazone formation)

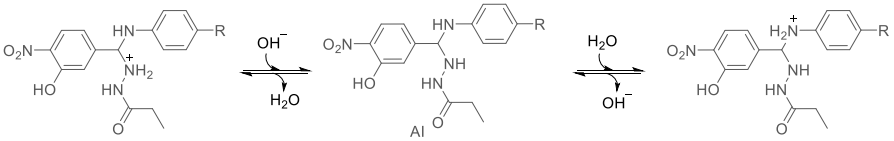
2a. Imine protonation



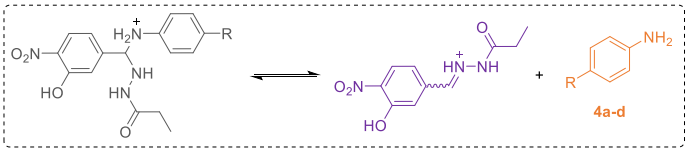
2b. Hydrazide nucleophilic attack



2c. Deprotonation-protonation of the tetrahedral intermediate



2d. Aniline elimination



2e. Hydrazonium deprotonation

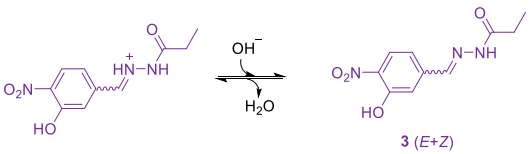
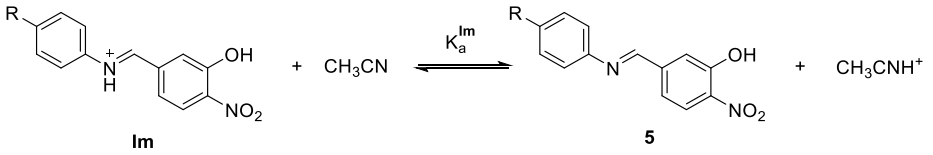


Figure S10. Complete mechanism proposed for acylhydrazone **3** formation from aldehyde **1** catalyzed by aniline derivatives **4a-d** in water, including hydrogen-transfer steps. The steps computed quantum mechanically are highlighted by a dashed line box.

Estimation of ΔG associated to imine protonation

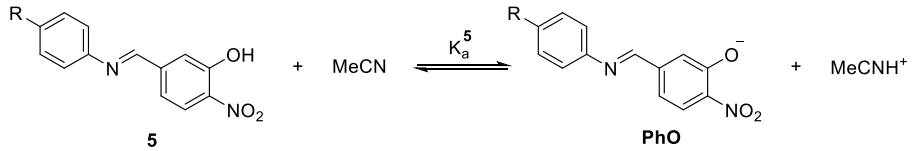
Due to the lack of experimental pK_b values for imines **5a-d** or similar compounds either in water or acetonitrile (CH_3CN), we predicted the free energy associated to imine protonation indirectly. Additionally, and given the extremely poor ability of CH_3CN to protonate **5a-d**, and the high acidic character of their nitrophenol groups, these moieties can be considered the proton source to generate the reactive iminium species.

First, the holistic model developed by Yang et al. (*Angew. Chem. Int. Ed.* **2020**, *59*, 19282–19291 (XGBoost algorithm; http://pka.luoszgroup.com) based on the *i*BonD experimental pK_a database (39 solvents; J.-D. Yang, X.-S. Xue, P. Ji, X. Li, J.-P. Cheng, Internet Bond-energy Databank (pKa and BDE): iBonD Home Page http://ibond.chem.tsinghua.edu.cn or http://ibond.nankai.edu.cn), was used to derive the acidity constants of iminium species ($K_a^{\boldsymbol{Im}}$) in acetonitrile, whose logarithmic values were predicted to range between 12.7 and 14.2:



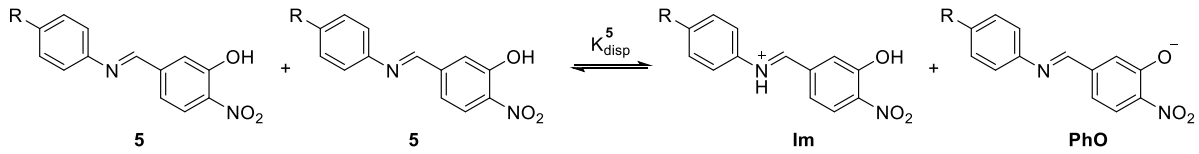
$$K_a^{\boldsymbol{Im}} = \frac{[\mathbf{5}][CH3CNH^+]}{[\boldsymbol{Im}]} \approx 10^{-12.7} \text{ to } 10^{-14.2} \quad (1)$$

On the other hand, the experimental pK_a of 2-nitrophenol in acetonitrile is 22.0 (*J. Phys. Chem.* **1965**, *69*, 3193–3196). Hence, the acidity constants of imine species ($K_a^{\mathbf{5}}$) were approximated to this value:



$$K_a^{\mathbf{5}} = \frac{[\boldsymbol{PhO}][CH3CNH^+]}{[\mathbf{5}]} \approx 10^{-22.0} \quad (2)$$

Considering both processes, the equilibrium constant for the disproportionation reaction ($K_{disp}^{\mathbf{5}}$) between two imine molecules to afford a protonated iminium (**Im**) and a deprotonated phenoxide (**PhO**) can be easily obtained from equations 1 and 2:



$$K_{disp}^{\mathbf{5}} = \frac{[\boldsymbol{Im}][\boldsymbol{PhO}]}{[\mathbf{5}]^2} = \frac{K_a^{\mathbf{5}}}{K_a^{\boldsymbol{Im}}} \quad (3)$$

Therefore:

$$\Delta G_{disp}^{\mathbf{5}} = -RT \ln K_{disp} = 2.303 \cdot RT \cdot pK_{disp} \approx 2.303 \cdot RT \cdot (pK_a^{\mathbf{5}} - pK_a^{\boldsymbol{Im}}) \quad (4)$$

$$\Delta G_{disp}^{\mathbf{5a}} \approx 2.303 \cdot RT \cdot (22.0 - 12.7) \approx 12.7\ kcal\ mol^{-1}$$

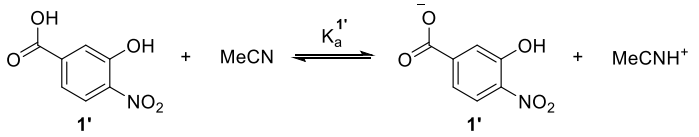
$$\Delta G_{disp}^{\mathbf{5b}} \approx 2.303 \cdot RT \cdot (22.0 - 14.2) \approx 10.6\ kcal\ mol^{-1}$$

$$\Delta G_{disp}^{\mathbf{5c}} \approx 2.303 \cdot RT \cdot (22.0 - 13.5) \approx 11.6\ kcal\ mol^{-1}$$

$$\Delta G_{disp}^{\mathbf{5d}} \approx 2.303 \cdot RT \cdot (22.0 - 13.5) \approx 11.6\ kcal\ mol^{-1}$$

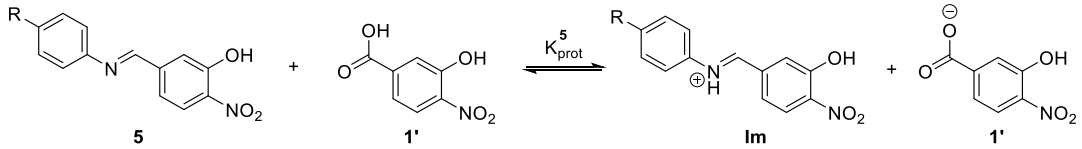
Hence, these estimated free energies for imine protonation through disproportionation, together with the intrinsic activation energies calculated quantum mechanically for the rate-limiting water elimination step (10.8 – 13.1 kcal mol^{-1}), would lead to total activation barriers for the hydrazone formation between 21.4 and 23.5 kcal mol^{-1} depending on the imine substituent.

Alternatively, impurities of the carboxylic acid **1'** generated by spontaneous oxidation of aldehyde **1** might be considered the source of imine protonation. The experimental pK$_a$ for 4-nitrobenzoic acid in CH_3CN is 19.1 (*Comb. Sci.* **2008**, *27*, 563–581):



$$K_a^{\mathbf{1'}} = \frac{[\mathbf{1'}-][CH3CNH^+]}{[\mathbf{1'}]} \approx 10^{-19.1} \quad (5)$$

Combining equations 1 and 5, the equilibrium constant for protonation of imines ($K_{prot}^{\mathbf{5}}$) by 3-hydroxy-4-nitrobenzoic acid can be obtained:



$$K_{prot}^{\mathbf{5}} = \frac{[\boldsymbol{Im}][\mathbf{1'}-]}{[\mathbf{5}][\mathbf{1'}-]} = \frac{K_a^{\mathbf{1'}}}{K_a^{\boldsymbol{Im}}} \quad (6)$$

Therefore:

$$\Delta G_{disp}^{\mathbf{5}} = -RT \ln K_{disp} = 2.303 \cdot RT \cdot pK_{disp} \approx 2.303 \cdot RT \cdot (pK_a^{\mathbf{5}} - pK_a^{\boldsymbol{Im}}) \quad (4)$$

$$\Delta G_{disp}^{\mathbf{5a}} = 2.303 \cdot RT \cdot (19.1 - 12.7) = 8.7\ kcal\ mol^{-1}$$

$$\Delta G_{disp}^{\mathbf{5b}} = 2.303 \cdot RT \cdot (19.1 - 14.2) = 6.7\ kcal\ mol^{-1}$$

$$\Delta G_{disp}^{\mathbf{5c}} = 2.303 \cdot RT \cdot (19.1 - 13.5) = 7.6\ kcal\ mol^{-1}$$

$$\Delta G_{disp}^{\mathbf{5d}} = 2.303 \cdot RT \cdot (19.1 - 13.5) = 7.6\ kcal\ mol^{-1}$$

Hence, these estimated free energies for imine protonation, together with the intrinsic activation energies calculated quantum mechanically for the rate-limiting water elimination step (10.8 – 13.1 kcal mol^{-1}), would lead to total activation barriers for the hydrazone formation between 17.5 and 19.5 kcal mol^{-1} depending on the imine substituent. However, the very low

concentration of 3-hydroxy-4-nitrobenzoic acid impurities expected for the purified imine samples makes this mechanism unlikely.

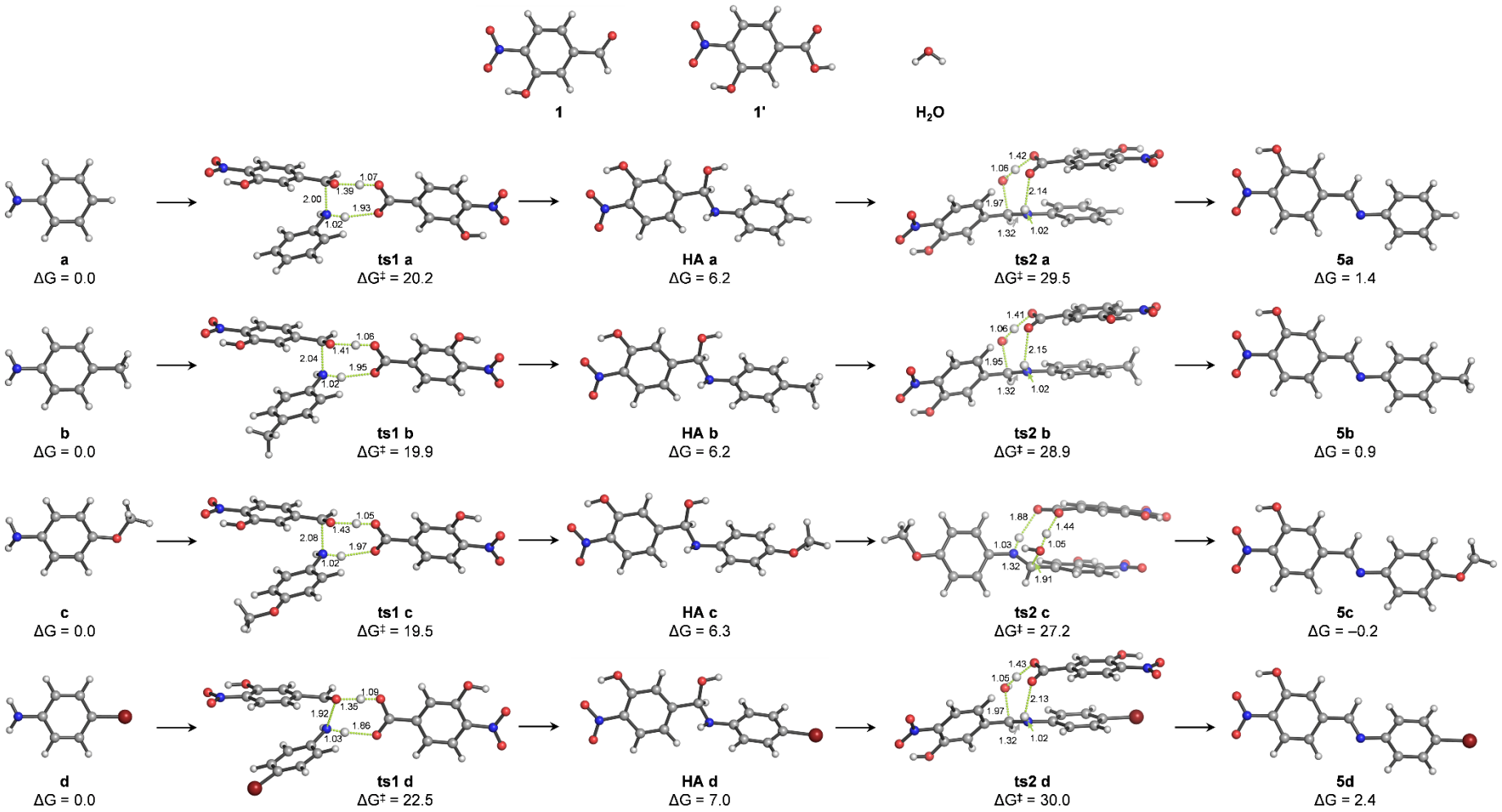


Figure S11. Lowest energy structures for the acid-catalyzed imine formation step optimized with PCM(CH_3CN)/M06-2X/6-31+G(d,p)**.**

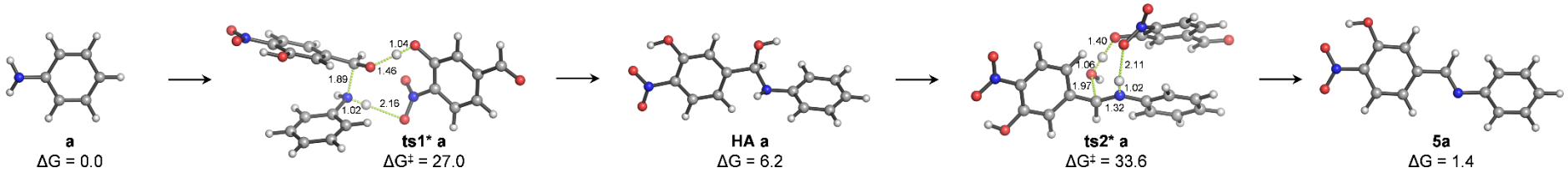


Figure S12. Lowest energy structures for the *o*-nitrophenol-catalyzed imine formation step optimized with PCM(CH_3CN)/M06-2X/6-31+G(d,p)**.**

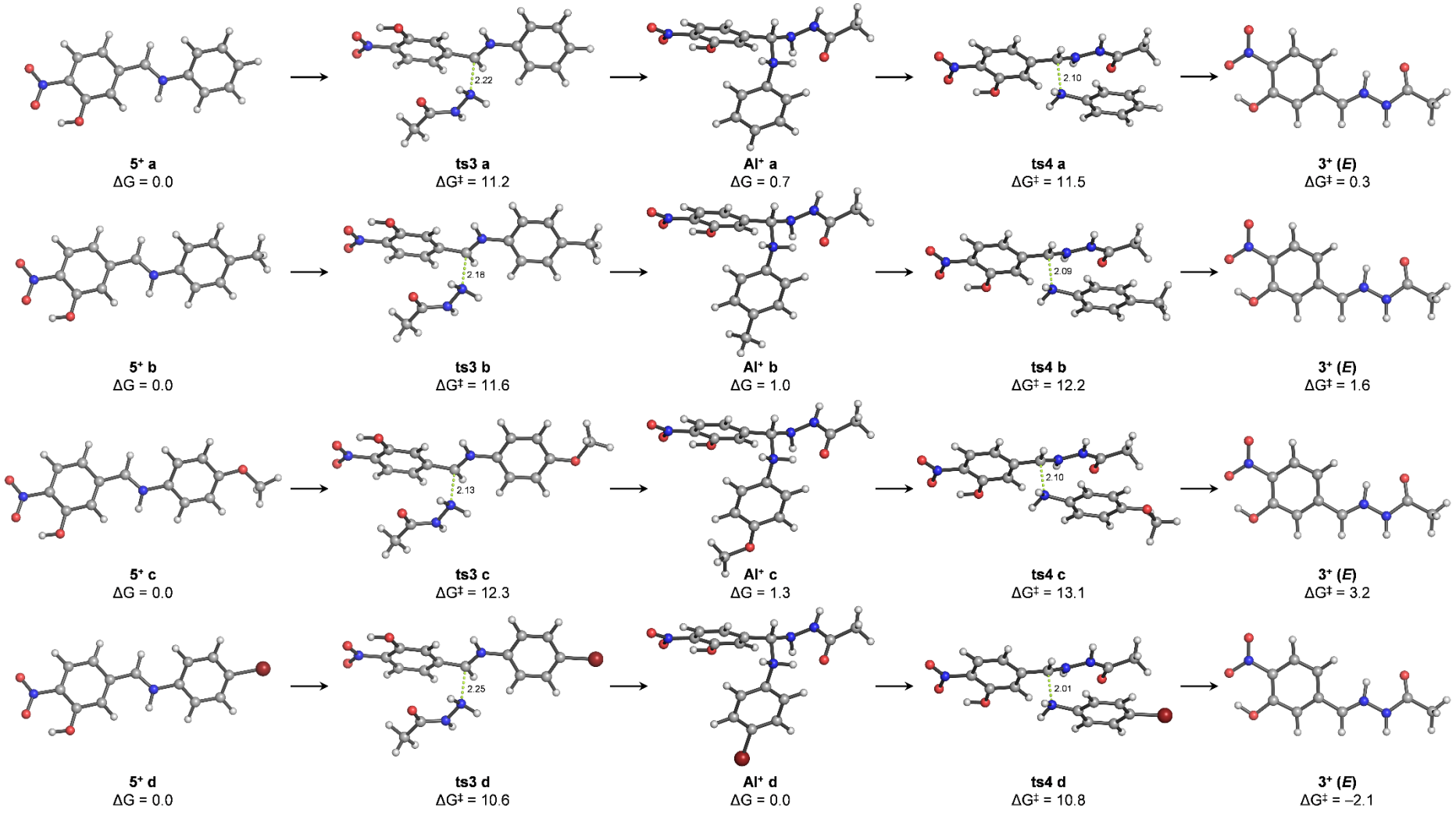


Figure S13. Lowest energy structures for the acylhydrazone formation step optimized with PCM(CH_3CN)/M06-2X/6-31+G(d,p)**.**

Table S1. Energies, entropies, and lowest frequencies of the lowest energy calculated structures for the imine formation step in acetonitrile.[a]

Structure	E_{elec} (Hartree)[a]	E_{elec} + ZPE (Hartree)[a]	H (Hartree)[a]	S (cal mol^{-1} K^{-1})[a]	G (Hartree)[a]	Lowest freq. (cm^{-1})[a]	# of imag freq.	$E_{elec\text{-}basis}$ (Hartree)[b]	G_{basis} (Hartree)[c]
1	–625.086971	–624.968947	–624.958265	98.1	–625.004173	59.2	0	–625.267805	–625.185007
a	–287.499924	–287.381907	–287.375225	75.3	–287.411008	222.2	0	–287.577350	–287.488434
b	–326.797758	–326.652296	–326.643765	85.3	–326.683668	52.1	0	–326.884324	–326.770233
c	–401.981525	–401.830516	–401.821282	88.3	–401.863035	81.3	0	–402.091592	–401.973102
d	–2858.704040	–2858.595462	–2858.587550	84.5	–2858.627695	129.5	0	–2861.149227	–2861.072882
1'	–700.322673	–700.199019	–700.187527	102.9	–700.235123	47.3	0	–700.527591	–700.440042
H_2O	–76.403212	–76.381716	–76.377936	45.1	–76.399363	1600.4	0	–76.430599	–76.426750
ts1 a	–1612.933702	–1612.570886	–1612.542217	196.8	–1612.624318	–172.4	1	–1613.390640	–1613.081256
HA a	–912.606414	–912.365912	–912.348975	131.3	–912.407623	22.0	0	–912.862316	–912.663524
ts2 a	–1612.918325	–1612.556080	–1612.527492	188.6	–1612.609277	–295.7	1	–1613.375545	–1613.066497
5a	–836.186347	–835.974395	–835.959106	123.0	–836.014826	32.5	0	–836.415915	–836.244394
ts1* a	-1537.686710	-1537.328650	-1537.300969	186.1	-1537.381318	-182.5	1	-1538.120854	-1537.815462
ts2* a	-1537.676203	-1537.319441	-1537.291711	182.1	-1537.372106	-319.2	1	-1538.109055	-1537.804958
ts1 b	–1652.232612	–1651.842455	–1651.811827	207.4	–1651.897626	–153.6	1	–1652.698600	–1652.363615
HA b	–951.904688	–951.636757	–951.617933	141.4	–951.680330	20.3	0	–952.169694	–951.945336
ts2 b	–1652.218119	–1651.828309	–1651.797949	197.0	–1651.883132	–298.3	1	–1652.684264	–1652.349277
5b	–875.485410	–875.246107	–875.228913	133.2	–875.288315	30.8	0	–875.724195	–875.527100
ts1 c	–1727.417447	–1727.021653	–1726.990369	208.8	–1727.077567	–125.5	1	–1727.906998	–1727.567119
HA c	–1027.088581	–1026.815094	–1026.795602	144.0	–1026.859450	19.9	0	–1027.377217	–1027.148086
ts2 c	–1727.407573	–1727.011347	–1726.980699	196.6	–1727.066360	–290.6	1	–1727.895967	–1727.554754
5c	–950.670954	–950.426194	–950.408297	136.2	–950.469237	24.7	0	–950.933397	–950.731679
ts1 d	–4184.139102	–4183.786142	–4183.756449	200.5	–4183.841218	–245.1	1	–4186.959976	–4186.662092
HA d	–3483.811559	–3483.580531	–3483.562289	140.1	–3483.624548	17.1	0	–3486.433776	–3486.246765
ts2 d	–4184.131390	–4183.779206	–4183.749167	197.3	–4183.834210	–292.8	1	–4186.947301	–4186.650120
5a	–3407.390915	–3407.188717	–3407.172064	132.3	–3407.231295	29.7	0	–3409.986946	–3409.827325

[a]Energy and entropy values calculated at the PCM(CH_3CN)/M06-2X/6-31+G(d,p) level. [b]Single-point energy calculated at the SMD(CH_3CN)/M06-2X/6-311++G(2d,p) level. [c]Free energies calculated with the formula $G_{basis} = E_{elec\text{-}basis} + (G - E_{elec})$. 1 Hartree = 627.51 kcal mol^{-1}. Thermal corrections calculated at 298.15 K.

Table S2. Energies, entropies, and lowest frequencies of the lowest energy calculated structures for the hydrazone formation step in acetonitrile.[a]

Structure	E_{elec} (Hartree)[a]	E_{elec} + ZPE (Hartree)[a]	H (Hartree)[a]	S (cal mol^{-1} K^{-1})[a]	G (Hartree)[a]	Lowest freq. (cm^{-1})[a]	# of imag freq.	$E_{elec\text{-}basis}$ (Hartree)[b]	G_{basis} (Hartree)[c]
2'	–264.447641	–264.355707	–264.348419	78.0	–264.385121	69.0	0	–264.524844	–264.462324
5$^+$ a	–836.611942	–836.385858	–836.370422	123.8	–836.426298	30.5	0	–836.855831	–836.670187
ts3 a	–1101.069671	–1100.749434	–1100.727561	155.1	–1100.796403	–130.3	1	–1101.388004	–1101.114736
AI$^+$ a	–1101.090939	–1100.768100	–1100.746727	152.8	–1100.814479	18.1	0	–1101.407840	–1101.131380
ts4 a	–1101.068105	–1100.748492	–1100.726665	154.1	–1100.795521	–157.2	1	–1101.386806	–1101.114222
5$^+$ b	–875.912233	–875.658825	–875.641412	138.3	–875.701002	4.6	0	–876.165238	–875.954007
ts3 b	–1140.369303	–1140.021617	–1139.997822	166.4	–1140.070339	–141.6	1	–1140.696835	–1140.397871
AI$^+$ b	–1140.390904	–1140.040681	–1140.017367	164.9	–1140.088722	12.2	0	–1140.716986	–1140.414804
ts4 b	–1140.368112	–1140.020724	–1139.997190	161.8	–1140.069328	–153.9	1	–1140.695624	–1140.396840
5$^+$ c	–951.098544	–950.839642	–950.821551	137.9	–950.882669	19.7	0	–951.375351	–951.159476
ts3 c	–1215.554457	–1215.201228	–1215.176772	168.3	–1215.250755	–154.3	1	–1215.905943	–1215.602241
AI$^+$ c	–1215.576454	–1215.220950	–1215.196899	166.0	–1215.269834	18.1	0	–1215.926359	–1215.619739
ts4 c	–1215.553137	–1215.200266	–1215.176032	164.0	–1215.249587	–145.4	1	–1215.904549	–1215.600999
5$^+$ d	–3407.814231	–3407.597690	–3407.580984	132.2	–3407.640253	29.6	0	–3410.424844	–3410.250866
ts3 d	–3672.272941	–3671.962489	–3671.939219	165.5	–3672.011607	–127.7	1	–3674.957584	–3674.696250
AI$^+$ d	–3672.293945	–3671.981565	–3671.958650	166.2	–3672.029948	4.2	0	–3674.977149	–3674.713152
ts4 d	–3672.275002	–3671.964856	–3671.941856	161.1	–3672.013501	–186.9	1	–3674.957467	–3674.695966
3$^+$ (*Z*)	–813.554095	–813.355513	–813.339609	126.4	–813.396465	27.4	0	–813.800783	–813.643154
3$^+$ (*E*)	–813.554756	–813.355992	–813.340140	125.7	–813.397034	24.5	0	–813.801350	–813.643628

[a]Energy and entropy values calculated at the PCM(CH_3CN)/M06-2X/6-31+G(d,p)level. [b]Single-point energy calculated at the SMD(CH_3CN)/M06-2X/6-311++G(2d,p) level. [c]Free energies calculated with the formula $G_{basis} = E_{elec\text{-}basis} + (G - E_{elec})$. 1 Hartree = 627.51 kcal mol^{-1}. Thermal corrections calculated at 298.15 K.

Table S3. Energies, entropies, and lowest frequencies of the lowest energy calculated structures for the hydrazone formation step in water.[a]

Structure	E_{elec} (Hartree)[a]	E_{elec} + ZPE (Hartree)[a]	H (Hartree)[a]	S (cal mol^{-1} K^{-1})[a]	G (Hartree)[a]	Lowest freq. (cm^{-1})[a]	# of imag freq.	$E_{elec\text{-}basis}$ (Hartree)[b]	G_{basis} (Hartree)[c]
2'	–264.447945	–264.356001	–264.348723	77.9	–264.385423	73.1	0	–264.526419	–264.463897
5$^+$ a	–836.613482	–836.387432	–836.371991	123.7	–836.427898	31.3	0	–836.8453903	–836.659805
ts3 a	–1101.071508	–1100.751409	–1100.729472	155.8	–1100.798436	–130.9	1	–1101.379962	–1101.106891
AI$^+$ a	–1101.092520	–1100.769853	–1100.748413	154.1	–1100.816242	11.8	0	–1101.398985	–1101.122707
ts4 a	–1101.069910	–1100.750527	–1100.728599	155.2	–1100.797594	–163.1	1	–1101.377322	–1101.105005
5$^+$ b	–875.913756	–875.660372	–875.642988	134.9	–875.702622	29.0	0	–876.153812	–875.942679
ts3 b	–1140.371115	–1140.023519	–1139.999689	166.7	–1140.072292	–141.7	1	–1140.687726	–1140.388903
AI$^+$ b	–1140.392475	–1140.042286	–1140.018957	164.8	–1140.090349	14.1	0	–1140.707088	–1140.404962
ts4 b	–1140.369911	–1140.022589	–1139.999042	162.1	–1140.071192	–154.5	1	–1140.685666	–1140.386948
5$^+$ c	–951.100079	–950.841187	–950.823106	137.6	–950.884226	22.2	0	–951.3646151	–951.148763
ts3 c	–1215.556325	–1215.203058	–1215.178610	168.2	–1215.252585	–152.9	1	–1215.897718	–1215.593978
AI$^+$ c	–1215.578068	–1215.222563	–1215.198514	165.9	–1215.271460	18.3	0	–1215.917336	–1215.610728
ts4 c	–1215.554954	–1215.202232	–1215.177934	164.6	–1215.251594	–148.3	1	–1215.895815	–1215.592455
5$^+$ d	–3407.815867	–3407.599442	–3407.582695	132.7	–3407.642031	29.4	0	–3410.41382	–3410.239984
ts3 d	–3672.274883	–3671.964474	–3671.941195	165.2	–3672.013622	–127.4	1	–3674.948967	–3674.687706
AI$^+$ d	–3672.295639	–3671.983145	–3671.960275	165.0	–3672.031555	5.3	0	–3674.967761	–3674.703676
ts4 d	–3672.276905	–3671.966965	–3671.943882	162.2	–3672.015604	–189.1	1	–3674.947713	–3674.686413
3$^+$ (*Z*)	–813.555900	–813.357280	–813.341382	126.4	–813.398215	27.6	0	–813.795004	–813.637319
3$^+$ (*E*)	–813.556550	–813.357754	–813.341917	125.6	–813.398771	26.2	0	–813.795500	–813.637720

[a]Energy and entropy values calculated at the PCM(H_2O)/M06-2X/6-31+G(d,p)level. [b]Single-point energy calculated at the SMD(H_2O)/M06-2X/6-311++G(2d,p) level. [c]Free energies calculated with the formula $G_{basis} = E_{elec\text{-}basis} + (G - E_{elec})$. 1 Hartree = 627.51 kcal mol^{-1}. Thermal corrections calculated at 298.15 K.

Cartesian coordinates optimized with PCM(CH_3CN)/M06-2X/6-31+G(d,p)

1

C	-3.282612	0.325993	0.000177
O	-4.089193	-0.578348	0.000077
C	-1.809014	0.104227	-0.000081
C	-0.975726	1.209428	-0.000035
C	-1.290467	-1.202461	-0.000230
C	0.420406	1.056081	-0.000120
H	-1.375447	2.219221	0.000104
C	0.075771	-1.377343	-0.000166
H	-1.965222	-2.050379	-0.000433
C	0.923332	-0.259169	-0.000087
H	0.519995	-2.364862	-0.000215
N	2.354401	-0.504801	-0.000025
O	3.115094	0.467625	-0.000338
O	2.755129	-1.651600	0.000502
O	1.153922	2.171793	0.000163
H	2.100098	1.932419	0.000414
H	-3.610000	1.380912	0.000335

1'

C	2.973129	-0.141430	0.000002
O	3.482484	1.093519	0.001188
H	4.451534	1.030593	0.000639
O	3.654586	-1.142020	-0.001365
C	1.475981	-0.158834	0.000109
C	0.753238	1.022010	-0.000092
C	0.834919	-1.407888	0.000293
C	-0.650002	0.998186	-0.000173
H	1.246304	1.986955	-0.000216
C	-0.542925	-1.453356	0.000312
H	1.424861	-2.316177	0.000434
C	-1.279056	-0.261950	0.000070
H	-1.075801	-2.395877	0.000524
N	-2.727340	-0.368269	0.000119
O	-3.236172	-1.471264	0.000272
O	-3.389804	0.673359	-0.000242
O	-1.274611	2.179090	-0.000462
H	-2.239094	2.030496	-0.000474

H_2O

O	0.000000	-0.000000	0.117007
H	0.000000	0.765876	-0.468028
H	-0.000000	-0.765876	-0.468028

a

C	0.937663	0.000193	-0.008309
C	0.222081	1.207515	-0.005142
C	0.222211	-1.207387	-0.005187
C	-1.170423	1.201783	0.003449
H	0.764473	2.149261	-0.010183
C	-1.170095	-1.201985	0.003374
H	0.765177	-2.148821	-0.010126
C	-1.880227	-0.000107	0.007501
H	-1.702971	-2.148299	0.008208
H	-2.964948	-0.000230	0.015032
H	-1.703385	2.148045	0.008480
N	2.331558	-0.000064	-0.077453
H	2.776909	0.836114	0.277457
H	2.776582	-0.835700	0.279189

b

C	1.440046	0.000008	-0.004539
C	0.720888	1.203229	-0.008760
C	0.720848	-1.203226	-0.008795
C	-0.671809	1.194677	-0.011350
H	1.258582	2.147861	-0.014512
C	-0.671817	-1.194653	-0.011350
H	1.258555	-2.147850	-0.014607
C	-1.399418	0.000033	-0.010118
H	-1.204086	-2.143155	-0.015215
H	-1.204041	2.143197	-0.015212
N	2.837962	-0.000060	-0.066606
H	3.275148	0.834148	0.303594
H	3.275109	-0.834009	0.304221
C	-2.908009	-0.000013	0.023366
H	-3.313997	-0.884963	-0.474246
H	-3.281389	-0.001351	1.053474
H	-3.313981	0.886213	-0.471973

c

C	-1.843940	-0.112148	-0.007805
C	-0.962347	-1.194946	-0.007011
C	-1.301491	1.183018	-0.006179
C	0.422728	-1.004982	-0.002250
H	-1.356957	-2.207488	-0.010920
C	0.072287	1.379240	-0.000331
H	-1.966018	2.042872	-0.010362
C	0.946970	0.287404	0.000648
H	0.487291	2.382416	0.004020
H	1.069853	-1.874193	0.000655
N	-3.233591	-0.306266	-0.079525
H	-3.542590	-1.194424	0.295846
H	-3.773696	0.450013	0.322504
O	2.283191	0.583812	0.006226
C	3.189395	-0.505203	0.004846
H	4.187582	-0.069548	0.007229
H	3.060141	-1.127443	0.897560
H	3.062393	-1.123143	-0.891171

d

C	2.463529	0.000010	-0.006980
C	1.748482	1.207250	-0.006883
C	1.748462	-1.207245	-0.006911
C	0.358112	1.207554	-0.003708
H	2.285385	2.151261	-0.009829
C	0.358115	-1.207547	-0.003710
H	2.285393	-2.151239	-0.009910
C	-0.332703	0.000016	-0.001664
H	-0.182542	-2.148049	-0.001091
H	-0.182518	2.148072	-0.001087
N	3.853377	-0.000044	-0.068241
H	4.301536	0.837297	0.279815
H	4.301509	-0.837172	0.280360
Br	-2.224182	-0.000003	0.003387

ts1 a

C	2.330167	-0.283003	-0.104691
O	1.733943	-0.807781	-1.137504
C	-1.281578	-1.043433	0.017482
O	-0.720310	-0.649134	-1.040716
N	-1.112280	0.482618	1.304136
H	-0.745246	-1.710418	0.707324
H	0.671670	-0.735359	-1.068224
H	-0.088307	0.505842	1.341218
O	1.753499	0.223665	0.853458
C	-2.772921	-1.147790	0.055827
C	-3.509365	-0.513061	-0.927656
C	-3.405036	-1.835185	1.106330
C	-4.911085	-0.529113	-0.896097
H	-3.010048	0.022235	-1.728784

C	-4.782126	-1.870921	1.155686
H	-2.817044	-2.331958	1.871757
C	-5.531454	-1.220708	0.164341
H	-5.306434	-2.392674	1.946514
N	-6.974499	-1.282748	0.266315
O	-7.649531	-0.708834	-0.595318
O	-7.476148	-1.892533	1.191135
O	-5.549064	0.123371	-1.872638
H	-6.511647	0.039075	-1.734654
C	3.832952	-0.342530	-0.163667
C	4.547008	0.190768	0.895043
C	4.487864	-0.923319	-1.262070
C	5.948497	0.167360	0.900470
H	4.030976	0.636327	1.738145
C	5.867028	-0.957342	-1.278716
H	3.913630	-1.336057	-2.081656
C	6.591828	-0.417565	-0.208813
H	6.409924	-1.395110	-2.107044
N	8.039682	-0.478982	-0.280495
O	8.560784	-0.992593	-1.250760
O	8.693033	-0.003428	0.653422
O	6.562382	0.702863	1.960666
H	7.527760	0.624554	1.842885
C	-1.678372	1.639232	0.718474
C	-2.984364	2.022779	1.038850
C	-0.961882	2.324181	-0.266141
C	-3.565667	3.102961	0.381004
H	-3.537746	1.473353	1.796807
C	-1.555240	3.401787	-0.921728
H	0.050139	2.011585	-0.505756
C	-2.855374	3.793889	-0.602777
H	-4.577459	3.402291	0.635161
H	-0.996767	3.936157	-1.683572
H	-3.312107	4.634543	-1.114500
H	-1.505594	0.250708	2.213823

ts1* a

C	0.402870	-0.576180	-1.037870
O	-0.465490	-0.612741	-0.109080
N	0.613610	1.235700	-1.535830
H	0.111790	-0.894120	-2.051090
H	-0.350890	1.522589	-1.721040
C	1.838180	-0.871620	-0.693080
C	2.218050	-0.861260	0.635970
C	2.778090	-1.095820	-1.712850
C	3.557720	-1.053380	1.001330
H	1.481540	-0.684020	1.412810
C	4.101830	-1.292460	-1.379970
H	2.470150	-1.113140	-2.753900
C	4.491970	-1.266060	-0.033790
H	4.855410	-1.468440	-2.137460
N	5.894360	-1.471410	0.261750
O	6.255830	-1.445770	1.443470
O	6.670730	-1.660260	-0.655140
O	3.846530	-1.011670	2.305920
H	4.805180	-1.152820	2.423260
C	1.211299	1.995350	-0.483040
C	2.575709	2.287430	-0.526550
C	0.443109	2.332210	0.631220
C	3.173679	2.926530	0.556130
H	3.164499	2.008350	-1.396730
C	1.053269	2.970760	1.710340
H	-0.614811	2.090969	0.648760
C	2.415689	3.266530	1.677990
H	4.233709	3.156230	0.522720
H	0.458769	3.235880	2.578540
H	2.885009	3.763000	2.520840
H	1.141990	1.297070	-2.406190
C	-7.068920	-1.547051	1.365420
O	-8.094440	-0.960382	1.639690
H	-6.943280	-2.616331	1.615200
C	-5.912710	-0.905651	0.683970
C	-4.785800	-1.676491	0.435110
C	-5.968420	0.450289	0.323650
C	-3.660840	-1.131701	-0.209600
H	-4.737790	-2.715851	0.747600
C	-4.881130	1.012319	-0.316200
H	-6.856450	1.032189	0.541190
C	-3.768950	0.214669	-0.601930
H	-4.878571	2.050239	-0.630050
N	-2.699720	0.827519	-1.377310
O	-2.187390	0.178199	-2.275080
O	-2.374221	1.977709	-1.109450
O	-2.584970	-1.888581	-0.383240
H	-1.704790	-1.336961	-0.369040

ts1 b

C	-2.461810	-0.321709	-0.143770
O	-1.926960	-0.723980	0.975670
C	1.122310	-1.248980	-0.018260
O	0.541900	-0.702760	0.954460
N	1.071990	0.140350	-1.507610
H	0.580130	-1.963110	-0.653750
H	-0.866870	-0.717270	0.936070
H	0.053540	0.184140	-1.601080
O	-1.828620	0.010120	-1.140960
C	2.608020	-1.402840	0.005750
C	3.337790	-0.672970	0.926340
C	3.245420	-2.234470	-0.931260
C	4.738500	-0.736900	0.942870
H	2.834890	-0.024970	1.636940
C	4.620970	-2.319090	-0.930950
H	2.661950	-2.801860	-1.649460
C	5.364140	-1.574730	-0.002800
H	5.148990	-2.950640	-1.634380
N	6.806290	-1.693520	-0.050430
O	7.476940	-1.039270	0.755620
O	7.311960	-2.427850	-0.877540
O	5.370740	0.011440	1.852250
H	6.333340	-0.119580	1.758060
C	-3.965870	-0.288889	-0.138380
C	-4.668960	-0.666099	0.992700
C	-4.632080	0.131561	-1.300770
C	-6.071610	-0.636769	1.006610
H	-4.153230	-0.990349	1.889000
C	-6.010240	0.167581	-1.310540
H	-4.058690	0.421721	-2.172560
C	-6.725250	-0.212879	-0.167250
H	-6.560500	0.485821	-2.187110
N	-8.173390	-0.155609	-0.231680
O	-8.703590	0.205971	-1.263730
O	-8.817880	-0.478419	0.771170
O	-6.674920	-1.016419	2.137580
H	-7.641390	-0.948879	2.021600
C	1.644130	1.336490	-1.018320
C	2.978380	1.649890	-1.296480
C	0.907850	2.145650	-0.151170
C	3.558480	2.775540	-0.721540
H	3.558110	1.007880	-1.955830
C	1.505650	3.267900	0.419980
H	-0.125260	1.893420	0.069740
C	2.834820	3.603840	0.145820
H	4.595620	3.011540	-0.945670
H	0.924540	3.892900	1.092840

H	1.505300	-0.202940	-2.361670
C	3.466870	4.836740	0.740960
H	4.515480	4.658720	0.993300
H	3.435810	5.670790	0.031930
H	2.942380	5.150250	1.646610

ts1 c

C	-2.624700	-0.414210	-0.135020
O	-2.101900	-0.763240	1.009440
C	0.932800	-1.469540	0.045000
O	0.375570	-0.845640	0.978870
N	0.931790	-0.127750	-1.546380
H	0.362400	-2.185400	-0.562700
H	-1.049570	-0.802820	0.965570
H	-0.083630	-0.067170	-1.649720
O	-1.981170	-0.173210	-1.150460
C	2.412500	-1.658910	0.061600
C	3.171630	-0.886130	0.921920
C	3.017790	-2.568820	-0.823020
C	4.570400	-0.984470	0.928040
H	2.694010	-0.178550	1.592020
C	4.390530	-2.688970	-0.830350
H	2.411810	-3.168400	-1.494890
C	5.163300	-1.901810	0.036710
H	4.894190	-3.381060	-1.493560
N	6.601170	-2.061530	-0.016000
O	7.297270	-1.374060	0.739480
O	7.078920	-2.861510	-0.797580
O	5.232300	-0.190160	1.775230
H	6.189950	-0.354030	1.681650
C	-4.126010	-0.323811	-0.129490
C	-4.838300	-0.590271	1.027050
C	-4.780200	0.035889	-1.318770
C	-6.238780	-0.506371	1.040270
H	-4.332070	-0.867911	1.944160
C	-6.156060	0.122889	-1.329760
H	-4.199620	0.239779	-2.210030
C	-6.880440	-0.145661	-0.160950
H	-6.697310	0.396479	-2.226800
N	-8.325840	-0.040091	-0.228510
O	-8.845600	0.266469	-1.283380
O	-8.978630	-0.267391	0.794940
O	-6.851730	-0.778251	2.196740
H	-7.815490	-0.684031	2.076790
C	1.524290	1.071220	-1.093110
C	2.864590	1.349670	-1.357420
C	0.794060	1.930120	-0.261880
C	3.478410	2.479850	-0.816410
H	3.441280	0.678370	-1.989370
C	1.399720	3.053120	0.282430
H	-0.248800	1.712390	-0.050980
C	2.744580	3.333830	0.011270
H	4.519770	2.672690	-1.043600
H	0.843640	3.728990	0.923770
H	1.364620	-0.512060	-2.382360
O	3.247809	4.458240	0.591300
C	4.612449	4.766680	0.353310
H	4.814679	5.683040	0.905330
H	5.264850	3.966510	0.719140
H	4.797449	4.933060	-0.713290

ts1 d

C	3.078981	-0.308460	0.001331
O	2.658141	-1.132430	-0.910219
C	-0.406729	-1.757300	-0.063179
O	0.227321	-1.221210	-1.028549
N	-0.362949	-0.475240	1.361941
H	0.082421	-2.536400	0.537821
H	1.571031	-1.188530	-0.938629
H	0.622571	-0.182490	1.286491
O	2.353951	0.294140	0.792601
C	-1.894169	-1.901780	-0.210309
C	-2.607849	-2.670640	0.691801
C	-2.547989	-1.173530	-1.217309
C	-4.008929	-2.719411	0.641441
H	-2.110399	-3.237490	1.473921
C	-3.925009	-1.193161	-1.278789
H	-1.962879	-0.586080	-1.914449
C	-4.651819	-1.956331	-0.355119
H	-4.465059	-0.628861	-2.029319
N	-6.096169	-1.942421	-0.462739
O	-6.751949	-2.607851	0.346391
O	-6.616639	-1.280321	-1.339719
O	-4.624869	-3.480971	1.551531
H	-5.589639	-3.419111	1.416171
C	4.572451	-0.123330	0.043011
C	5.380981	-0.785320	-0.864609
C	5.120041	0.727390	1.016771
C	6.774021	-0.622260	-0.835059
H	4.955821	-1.441420	-1.615149
C	6.486671	0.903370	1.064891
H	4.465721	1.233680	1.715701
C	7.308111	0.234600	0.147631
H	6.947171	1.550840	1.800531
N	8.738741	0.454800	0.243191
O	9.164471	1.200261	1.103541
O	9.476441	-0.127539	-0.558209
O	7.483471	-1.296250	-1.746089
H	8.430851	-1.098780	-1.621739
C	-1.275399	0.576130	1.079391
C	-2.532609	0.592280	1.685751
C	-0.962009	1.482600	0.066341
C	-3.495559	1.495469	1.251981
H	-2.767099	-0.109380	2.481071
C	-1.930050	2.377570	-0.381499
H	0.023321	1.460470	-0.388329
C	-3.191660	2.358570	0.202831
H	-4.477789	1.511329	1.711011
H	-1.704370	3.073250	-1.181689
H	-0.533269	-0.920750	2.262631
Br	-4.518780	3.550239	-0.423049

HA a

C	0.936338	0.648720	-0.444980
O	1.129204	1.970739	0.023641
N	1.730196	-0.336236	0.243795
H	1.187139	0.598602	-1.512560
H	2.045256	2.229857	-0.143332
C	3.129750	-0.298151	0.157065
C	3.802441	0.313195	-0.911600
C	3.887712	-0.930729	1.156323
C	5.196381	0.280229	-0.973744
H	3.256550	0.809244	-1.707842
C	5.275181	-0.956970	1.083043
H	3.376267	-1.405549	1.989394
C	5.944224	-0.351310	0.016471
H	5.695142	0.759752	-1.810448
H	5.837772	-1.452809	1.868207
H	7.027335	-0.369694	-0.037228
C	-0.532564	0.300646	-0.302150
C	-1.449398	1.254346	0.099383
C	-0.952225	-1.008399	-0.609516
C	-2.813071	0.940955	0.215675
H	-1.136868	2.264267	0.334908

C	-2.284987	-1.338371	-0.506256
H	-0.225967	-1.750257	-0.921273
C	-3.215229	-0.372435	-0.094391
H	-2.637726	-2.335953	-0.736807
N	-4.601115	-0.768564	0.001010
O	-5.431483	0.074542	0.361299
O	-4.910956	-1.912734	-0.273669
O	-3.627824	1.923195	0.615583
H	-4.540809	1.579649	0.655089
H	1.393494	-0.529806	1.181485

HA b

C	0.503030	0.657499	-0.449379
O	0.687740	1.984169	0.010881
N	1.302851	-0.318811	0.244571
H	0.754990	0.602829	-1.516619
H	1.606690	2.240649	-0.144439
C	2.705091	-0.255291	0.161301
C	3.374270	0.353540	-0.906869
C	3.474311	-0.863180	1.167201
C	4.770700	0.342130	-0.961409
H	2.828050	0.833010	-1.713299
C	4.860481	-0.865390	1.096291
H	2.972551	-1.339830	2.005361
C	5.542061	-0.262190	0.029781
H	5.262690	0.822640	-1.803299
H	5.428331	-1.344860	1.890261
C	-0.963810	0.301978	-0.305309
C	-1.886030	1.251388	0.094161
C	-1.376239	-1.010362	-0.608669
C	-3.247790	0.930458	0.212201
H	-1.579240	2.263768	0.326681
C	-2.706939	-1.347812	-0.503619
H	-0.645689	-1.748721	-0.918639
C	-3.642599	-0.386132	-0.093789
H	-3.054019	-2.348092	-0.731069
N	-5.026019	-0.789893	0.003601
O	-5.861200	0.049627	0.361311
O	-5.329459	-1.936803	-0.266939
O	-4.068030	1.909078	0.609941
H	-4.978990	1.560327	0.650601
H	0.971441	-0.495721	1.187671
C	7.049191	-0.267289	-0.027419
H	7.478730	0.255031	0.833211
H	7.441161	-1.288999	-0.017549
H	7.408710	0.224241	-0.934409

HA c

C	0.129979	0.625980	-0.385590
O	0.322349	1.943960	0.096650
N	0.898439	-0.372310	0.313500
H	0.406689	0.582090	-1.447250
H	1.251269	2.183840	-0.021740
C	2.307189	-0.308070	0.271550
C	3.009249	0.293680	-0.774380
C	3.046519	-0.914260	1.302190
C	4.409649	0.288710	-0.803070
H	2.488849	0.771810	-1.598230
C	4.430729	-0.923500	1.277890
H	2.521719	-1.387530	2.127680
C	5.127249	-0.320629	0.222330
H	4.912529	0.768221	-1.634180
H	4.994709	-1.394199	2.076900
C	-1.344761	0.290110	-0.281700
C	-2.261641	1.243680	0.120060
C	-1.769281	-1.008830	-0.623760
C	-3.630051	0.940199	0.202280
H	-1.945491	2.245950	0.382060
C	-3.106501	-1.329010	-0.554280
H	-1.042671	-1.750510	-0.934990
C	-4.036891	-0.363201	-0.141860
H	-3.462950	-2.318611	-0.811920
N	-5.427481	-0.749001	-0.081710
O	-6.257951	0.094299	0.278160
O	-5.741430	-1.885061	-0.384220
O	-4.444611	1.921619	0.604870
H	-5.361111	1.585499	0.617910
H	0.546619	-0.537340	1.251710
O	6.489729	-0.377679	0.289980
C	7.219069	0.220951	-0.768340
H	7.010169	1.294551	-0.832200
H	8.271659	0.068241	-0.535030
H	6.983549	-0.254809	-1.726730

HA d

C	-0.649411	0.768230	-0.351550
O	-0.528361	2.092650	0.132470
N	0.178480	-0.183279	0.340970
H	-0.378191	0.739301	-1.414830
H	0.368609	2.410251	-0.035400
C	1.570530	-0.130259	0.235180
C	2.223829	0.520671	-0.821520
C	2.348380	-0.794329	1.198230
C	3.613889	0.496662	-0.919230
H	1.668219	1.046031	-1.590940
C	3.732440	-0.818288	1.103050
H	1.859100	-1.302149	2.024260
C	4.360210	-0.172018	0.040820
H	4.103509	1.005122	-1.742510
H	4.318440	-1.335378	1.855080
C	-2.103761	0.351930	-0.242690
C	-3.076111	1.272860	0.100620
C	-2.453250	-0.981670	-0.530990
C	-4.427691	0.901129	0.177280
H	-2.817321	2.301200	0.321040
C	-3.773370	-1.368461	-0.467410
H	-1.684600	-1.697460	-0.798630
C	-4.759760	-0.435941	-0.114260
H	-4.072820	-2.386151	-0.684970
N	-6.129780	-0.891731	-0.058720
O	-7.009080	-0.078222	0.249360
O	-6.378400	-2.054891	-0.314880
O	-5.299021	1.854909	0.522800
H	-6.196881	1.471939	0.537160
H	-0.154590	-0.408299	1.272420
Br	6.249400	-0.185657	-0.082330

ts2 a

C	-1.825630	1.332591	0.044979
O	-1.534720	1.020341	1.964169
N	-0.807870	0.805981	-0.603221
H	-1.829030	2.411021	0.165889
H	-1.393020	1.828381	2.476979
H	-0.852010	-0.190539	-0.818671
H	-0.676440	0.410771	2.060459
O	0.544960	-0.312799	2.118719
C	0.840640	-1.055829	1.130099
O	0.034360	-1.690449	0.421389
C	0.483860	1.381001	-0.745641
C	0.914370	2.434041	0.061459
C	1.333510	0.818691	-1.700391
C	2.203940	2.934511	-0.108301
H	0.273160	2.845731	0.833239
C	2.622380	1.319621	-1.852481

H	0.987600	-0.012449	-2.308571
C	3.060580	2.380161	-1.059151
H	2.543870	3.748651	0.523109
H	3.285190	0.874471	-2.587611
C	-3.130060	0.632201	-0.007341
C	-3.189020	-0.771269	0.081269
C	-4.273830	1.394071	-0.161811
C	-4.416720	-1.389259	-0.008181
H	-2.287540	-1.354579	0.253069
C	-5.533480	0.780251	-0.260061
H	-4.234450	2.476811	-0.219141
C	-5.578450	-0.624479	-0.183051
H	-4.509000	-2.465909	0.062279
C	2.312430	-1.104949	0.753209
C	2.757620	-2.022609	-0.215191
C	3.181520	-0.179639	1.301339
C	4.070750	-1.987749	-0.629271
H	2.056960	-2.732339	-0.638371
C	4.518890	-0.110169	0.885399
H	2.828160	0.535411	2.035639
C	4.947360	-1.032509	-0.089981
N	-6.840820	-1.331919	-0.275131
O	-7.872930	-0.669709	-0.421661
O	-6.842600	-2.544959	-0.206881
N	6.308210	-1.018829	-0.577141
O	6.648910	-1.839019	-1.409251
O	7.086330	-0.166669	-0.131061
O	-6.586190	1.584781	-0.418161
H	-7.396520	1.042451	-0.470041
O	5.282720	0.837041	1.443509
H	6.178590	0.786561	1.059839
H	4.448230	-2.676369	-1.375011
H	4.068980	2.764761	-1.172211

ts2* a

C	0.921640	-1.543940	-0.064940
O	0.469860	-1.269530	1.831260
N	-0.015500	-0.945930	-0.774090
H	0.861360	-2.622790	0.027410
H	-0.109660	-1.946170	2.207850
H	0.104300	0.049470	-0.980950
H	-0.062150	-0.350560	1.757510
C	-1.328980	-1.449000	-0.972120
C	-1.801640	-2.570530	-0.289850
C	-2.163530	-0.742950	-1.841690
C	-3.122830	-2.974320	-0.476680
H	-1.172050	-3.123150	0.398140
C	-3.481810	-1.149670	-2.011900
H	-1.781170	0.128140	-2.367060
C	-3.967990	-2.265280	-1.327940
H	-3.491660	-3.841260	0.061420
H	-4.131100	-0.588470	-2.675680
C	2.264110	-0.924500	0.013370
C	2.401970	0.465560	0.182080
C	3.368720	-1.751440	-0.092720
C	3.669720	1.004790	0.222060
H	1.526860	1.095310	0.315750
C	4.666960	-1.218090	-0.061890
H	3.268550	-2.825370	-0.209830
C	4.791780	0.175480	0.094830
H	3.821830	2.068250	0.358200
N	6.099240	0.802600	0.141380
O	7.097030	0.082660	0.036910
O	6.169630	2.007480	0.279500
O	5.677600	-2.081750	-0.182090
H	6.521410	-1.592600	-0.142010
H	-4.999400	-2.576670	-1.455670
C	-5.204660	-0.460550	1.531510
O	-6.372300	-0.405130	1.202310
C	-4.155660	0.459380	1.024230
C	-2.860720	0.270810	1.471050
C	-4.482940	1.470050	0.097980
C	-1.771640	1.050360	0.980620
H	-2.640030	-0.504150	2.202320
C	-3.464220	2.251450	-0.402760
H	-5.509170	1.598870	-0.225340
C	-2.143110	2.008100	-0.002550
H	-3.652199	3.023600	-1.141180
N	-1.110189	2.743340	-0.699670
O	-0.082370	2.147220	-1.021990
O	-1.313219	3.913600	-0.987220
O	-0.562020	0.906200	1.405970
H	-4.855370	-1.232830	2.242520

ts2 b

C	-1.968410	1.338311	0.135771
O	-1.735320	0.998961	2.042381
N	-0.933190	0.823411	-0.496039
H	-1.977150	2.415321	0.269491
H	-1.607960	1.803141	2.565001
H	-0.971080	-0.169799	-0.726739
H	-0.880250	0.383521	2.163361
O	0.329260	-0.340090	2.265731
C	0.668920	-1.061570	1.274231
O	-0.104770	-1.685870	0.522691
C	0.364030	1.396490	-0.584849
C	0.775090	2.438460	0.242991
C	1.249870	0.842930	-1.512259
C	2.076510	2.925910	0.128521
H	0.111440	2.854590	0.993461
C	2.545820	1.332080	-1.603229
H	0.925660	0.021210	-2.144889
C	2.983730	2.379440	-0.782919
H	2.395200	3.732000	0.783181
H	3.233400	0.885800	-2.317579
C	-3.270980	0.639091	0.026801
C	-3.331390	-0.765189	0.101831
C	-4.409120	1.400481	-0.166189
C	-4.553660	-1.384329	-0.039019
H	-2.435530	-1.348279	0.301841
C	-5.663100	0.785691	-0.316919
H	-4.369840	2.483721	-0.214499
C	-5.709190	-0.619649	-0.251979
H	-4.646890	-2.461599	0.019651
C	2.157440	-1.090800	0.963631
C	2.630920	-1.950780	-0.012999
C	3.020990	-0.184630	1.600341
C	3.973160	-1.923230	-0.409809
H	1.955440	-2.637880	-0.510809
C	4.345480	-0.128340	1.220831
H	2.629780	0.481260	2.359381
C	4.819430	-0.982640	0.215611
H	5.033950	0.574300	1.674941
N	-6.966160	-1.327349	-0.395869
O	-7.993010	-0.665039	-0.576199
O	-6.969420	-2.540899	-0.335909
N	6.207150	-0.857830	-0.171959
O	6.651920	-1.628450	-1.030469
O	6.892930	0.002130	0.349841
O	4.347870	-2.781160	-1.368379
H	5.298140	-2.656500	-1.550449
O	-6.710290	1.590151	-0.509129
H	-7.517160	1.047101	-0.595769
C	4.405080	2.871060	-0.868689

H	5.103320	2.089160	-0.548569
H	4.666250	3.140090	-1.896219
H	4.561600	3.744610	-0.232429

ts2 c

C	1.930749	1.155740	0.707250
O	1.896019	0.127530	2.318340
N	2.586729	0.457059	-0.205400
H	2.476970	1.945749	1.214100
H	2.810989	-0.124441	2.514040
H	2.064759	-0.326140	-0.623480
H	1.366079	-0.737920	2.056840
O	0.438429	-1.755990	1.631710
C	0.106509	-1.773240	0.405080
O	0.886959	-1.783960	-0.568480
C	4.006139	0.350959	-0.242490
C	4.822080	1.471779	-0.061230
C	4.575169	-0.895711	-0.478720
C	6.199890	1.329919	-0.095070
H	4.387630	2.455619	0.085250
C	5.961869	-1.041601	-0.526890
H	3.934319	-1.761201	-0.621580
C	6.778759	0.074019	-0.326260
H	6.849520	2.187869	0.040750
H	6.382129	-2.022051	-0.712450
C	0.461670	1.357400	0.515440
C	-0.386300	1.585700	1.616400
C	-0.040840	1.358280	-0.776050
C	-1.736420	1.754280	1.400140
H	0.014370	1.589290	2.621840
C	-1.411450	1.549920	-1.019270
H	0.600899	1.213090	-1.638080
C	-2.250020	1.724840	0.096020
H	-2.422440	1.895160	2.226590
C	-1.385151	-1.693160	0.117080
C	-2.273081	-1.545680	1.168390
C	-1.835951	-1.646580	-1.213710
C	-3.635521	-1.303070	0.936860
H	-1.916421	-1.564960	2.192120
C	-3.170471	-1.416200	-1.470830
H	-1.121261	-1.751970	-2.021330
C	-4.063981	-1.230940	-0.404440
H	-3.549331	-1.348960	-2.483470
N	-3.685730	1.826070	-0.065180
O	-4.150540	1.839130	-1.210900
O	-4.388940	1.861750	0.926020
N	-5.444261	-0.931730	-0.730940
O	-6.229551	-0.702699	0.195040
O	-5.783181	-0.907870	-1.898270
O	-4.416231	-1.136100	2.010840
H	-5.317871	-0.909060	1.714640
O	-1.803230	1.534470	-2.294550
H	-2.770530	1.660260	-2.333750
O	8.134919	0.042259	-0.345270
C	8.764739	-1.209101	-0.582970
H	8.503499	-1.932311	0.196360
H	8.486559	-1.606321	-1.564550
H	9.835419	-1.014971	-0.557340

ts2 d

C	-2.357270	1.119449	0.378149
O	-2.158530	0.294589	2.159169
N	-1.395120	0.651049	-0.388331
H	-2.235181	2.122169	0.775189
H	-1.897210	0.907439	2.860689
H	-1.554710	-0.245551	-0.850671
H	-1.418670	-0.448371	2.076289
O	-0.323500	-1.355971	1.936129
C	0.012320	-1.779481	0.785259
O	-0.763960	-2.093111	-0.138631
C	-0.037730	1.064379	-0.391291
C	0.526589	1.775409	0.666979
C	0.742250	0.661349	-1.475901
C	1.883739	2.085750	0.636709
H	-0.064491	2.064169	1.528649
C	2.096890	0.963400	-1.504141
H	0.293850	0.096389	-2.287511
C	2.656599	1.658980	-0.438311
H	2.335899	2.627340	1.459689
H	2.711230	0.643600	-2.338441
C	-3.730230	0.609229	0.159409
C	-3.944010	-0.756501	-0.105971
C	-4.779241	1.508659	0.206359
C	-5.229290	-1.191611	-0.341671
H	-3.116680	-1.462531	-0.092831
C	-6.095630	1.083329	-0.038321
H	-4.620851	2.560399	0.420179
C	-6.295540	-0.282141	-0.314991
H	-5.440430	-2.234531	-0.542571
C	1.508360	-1.823210	0.510409
C	1.996700	-2.399890	-0.676051
C	2.367280	-1.189760	1.389799
C	3.336960	-2.295650	-0.978581
H	1.307490	-2.889050	-1.354271
C	3.734220	-1.063210	1.104849
H	1.983770	-0.737940	2.297599
C	4.201100	-1.616820	-0.103541
N	-7.625250	-0.798881	-0.576931
O	-8.574220	-0.009071	-0.554531
O	-7.761020	-1.983501	-0.809461
N	5.587810	-1.484960	-0.491291
O	5.949800	-1.940980	-1.560421
O	6.364220	-0.909140	0.279469
O	-7.049031	2.015099	0.012639
H	-7.912491	1.598769	-0.172801
Br	4.503629	2.063020	-0.479071
O	4.481480	-0.405760	1.999749
H	5.397830	-0.354120	1.667809
H	3.745290	-2.711520	-1.891481

5a

C	-1.049051	0.379439	-0.096160
N	-1.888131	-0.563861	0.074860
H	-1.359991	1.410709	-0.305710
C	-3.268151	-0.263071	0.055360
C	-3.799331	0.897229	0.635160
C	-4.127501	-1.200501	-0.530250
C	-5.173261	1.126029	0.596170
H	-3.143511	1.599729	1.140650
C	-5.496851	-0.956311	-0.581470
H	-3.704261	-2.106901	-0.951810
C	-6.024631	0.207609	-0.018900
H	-5.579501	2.021499	1.055860
H	-6.154591	-1.680211	-1.051940
H	-7.093881	0.390269	-0.046850
C	0.405659	0.134099	-0.042190
C	0.918549	-1.156381	0.202440
C	1.263759	1.205699	-0.239070
C	2.280739	-1.345071	0.242340
H	0.235909	-1.983471	0.354930
C	2.656119	1.038089	-0.201510
H	0.882199	2.204409	-0.427750
C	3.148039	-0.258911	0.042360
H	2.708969	-2.322581	0.426530

N	4.570109	-0.515041	0.094010
O	5.344849	0.432309	-0.083130
O	4.960319	-1.647031	0.308300
O	3.405189	2.126649	-0.401400
H	4.347409	1.875759	-0.351790

5b

C	-0.588330	0.353420	-0.088181
N	-1.416210	-0.602060	0.071459
H	-0.910270	1.383610	-0.285481
C	-2.800430	-0.322610	0.057629
C	-3.353490	0.840300	0.609599
C	-3.651860	-1.283340	-0.499781
C	-4.730650	1.042490	0.571059
H	-2.712580	1.571060	1.094029
C	-5.023830	-1.060440	-0.549241
H	-3.220480	-2.192650	-0.907091
C	-5.588240	0.103580	-0.012931
H	-5.147490	1.945150	1.010369
H	-5.670190	-1.806520	-1.004151
C	0.868780	0.123400	-0.037551
C	1.395800	-1.163600	0.196599
C	1.716150	1.205030	-0.227311
C	2.759790	-1.338810	0.232909
H	0.721840	-1.998680	0.343999
C	3.110050	1.051230	-0.193531
H	1.324360	2.201320	-0.407681
C	3.615980	-0.242470	0.039879
H	3.198110	-2.313290	0.409269
N	5.040220	-0.484260	0.087749
O	5.805260	0.472330	-0.082941
O	5.442680	-1.613820	0.292829
O	3.847980	2.148720	-0.386681
H	4.792680	1.906610	-0.340091
C	-7.080470	0.316280	-0.024031
H	-7.536780	-0.140880	-0.905501
H	-7.542560	-0.136670	0.859629
H	-7.327590	1.380560	-0.018161

5c

C	-0.179790	0.281400	-0.114660
N	-0.979740	-0.697240	0.051370
H	-0.529080	1.298530	-0.331330
C	-2.372100	-0.471940	0.020780
C	-2.979720	0.699520	0.481840
C	-3.184490	-1.511070	-0.459090
C	-4.365390	0.853940	0.436310
H	-2.377530	1.492640	0.914560
C	-4.559080	-1.360461	-0.527250
H	-2.714480	-2.431500	-0.791250
C	-5.159010	-0.174031	-0.081310
H	-4.807190	1.767089	0.815950
H	-5.192050	-2.153201	-0.912290
C	1.282200	0.095100	-0.046930
C	1.844420	-1.173500	0.207000
C	2.100800	1.198060	-0.242720
C	3.212310	-1.309649	0.255310
H	1.193200	-2.025520	0.359370
C	3.497950	1.084221	-0.196370
H	1.682829	2.180790	-0.438130
C	4.039020	-0.191929	0.055450
H	3.676450	-2.269339	0.446230
N	5.468520	-0.392479	0.115470
O	6.207600	0.583251	-0.062770
O	5.901910	-1.507559	0.337190
O	4.206609	2.199791	-0.396370
H	5.157240	1.984021	-0.341060
O	-6.512680	-0.121501	-0.173900
C	-7.161650	1.061739	0.269250
H	-6.983200	1.229949	1.336380
H	-6.823160	1.931609	-0.303090
H	-8.224800	0.902709	0.097860

5d

C	0.622509	0.321489	-0.075760
N	-0.189701	-0.651511	0.053241
H	0.284549	1.350479	-0.251770
C	-1.576641	-0.398641	0.040611
C	-2.150841	0.728779	0.642011
C	-2.402841	-1.367251	-0.540580
C	-3.531851	0.899879	0.634751
H	-1.525061	1.457349	1.147641
C	-3.781421	-1.192841	-0.569800
H	-1.950261	-2.250871	-0.978540
C	-4.332121	-0.059271	0.022291
H	-3.978221	1.767709	1.107391
H	-4.419881	-1.933951	-1.037360
C	2.082389	0.112590	-0.025390
C	2.625939	-1.164560	0.222031
C	2.913269	1.203380	-0.232590
C	3.992449	-1.321250	0.253621
H	1.963149	-2.006020	0.383251
C	4.309429	1.068430	-0.202610
H	2.507189	2.192080	-0.422480
C	4.832439	-0.216100	0.042261
H	4.444729	-2.287400	0.440151
N	6.260919	-0.438700	0.086111
O	7.011729	0.525820	-0.099970
O	6.678739	-1.560250	0.302491
O	5.031619	2.173230	-0.411360
H	5.979769	1.944700	-0.367330
Br	-6.205641	0.188548	-0.016880

2'

N	-1.935230	-0.215778	0.000549
H	-2.069650	0.375802	0.818109
N	-0.614141	-0.673669	-0.000871
C	0.450390	0.163050	-0.000631
O	0.310591	1.385970	-0.000121
C	1.805939	-0.499152	0.000319
H	1.748908	-1.588362	-0.013102
H	2.360650	-0.156102	-0.875362
H	2.348330	-0.178022	0.892069
H	-0.494492	-1.675580	-0.000781
H	-2.070850	0.377252	-0.815822

5⁺ a

C	-3.266990	0.169049	-0.015261
C	-3.855080	-0.882181	0.686389
C	-5.241770	-0.993791	0.675949
C	-6.019000	-0.061351	-0.012561
C	-5.412200	0.996029	-0.690681
C	-4.026580	1.120529	-0.693811
H	-5.714130	-1.802301	1.222479
H	-6.015020	1.725309	-1.220001
H	-3.254040	-1.580671	1.258559
H	-3.542670	1.933229	-1.226201
N	-1.844820	0.308719	-0.053271
C	-0.986560	-0.652922	0.003459
H	-1.382690	-1.665192	0.025809
C	0.457750	-0.468992	0.007939
C	1.046620	0.764378	0.272009
C	1.241330	-1.603562	-0.271821
C	2.438670	0.909478	0.243189

H	0.474570	1.646518	0.539339
C	2.615630	-1.476562	-0.311381
H	0.775810	-2.563082	-0.464411
C	3.204120	-0.236692	-0.059441
H	3.251950	-2.324442	-0.531101
N	4.661080	-0.167022	-0.103721
O	5.195900	0.917878	0.128709
O	5.284110	-1.173202	-0.366931
O	2.922640	2.121178	0.512109
H	3.897310	2.099298	0.467169
H	-1.501960	1.264649	-0.157901
H	-7.099780	-0.152491	-0.009811

5⁺ b

C	2.803399	0.188450	0.014600
C	3.404919	-0.865770	-0.668060
C	4.792509	-0.961260	-0.659290
C	5.582709	-0.017750	0.006680
C	4.945759	1.043510	0.664740
C	3.562639	1.157260	0.671480
H	5.267710	-1.776350	-1.195860
H	5.542119	1.790300	1.180320
H	2.814500	-1.583570	-1.227510
H	3.077559	1.977570	1.191520
N	1.382679	0.315839	0.057290
C	0.528149	-0.648971	-0.005310
H	0.927270	-1.659741	-0.033940
C	-0.916941	-0.468701	-0.009410
C	-1.509061	0.763999	-0.268970
C	-1.698420	-1.605931	0.266000
C	-2.901401	0.905909	-0.239140
H	-0.939131	1.648339	-0.533630
C	-3.072930	-1.482481	0.305580
H	-1.230780	-2.565141	0.455060
C	-3.664621	-0.242921	0.058660
H	-3.707160	-2.332871	0.521600
N	-5.121151	-0.176572	0.102750
O	-5.658421	0.908578	-0.123790
O	-5.742520	-1.185542	0.360010
O	-3.388301	2.117689	-0.503360
H	-4.362871	2.093139	-0.457760
C	7.084049	-0.121370	0.011450
H	7.533849	0.775210	-0.424710
H	7.458889	-0.210870	1.035270
H	7.423119	-0.989220	-0.556710
H	1.033599	1.268699	0.169190

5⁺ c

C	-2.378321	0.068420	0.055981
C	-2.964261	-1.040310	0.677951
C	-4.340231	-1.154579	0.688181
C	-5.141591	-0.165939	0.090201
C	-4.547180	0.951471	-0.509239
C	-3.161580	1.064610	-0.519869
H	-4.823731	-1.995479	1.172311
H	-5.143300	1.730241	-0.966819
O	-6.469491	-0.371999	0.156291
C	-7.332891	0.603121	-0.421219
H	-7.144160	0.699271	-1.494539
H	-8.344091	0.237162	-0.256859
H	-7.205710	1.572061	0.070581
H	-2.361371	-1.790660	1.178131
H	-2.696910	1.924570	-0.992789
N	-0.965291	0.216420	-0.004839
C	-0.085701	-0.727700	0.039251
H	-0.456051	-1.748990	0.065031
C	1.353879	-0.506850	0.025481
C	1.915920	0.736609	0.300181
C	2.163549	-1.615301	-0.284959
C	3.302940	0.919259	0.248841
H	1.326410	1.598500	0.594301
C	3.532879	-1.451971	-0.344639
H	1.720059	-2.583451	-0.485779
C	4.093949	-0.200771	-0.083719
H	4.186959	-2.279671	-0.587989
N	5.546139	-0.091411	-0.150969
O	6.056940	1.002729	0.094341
O	6.191609	-1.075241	-0.444539
O	3.759680	2.139689	0.527361
H	4.733780	2.142969	0.466871
H	-0.635890	1.176580	-0.113909

5⁺ d

C	-1.593080	0.214950	-0.037251
C	-2.199180	-0.841210	0.640239
C	-3.585480	-0.924320	0.652719
C	-4.334470	0.053850	0.001839
C	-3.726670	1.119840	-0.656501
C	-2.340380	1.204930	-0.671661
H	-4.075810	-1.735520	1.177579
H	-4.324230	1.874510	-1.153751
H	-1.613890	-1.574620	1.183649
H	-1.850080	2.025970	-1.184651
N	-0.171970	0.333350	-0.077411
C	0.677300	-0.636450	-0.012881
H	0.274110	-1.645830	0.011199
C	2.121770	-0.463360	-0.002361
C	2.718590	0.766820	0.260009
C	2.897810	-1.605610	-0.271831
C	4.111690	0.900810	0.238139
H	2.152150	1.654630	0.520549
C	4.273310	-1.489550	-0.303881
H	2.426000	-2.562510	-0.462231
C	4.869580	-0.252960	-0.054841
H	4.904320	-2.343490	-0.515251
N	6.327580	-0.194920	-0.090611
O	6.869100	0.887680	0.136599
O	6.944130	-1.207940	-0.342311
O	4.603770	2.109790	0.504249
H	5.578440	2.080390	0.464179
Br	-6.212120	-0.075140	0.006839
H	0.183110	1.284640	-0.183251

ts3 a

C	3.517231	-0.649059	0.104030
C	4.060960	0.568911	0.513380
C	5.446350	0.706272	0.561040
C	6.277641	-0.351538	0.195450
C	5.719491	-1.559558	-0.223350
C	4.337991	-1.713799	-0.270590
H	5.873090	1.651612	0.878060
N	2.110891	-0.853159	0.044340
C	1.197311	-0.060230	0.547360
C	-0.234689	-0.398730	0.521260
C	-0.767689	-1.232030	-0.452560
C	-1.059549	0.209969	1.482170
C	-2.144379	-1.478621	-0.507230
H	-0.165379	-1.684210	-1.234180
C	-2.420519	-0.024751	1.447790
H	-0.637550	0.854460	2.245200
C	-2.957169	-0.852611	0.460790
H	-3.086369	0.427179	2.172590
N	-4.399679	-1.044392	0.458370
O	-4.888439	-1.769052	-0.411310

O	-5.065499	-0.486692	1.306120
O	-2.575589	-2.276531	-1.484530
H	-3.546298	-2.360421	-1.427970
H	3.898502	-2.654449	-0.589100
H	6.358242	-2.386998	-0.512380
H	1.525150	0.668670	1.279570
N	0.921670	1.630870	-0.863990
H	1.756260	2.095461	-1.223460
H	0.444590	1.182560	-1.652610
N	0.027060	2.593210	-0.379520
C	-1.282240	2.513459	-0.746690
O	-1.639620	1.721799	-1.615980
C	-2.221401	3.451139	-0.039820
H	-2.970990	2.855279	0.487040
H	-1.713871	4.105319	0.670040
H	-2.735271	4.055749	-0.789470
H	0.318880	3.100540	0.445260
H	1.810521	-1.662609	-0.491760
H	3.432920	1.410411	0.784360
H	7.355111	-0.233397	0.231830

ts3 b

C	3.145910	-0.629580	0.065249
C	3.697960	0.581600	0.486459
C	5.081240	0.715281	0.530009
C	5.931770	-0.330889	0.152169
C	5.351670	-1.528839	-0.275311
C	3.969830	-1.685059	-0.320971
H	5.507440	1.659151	0.858059
N	1.739890	-0.832390	0.009179
C	0.826610	-0.033550	0.509179
C	-0.604350	-0.385670	0.501369
C	-1.141560	-1.222900	-0.466441
C	-1.423590	0.215060	1.471899
C	-2.516600	-1.481910	-0.505211
H	-0.544240	-1.670000	-1.254871
C	-2.782990	-0.030020	1.452239
H	-0.998280	0.861930	2.231109
C	-3.324100	-0.862320	0.471279
H	-3.444340	0.416550	2.184449
N	-4.764400	-1.066880	0.485549
O	-5.256580	-1.798751	-0.376331
O	-5.425960	-0.512661	1.339039
O	-2.951850	-2.284370	-1.477161
H	-3.920960	-2.377460	-1.408641
H	3.535200	-2.625130	-0.648381
H	5.986950	-2.356689	-0.575521
H	1.155880	0.686750	1.249599
N	0.550240	1.624990	-0.878031
H	1.393390	2.076850	-1.234261
H	0.066150	1.186180	-1.668051
N	-0.328910	2.597560	-0.387591
C	-1.642390	2.530150	-0.745601
O	-2.012070	1.741840	-1.612101
C	-2.567300	3.476080	-0.031451
H	-2.047530	4.129790	0.669899
H	-3.086880	4.080540	-0.777201
H	-3.313490	2.886080	0.506749
H	-0.023970	3.105010	0.432439
H	1.437630	-1.641330	-0.525931
H	3.075880	1.422670	0.772979
C	7.427010	-0.154699	0.198809
H	7.941410	-1.080449	-0.066061
H	7.746740	0.625531	-0.498521
H	7.752240	0.146201	1.198769

ts3 c

C	2.806240	-0.467551	0.065051
C	3.325550	0.755229	0.502671
C	4.698150	0.929709	0.570791
C	5.567860	-0.103411	0.196471
C	5.045450	-1.320411	-0.252239
C	3.665410	-1.494881	-0.313719
H	5.118320	1.871349	0.906631
N	1.407310	-0.705801	-0.007929
C	0.466730	0.067939	0.489431
C	-0.951320	-0.342371	0.486771
C	-1.456800	-1.206011	-0.474679
C	-1.792640	0.228429	1.456411
C	-2.819770	-1.523781	-0.506669
H	-0.844520	-1.634181	-1.262089
C	-3.140940	-0.071821	1.441821
H	-1.392980	0.896079	2.211451
C	-3.650160	-0.932201	0.467941
H	-3.817920	0.351559	2.173571
N	-5.079470	-1.199761	0.490451
O	-5.541170	-1.967331	-0.357279
O	-5.762820	-0.661581	1.337131
O	-3.223560	-2.350951	-1.471699
H	-4.186930	-2.488351	-1.396259
H	3.262300	-2.444401	-0.653809
H	5.691740	-2.135771	-0.551309
H	0.770550	0.776409	1.252731
N	0.159900	1.690639	-0.856179
H	1.004630	2.160779	-1.184799
H	-0.296170	1.251909	-1.663339
N	-0.748360	2.639659	-0.375179
C	-2.054510	2.540399	-0.756489
O	-2.387100	1.745639	-1.631209
C	-3.014870	3.459439	-0.055069
H	-2.520550	4.141569	0.637421
H	-3.557280	4.033059	-0.808679
H	-3.737460	2.848059	0.491531
H	-0.467330	3.153259	0.449721
H	1.130240	-1.512991	-0.557989
H	2.680560	1.579189	0.787741
O	6.889880	0.169049	0.296921
C	7.808670	-0.852561	-0.069769
H	7.687700	-1.126041	-1.122779
H	8.800180	-0.432501	0.087641
H	7.679110	-1.737561	0.561271

ts3 d

C	2.145851	-0.614500	0.042820
C	2.681151	0.611810	0.435350
C	4.061781	0.779670	0.449890
C	4.884151	-0.274110	0.064290
C	4.352990	-1.496340	-0.338400
C	2.974520	-1.665790	-0.349860
H	4.487861	1.728910	0.752710
N	0.744141	-0.837490	0.012530
C	-0.167429	-0.058220	0.537760
C	-1.596649	-0.399859	0.522600
C	-2.135800	-1.234289	-0.447240
C	-2.414589	0.207721	1.490260
C	-3.512480	-1.482759	-0.490890
H	-1.539770	-1.684419	-1.234860
C	-3.775199	-0.030349	1.467640
H	-1.987669	0.852951	2.249810
C	-4.317829	-0.858559	0.484400
H	-4.436059	0.420061	2.197900
N	-5.760609	-1.052159	0.493710
O	-6.255020	-1.779619	-0.370170
O	-6.420139	-0.493009	1.345260

O	-3.950530	-2.279819	-1.465590
H	-4.920510	-2.366059	-1.400870
H	2.548090	-2.616000	-0.656210
H	5.004090	-2.309280	-0.637810
H	0.166091	0.676160	1.261720
N	-0.478009	1.656600	-0.882920
H	0.336671	2.147000	-1.253450
H	-0.949349	1.193780	-1.666500
N	-1.397259	2.592580	-0.391700
C	-2.705279	2.478461	-0.752430
O	-3.045769	1.680371	-1.623010
C	-3.666549	3.390591	-0.041630
H	-4.444519	2.778071	0.420300
H	-3.185559	4.004141	0.721050
H	-4.140619	4.038101	-0.782140
H	-1.115139	3.105880	0.432600
H	0.442170	-1.647180	-0.522610
H	2.050181	1.446340	0.719860
Br	6.755601	-0.040841	0.092510

AI⁺ a

C	1.218400	1.468420	-0.748090
C	-0.007320	2.010901	-1.124100
C	-0.390190	3.235261	-0.584170
C	0.443870	3.896521	0.318990
C	1.671410	3.342330	0.675420
C	2.071720	2.118510	0.138350
H	-1.341200	3.670801	-0.870380
N	1.618720	0.160150	-1.271080
C	1.169050	-1.061029	-0.408420
C	-0.335720	-1.006419	-0.260090
C	-0.923200	-0.558709	0.908680
C	-1.123530	-1.377869	-1.363010
C	-2.318440	-0.443899	1.014520
H	-0.340600	-0.284119	1.781110
C	-2.496890	-1.275969	-1.281630
H	-0.666481	-1.754539	-2.272550
C	-3.091050	-0.805529	-0.106210
H	-3.131511	-1.559009	-2.112170
N	-4.539000	-0.715738	-0.073150
O	-5.074900	-0.304888	0.960190
O	-5.170860	-1.043778	-1.057240
O	-2.799160	0.004691	2.175250
H	-3.773540	0.040971	2.125290
H	1.460379	-1.932040	-0.999090
N	1.872320	-1.106240	0.827490
N	3.098589	-1.756940	0.838710
C	4.198630	-1.319540	0.181110
O	4.159490	-0.341200	-0.575720
C	5.464249	-2.090360	0.419250
H	5.312609	-2.979920	1.030210
H	5.884709	-2.372590	-0.547080
H	6.173869	-1.426420	0.918400
H	3.150189	-2.560930	1.450080
H	2.666860	0.087660	-1.258220
H	2.327190	3.861360	1.365650
H	-0.652610	1.488301	-1.824350
H	3.038300	1.689580	0.385830
H	1.289410	0.042420	-2.233930
H	1.887320	-0.243760	1.366110
H	0.138231	4.849291	0.737850

AI⁺ b

C	1.191131	1.174429	-0.878520
C	-0.040539	1.658659	-1.313270
C	-0.468329	2.900990	-0.862870
C	0.312881	3.663899	0.017070
C	1.546041	3.152799	0.427040
C	1.997271	1.909669	-0.018280
H	-1.426769	3.285550	-1.199520
N	1.639090	-0.153281	-1.304060
C	1.210520	-1.326211	-0.367530
C	-0.294820	-1.285340	-0.219350
C	-0.885880	-0.766310	0.917810
C	-1.080470	-1.740110	-1.292110
C	-2.281950	-0.659750	1.019120
H	-0.305350	-0.425580	1.768010
C	-2.454830	-1.648840	-1.214090
H	-0.620690	-2.171390	-2.175540
C	-3.052540	-1.106170	-0.072000
H	-3.087570	-1.995190	-2.021770
N	-4.501340	-1.031259	-0.041210
O	-5.040260	-0.558699	0.963780
O	-5.131180	-1.431889	-0.999400
O	-2.765260	-0.136840	2.147370
H	-3.740010	-0.114529	2.097730
H	1.517650	-2.228501	-0.900920
N	1.913420	-1.280351	0.869650
N	3.153450	-1.902791	0.918490
C	4.248840	-1.467022	0.251740
O	4.191850	-0.524222	-0.547570
C	5.530450	-2.195652	0.533730
H	5.394139	-3.060942	1.182090
H	5.965330	-2.510522	-0.416030
H	6.220510	-1.493992	1.008040
H	3.220720	-2.670721	1.573160
H	2.688000	-0.191241	-1.272620
H	2.172271	3.732579	1.098060
H	-0.657809	1.075920	-1.991480
H	2.969971	1.531489	0.282790
H	1.331080	-0.344111	-2.262260
H	1.913610	-0.383711	1.349780
C	-0.167938	5.012700	0.483780
H	-1.186078	4.947490	0.876770
H	0.480182	5.414559	1.264710
H	-0.181748	5.723380	-0.348200

AI⁺ c

C	1.158680	1.044271	-0.885670
C	-0.113180	1.416771	-1.300510
C	-0.660490	2.618301	-0.858270
C	0.076451	3.437141	0.006250
C	1.363640	3.054631	0.408290
C	1.908600	1.860831	-0.038470
H	-1.651240	2.898571	-1.192300
N	1.720160	-0.240239	-1.305940
C	1.400160	-1.443839	-0.364990
C	-0.102670	-1.538349	-0.215560
C	-0.737940	-1.058159	0.915030
C	-0.845140	-2.075129	-1.281220
C	-2.137980	-1.072159	1.015850
H	-0.190310	-0.655409	1.759950
C	-2.222410	-2.102079	-1.204000
H	-0.348850	-2.477509	-2.158420
C	-2.865810	-1.597419	-0.069470
H	-2.822290	-2.512479	-2.006710
N	-4.315860	-1.644128	-0.040880
O	-4.894470	-1.201398	0.955490
O	-4.907850	-2.112238	-0.992570
O	-2.665530	-0.578809	2.137610
H	-3.638570	-0.639939	2.087440
H	1.788910	-2.316049	-0.894720
N	2.095830	-1.329690	0.872110
N	3.388390	-1.833680	0.923440

C	4.439620	-1.298300	0.258170
O	4.296810	-0.366360	-0.543060
C	5.783080	-1.904240	0.541860
H	5.735670	-2.737300	1.242650
H	6.216960	-2.240230	-0.401490
H	6.425620	-1.121890	0.951630
H	3.525150	-2.595230	1.574850
H	2.767980	-0.182710	-1.275610
H	1.925121	3.710941	1.063710
O	-0.367869	4.615321	0.494480
C	-1.667689	5.051491	0.112590
H	-1.727919	5.192021	-0.971050
H	-2.429189	4.336551	0.439090
H	-1.820469	6.004691	0.614640
H	-0.688580	0.780391	-1.967160
H	2.916030	1.575510	0.249740
H	1.434110	-0.463889	-2.263800
H	2.011990	-0.436580	1.351620

AI⁺ d

C	1.033060	0.776459	-0.991510
C	-0.250810	0.789930	-1.527720
C	-1.124789	1.806121	-1.161570
C	-0.698168	2.779900	-0.261020
C	0.589452	2.773729	0.263560
C	1.469061	1.760608	-0.111250
H	-2.126848	1.837742	-1.573020
N	1.941029	-0.319432	-1.320010
C	1.909538	-1.517932	-0.310490
C	0.469318	-1.955431	-0.161510
C	-0.271512	-1.609070	0.953460
C	-0.118753	-2.666470	-1.221580
C	-1.633972	-1.936509	1.042990
H	0.157888	-1.076790	1.794880
C	-1.455044	-3.002829	-1.153900
H	0.465197	-2.957291	-2.089370
C	-2.210123	-2.634648	-0.035700
H	-1.937114	-3.552268	-1.952910
N	-3.613374	-3.004687	-0.018870
O	-4.290623	-2.678936	0.960150
O	-4.070934	-3.616696	-0.962910
O	-2.273052	-1.551798	2.148470
H	-3.207752	-1.827907	2.090840
H	2.501927	-2.294813	-0.798310
N	2.542778	-1.179293	0.914660
N	3.923748	-1.305004	0.977770
C	4.790349	-0.512435	0.303960
O	4.400820	0.322935	-0.523220
C	6.246179	-0.709807	0.607010
H	6.426168	-1.503557	1.331320
H	6.765149	-0.936207	-0.326000
H	6.639990	0.232093	0.995110
H	4.261808	-1.980295	1.650890
H	1.765539	-0.663462	-2.268700
H	0.912773	3.551309	0.945360
H	-0.573150	0.020630	-2.222770
H	2.489151	1.757317	0.260230
Br	-1.881056	4.163372	0.222010
H	2.936960	0.023807	-1.256920
H	2.207589	-0.343153	1.385770

ts4 a

C	-2.152671	-1.556521	0.628631
C	-2.496511	-0.619240	1.603871
C	-3.834401	-0.265960	1.771711
C	-4.820071	-0.843330	0.973441
C	-4.468421	-1.803130	0.019451
C	-3.137921	-2.163830	-0.156629
H	-4.100971	0.474570	2.518781
N	-0.783761	-1.767031	0.326371
C	-0.256531	-0.249781	-1.019809
C	1.187179	-0.173421	-0.700199
C	1.640109	0.521669	0.412311
C	2.081809	-0.840851	-1.550879
C	3.008939	0.590949	0.703291
H	0.967669	1.012179	1.109891
C	3.435189	-0.783041	-1.281469
H	1.720439	-1.390101	-2.412569
C	3.895009	-0.073931	-0.169869
H	4.154909	-1.280291	-1.919589
N	5.328799	-0.052002	0.066991
O	5.746369	0.560928	1.052761
O	6.059959	-0.633442	-0.708129
O	3.360279	1.277269	1.790801
H	4.331269	1.249559	1.888571
H	-2.857291	-2.893130	-0.911299
H	-5.234241	-2.267160	-0.593419
H	-0.561641	-0.893981	-1.838709
N	-1.022441	0.794659	-0.789299
H	-0.782541	1.547789	-0.143669
N	-2.323681	0.896109	-1.237659
C	-3.097131	1.858960	-0.641839
O	-2.654090	2.492640	0.307581
C	-4.463420	2.050060	-1.233989
H	-4.482750	3.004360	-1.766359
H	-4.737851	1.246370	-1.918499
H	-5.184590	2.096260	-0.416729
H	-2.508981	0.554030	-2.173639
H	-0.592041	-2.661781	-0.121509
H	-0.168741	-1.657111	1.130811
H	-1.723161	-0.158031	2.212351
H	-5.858991	-0.556440	1.098531

ts4 b

C	-1.880291	-1.526880	0.546699
C	-2.243060	-0.579760	1.502519
C	-3.577890	-0.192120	1.612449
C	-4.561230	-0.734670	0.782429
C	-4.177301	-1.712960	-0.148291
C	-2.853791	-2.111920	-0.270441
H	-3.851190	0.562650	2.344679
N	-0.506341	-1.757230	0.281959
C	0.063010	-0.264760	-1.060881
C	1.500150	-0.187591	-0.710741
C	1.927320	0.502319	0.415389
C	2.415290	-0.848471	-1.544721
C	3.289240	0.572269	0.737189
H	1.239200	0.987839	1.101369
C	3.762140	-0.790201	-1.244601
H	2.075079	-1.393131	-2.417771
C	4.195950	-0.086591	-0.119081
H	4.496669	-1.282951	-1.869211
N	5.623730	-0.064442	0.150489
O	6.018010	0.542228	1.149729
O	6.373350	-0.639692	-0.611621
O	3.614960	1.253449	1.835929
H	4.583540	1.226189	1.955309
H	-2.567491	-2.850830	-1.013831
H	-4.929291	-2.159460	-0.793571
H	-0.224340	-0.911790	-1.884391
N	-0.700910	0.788000	-0.857151
H	-0.465800	1.549390	-0.219741
N	-1.993090	0.898680	-1.324321
C	-2.768160	1.875550	-0.763261

O	-2.320180	2.554380	0.153849
C	-4.141450	2.031990	-1.350131
H	-4.161450	2.936190	-1.963931
H	-4.434630	1.174220	-1.957801
H	-4.848970	2.157420	-0.528741
H	-2.207780	0.451380	-2.207161
H	-0.314381	-2.658640	-0.152351
H	0.089299	-1.647860	1.100989
H	-1.486190	-0.128740	2.138979
C	-6.001870	-0.305149	0.888969
H	-6.420190	-0.090599	-0.099091
H	-6.611840	-1.095499	1.337989
H	-6.101410	0.589911	1.507319

ts4 c

C	-1.602840	1.469470	-0.726100
C	-1.962730	0.336000	-1.448280
C	-3.291850	-0.090300	-1.478910
C	-4.259550	0.619850	-0.766920
C	-3.899020	1.780390	-0.062450
C	-2.582830	2.203970	-0.043820
H	-3.544970	-0.981820	-2.039140
N	-0.231070	1.767730	-0.531030
C	0.382690	0.564000	1.081710
C	1.794800	0.364060	0.686630
C	2.156040	-0.614420	-0.229360
C	2.759410	1.209010	1.258530
C	3.497230	-0.795570	-0.591750
H	1.431050	-1.259820	-0.716260
C	4.086750	1.045100	0.915100
H	2.470370	1.976080	1.967620
C	4.453860	0.053150	0.002930
H	4.857790	1.673540	1.342900
N	5.864630	-0.073290	-0.321000
O	6.201210	-0.944920	-1.126680
O	6.657540	0.677510	0.209490
O	3.757190	-1.757470	-1.477720
H	4.717940	-1.786600	-1.648270
H	-2.305770	3.091620	0.517960
H	-4.669850	2.330400	0.467110
H	0.158570	1.382620	1.758830
N	-0.424040	-0.474200	1.131700
H	-0.243900	-1.362060	0.661900
N	-1.692770	-0.437940	1.667020
C	-2.515700	-1.490810	1.381670
O	-2.122490	-2.387260	0.643300
C	-3.872830	-1.444370	2.023020
H	-3.957650	-2.276890	2.725130
H	-4.059050	-0.504480	2.544490
H	-4.625140	-1.576230	1.242590
H	-1.873420	0.235030	2.401340
H	-0.051870	2.740890	-0.290230
H	0.357670	1.507210	-1.320210
H	-1.205790	-0.233950	-1.980490
O	-5.569770	0.269530	-0.698530
C	-5.994090	-0.855350	-1.456930
H	-5.808950	-0.697350	-2.524360
H	-5.486020	-1.768450	-1.127670
H	-7.063700	-0.950000	-1.279320

ts4 d

C	1.092180	-1.468569	-0.456559
C	1.505750	-0.503499	-1.372569
C	2.840440	-0.109399	-1.399529
C	3.731960	-0.675969	-0.496719
C	3.335430	-1.680979	0.385471
C	2.007440	-2.082019	0.403171
H	3.169639	0.656721	-2.092329
N	-0.298440	-1.689460	-0.271629
C	-0.915960	-0.315920	1.062561
C	-2.351290	-0.229780	0.689581
C	-2.750140	0.474319	-0.437909
C	-3.286930	-0.889571	1.500141
C	-4.104940	0.558409	-0.786109
H	-2.044111	0.963710	-1.102919
C	-4.627430	-0.817111	1.174131
H	-2.968740	-1.444211	2.375171
C	-5.033170	-0.100421	0.046671
H	-5.378220	-1.309081	1.779801
N	-6.455590	-0.063972	-0.250329
O	-6.825340	0.555878	-1.250679
O	-7.224210	-0.640742	0.491251
O	-4.403371	1.252519	-1.884369
H	-5.369771	1.236089	-2.022119
H	1.677641	-2.841279	1.106161
H	4.053130	-2.134038	1.059931
H	-0.651870	-0.974850	1.885841
N	-0.178901	0.779670	0.952391
H	-0.411871	1.557190	0.335741
N	1.101259	0.876231	1.469871
C	1.897999	1.860061	0.935951
O	1.504419	2.511511	-0.022539
C	3.231269	2.039911	1.604911
H	3.159029	2.860181	2.324711
H	3.557549	1.135361	2.122131
H	3.962299	2.311102	0.842361
H	1.211630	0.584611	2.435541
H	-0.520739	-2.607660	0.112331
H	-0.846030	-1.549720	-1.120149
H	0.788470	-0.036189	-2.041219
Br	5.531030	-0.100438	-0.488329

3^+ (*Z*)

C	-1.413650	-1.175600	-0.231411
C	-0.008610	-0.789370	-0.158551
C	0.402670	0.536290	-0.253081
C	0.922940	-1.829740	0.008259
C	1.759430	0.868390	-0.157001
H	-0.283120	1.357890	-0.431961
C	2.264540	-1.518920	0.107099
H	0.595330	-2.860970	0.069049
C	2.676360	-0.187950	0.027799
H	3.010360	-2.291850	0.243069
N	4.106150	0.077550	0.130139
O	4.485340	1.247510	0.055279
O	4.862820	-0.857510	0.284729
O	2.070150	2.159890	-0.258771
H	3.037290	2.267650	-0.182851
H	-1.673500	-2.213840	-0.423591
N	-2.379190	-0.344580	-0.061371
H	-2.241500	0.648360	0.174139
N	-3.701460	-0.626840	-0.138061
C	-4.572680	0.421190	0.132099
O	-4.106130	1.507650	0.420939
C	-6.027370	0.079400	0.064649
H	-6.219280	-0.805300	-0.542541
H	-6.381500	-0.103860	1.082759
H	-6.563640	0.936960	-0.340601
H	-3.978190	-1.560440	-0.419021

3^+ (*E*)

C	2.305498	1.068056	-0.050539
C	0.951605	1.435238	0.011282

C	-0.042991	0.472938	0.131022
C	0.277295	-0.897004	0.216247
C	1.600603	-1.272942	0.159472
C	2.602599	-0.304666	0.023839
H	0.715630	2.492503	-0.046061
H	-0.479511	-1.660573	0.352114
H	1.887689	-2.314667	0.226937
N	3.981361	-0.770409	-0.026208
O	4.197369	-1.962572	0.034597
O	4.873998	0.072984	-0.129434
O	3.189454	2.056102	-0.172588
H	4.091002	1.682740	-0.198382
C	-1.412730	0.970947	0.164574
H	-1.592032	2.034646	0.296553
N	-2.441500	0.211795	0.033323
N	-3.735757	0.611046	0.068199
C	-4.691039	-0.382579	-0.116988
H	-2.385758	-0.801553	-0.140652
H	-3.934260	1.567257	0.341180
O	-4.314274	-1.514473	-0.357318
C	-6.111162	0.064647	0.028771
H	-6.372059	0.052265	1.090981
H	-6.259647	1.074716	-0.355586
H	-6.750217	-0.638505	-0.502432

4. DCL – ACYLHYDRAZONES CHARACTERIZATION

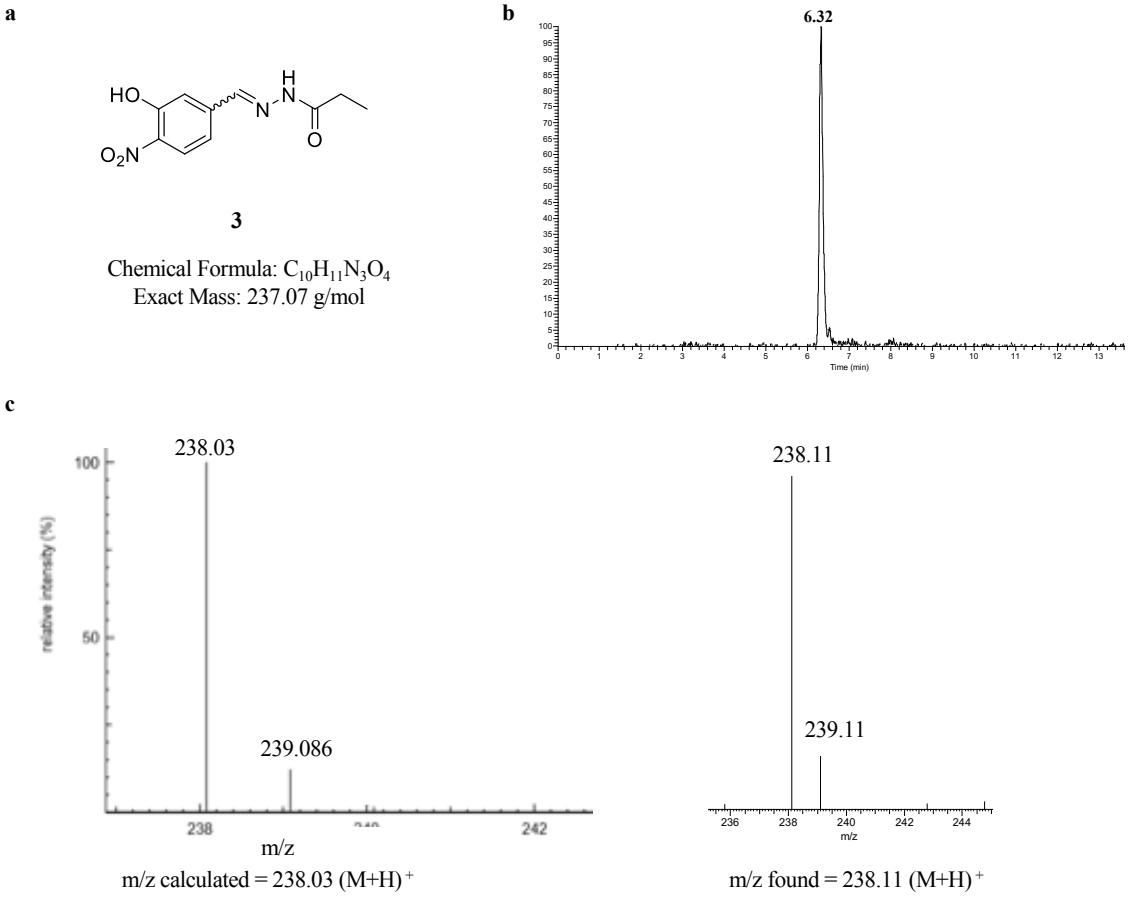


Figure S14. HPLC and MS of acylhydrazone **3**.

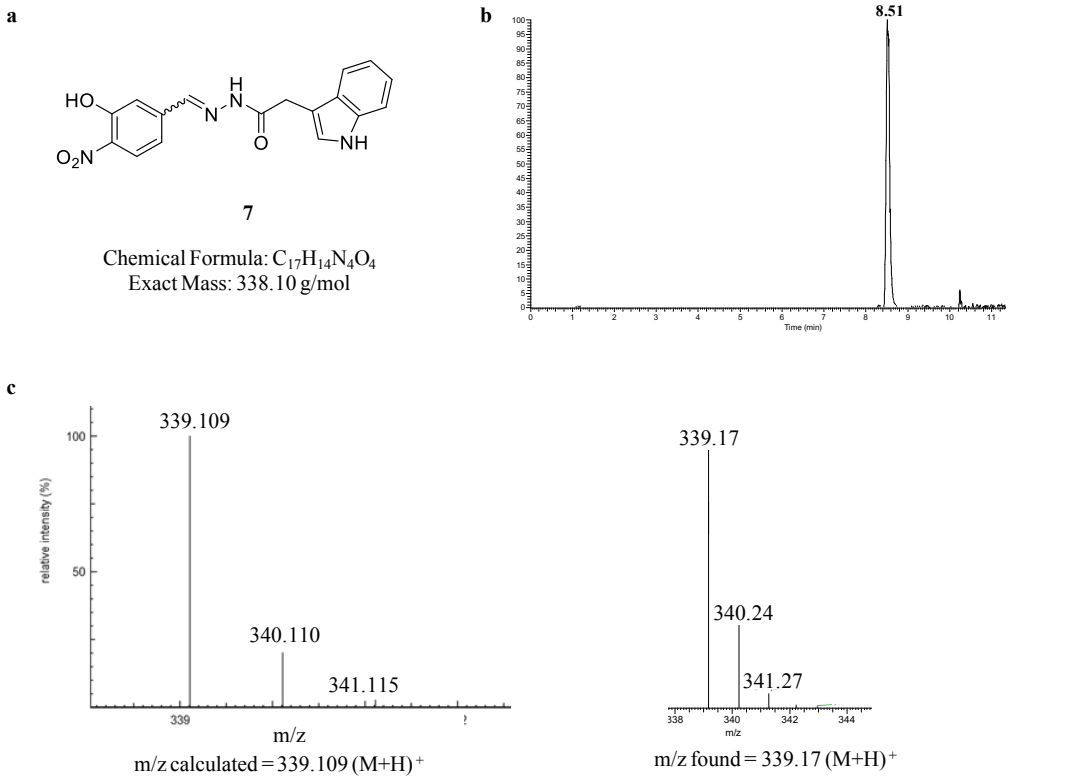


Figure S15. HPLC and MS of acylhydrazone **7**.

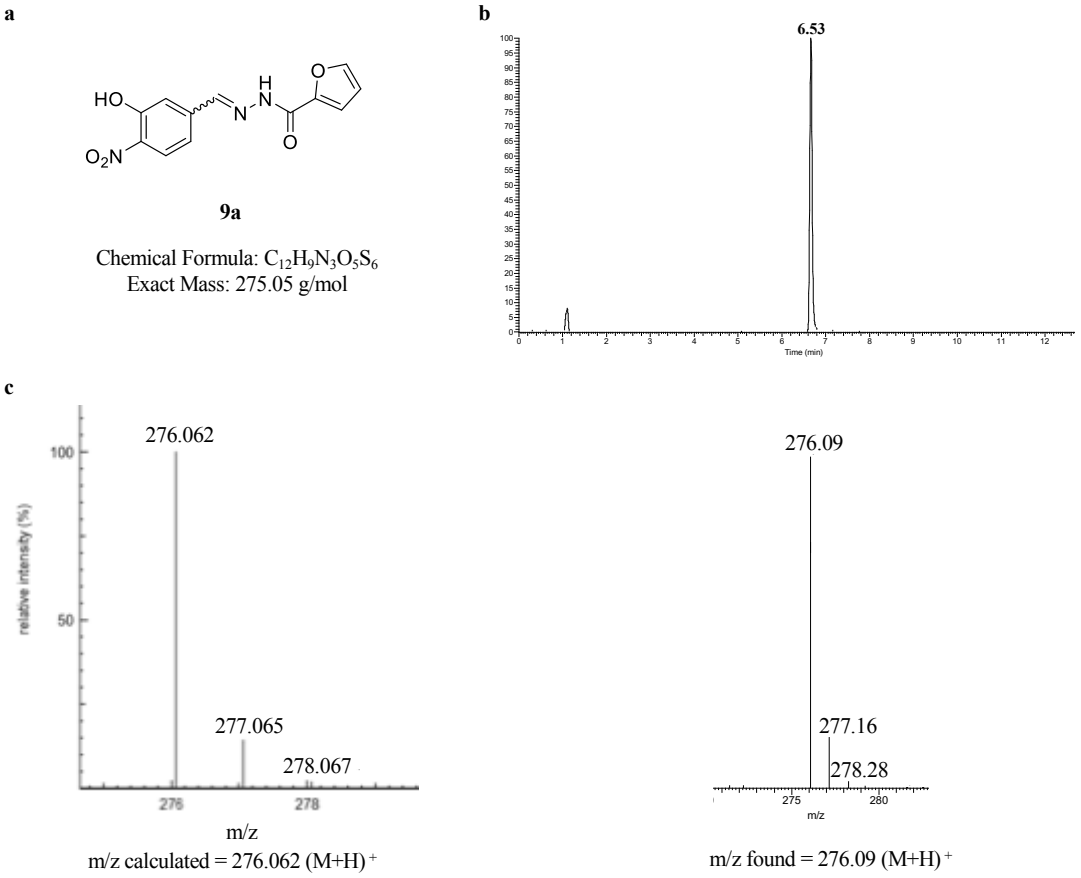


Figure S16. HPLC and MS of acylhydrazone **9a**.

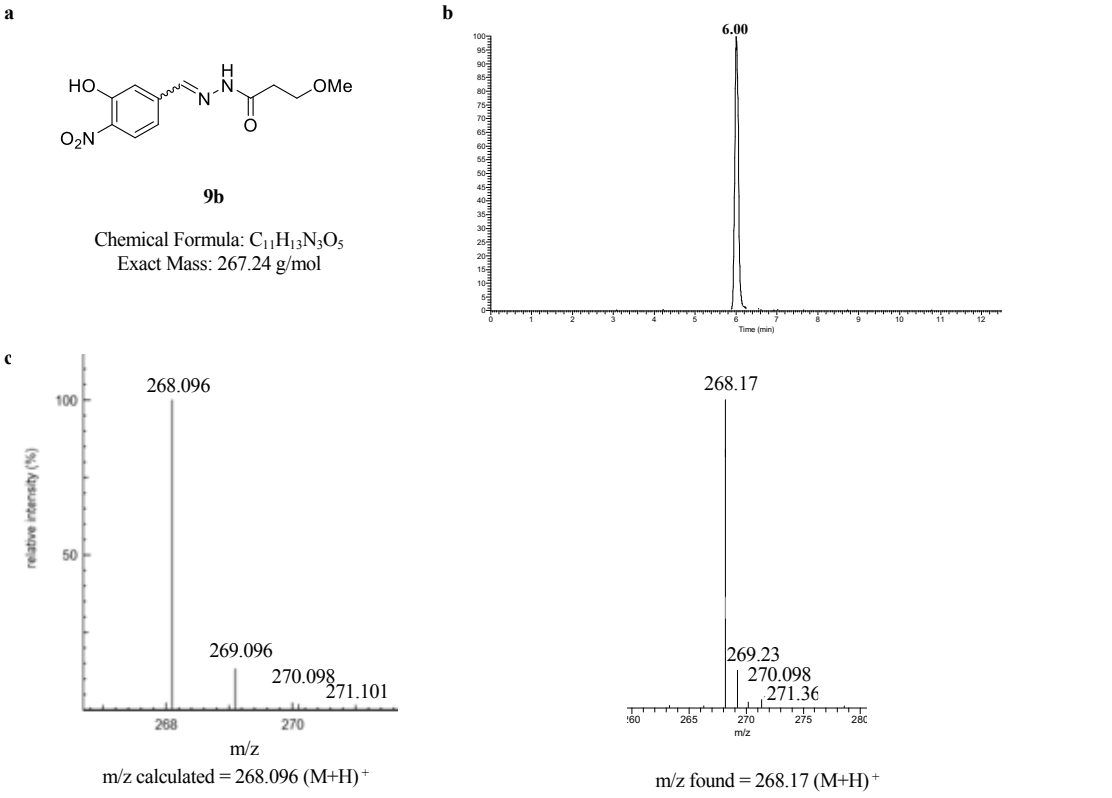


Figure S17. HPLC and MS of acylhydrazone **9b**.

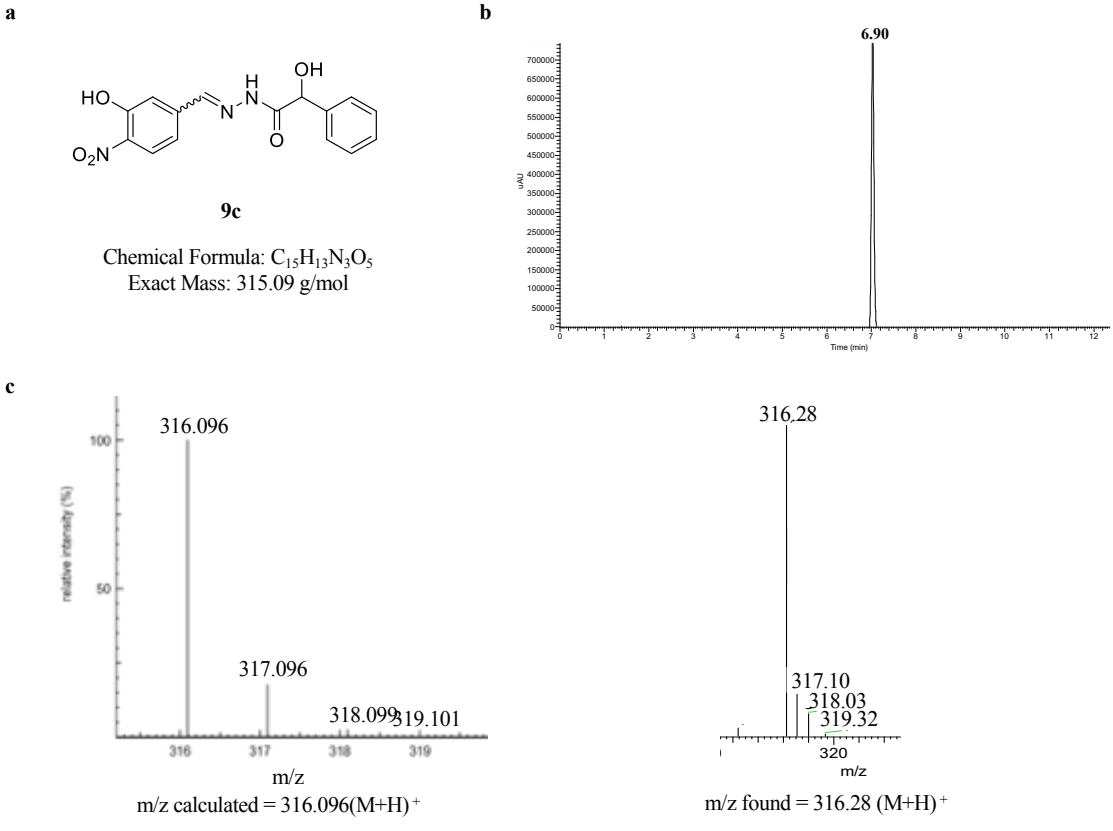
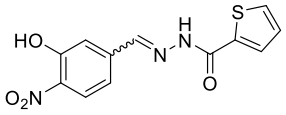


Figure S18. HPLC and MS of acylhydrazone **9c**.

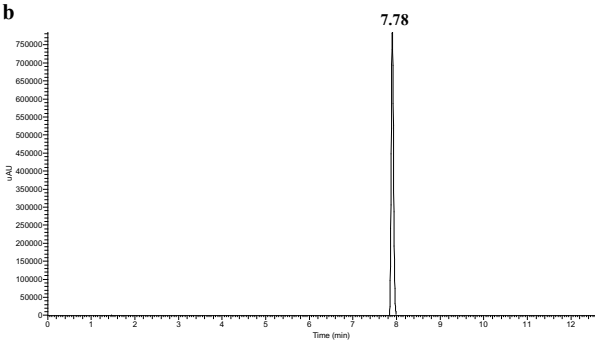
a



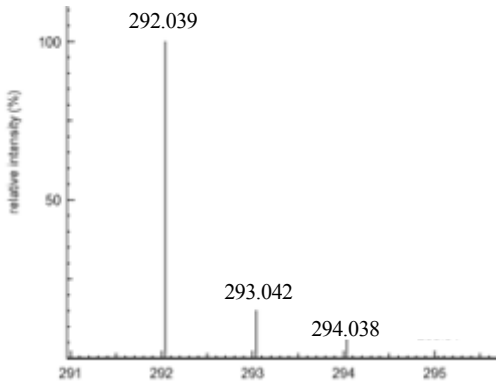
9d

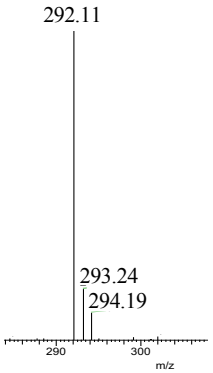
Chemical Formula: $C_{12}H_9N_3O_4S$
Exact Mass: 291.03 g/mol

b



c





m/z calculated = 292.039 $(M+H)^+$

m/z found = 292.11 $(M+H)^+$

Figure S19. HPLC and MS of acylhydrazone **9d**.

5. NMR SPECTRA OF SYNTHESIZED COMPOUNDS.

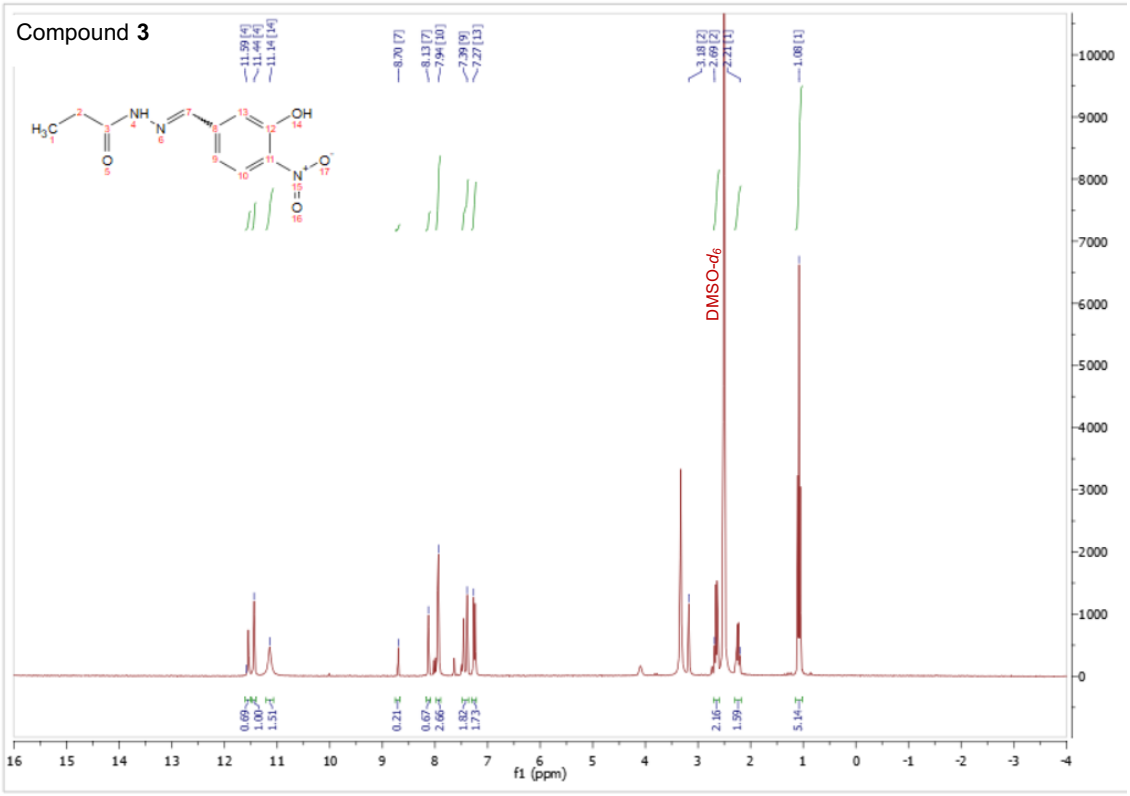


Figure S20. ^{1}H-NMR of acylhydrazone**3** (DMSO-d_6, 300 MHz).The characterization of both isomers (*E/Z*) is given.

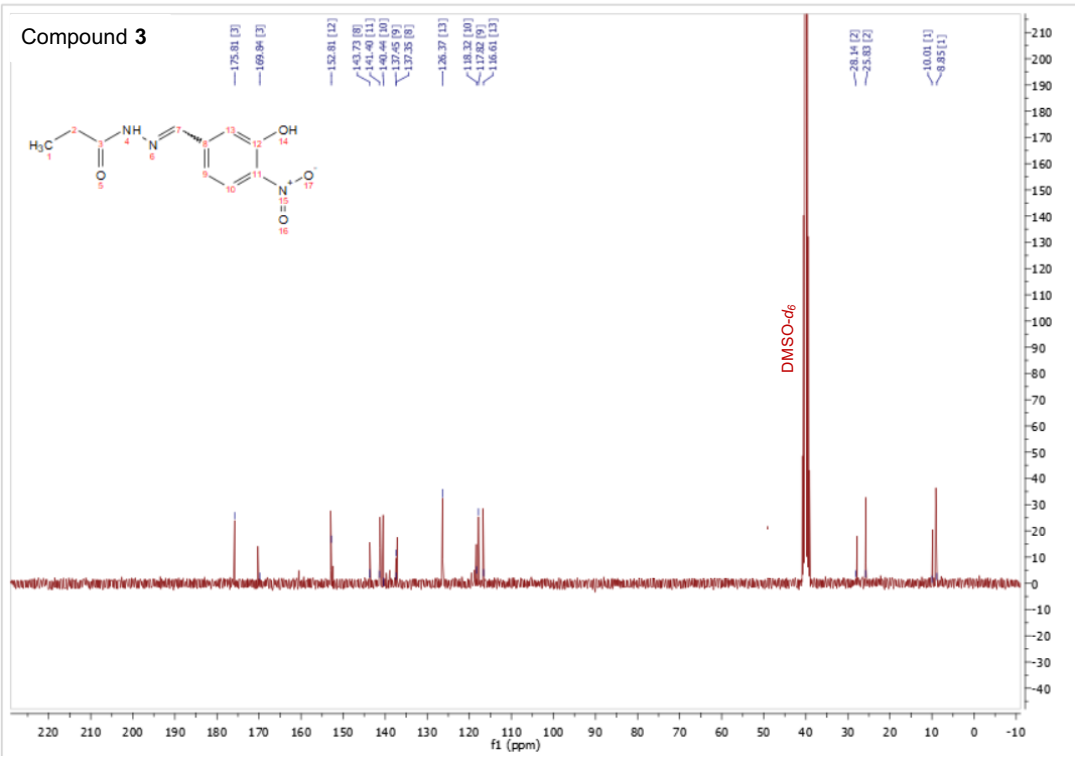


Figure S21. ^{13}C-NMR {1H} of acylhydrazone **3** (DMSO-d_6, 75 MHz). The characterization of both isomers (*E/Z*) is given.

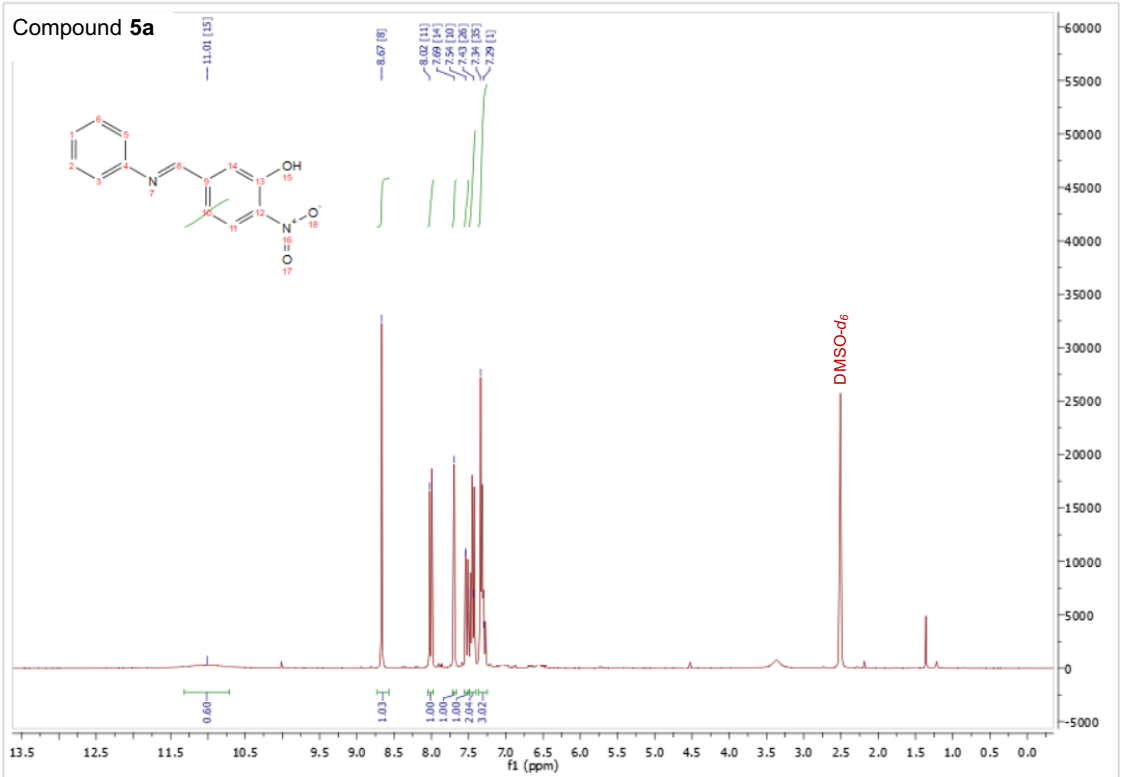


Figure S22. ^{1}H-NMR of compound **5a** (DMSO-*d*$_6$, 300 MHz).

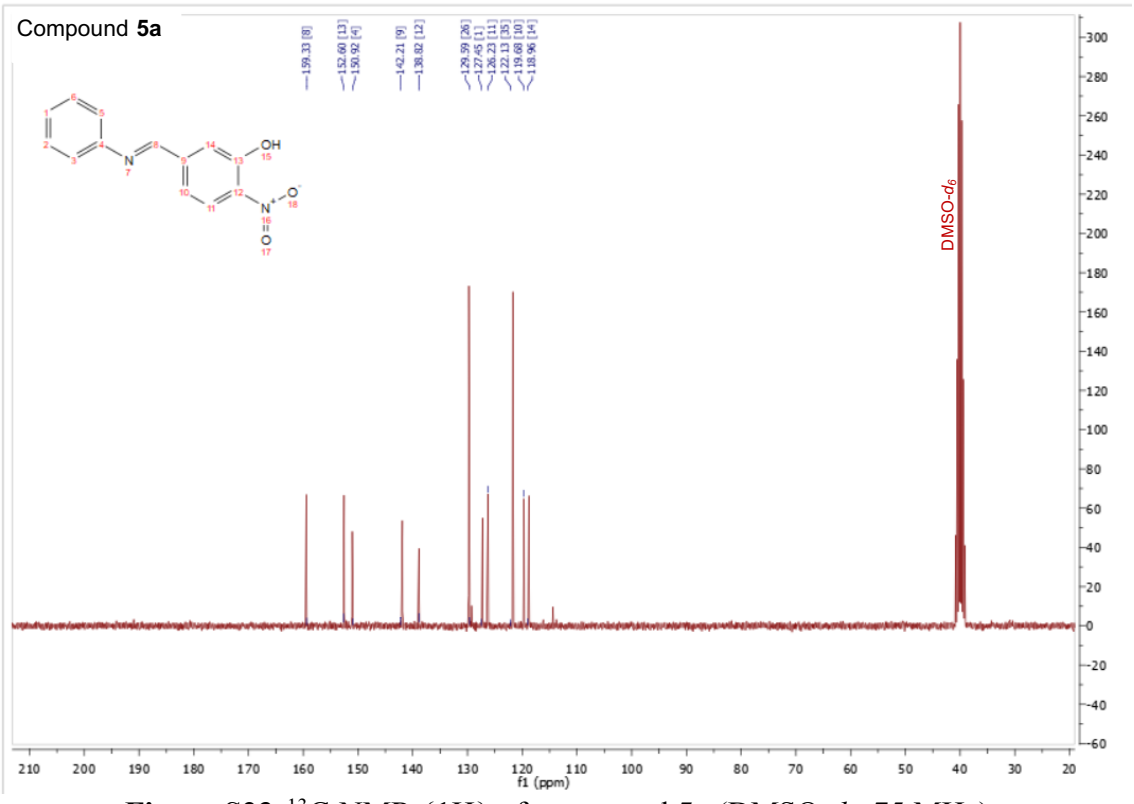


Figure S23. ^{13}C-NMR {1H} of compound **5a** (DMSO-*d*$_6$, 75 MHz).

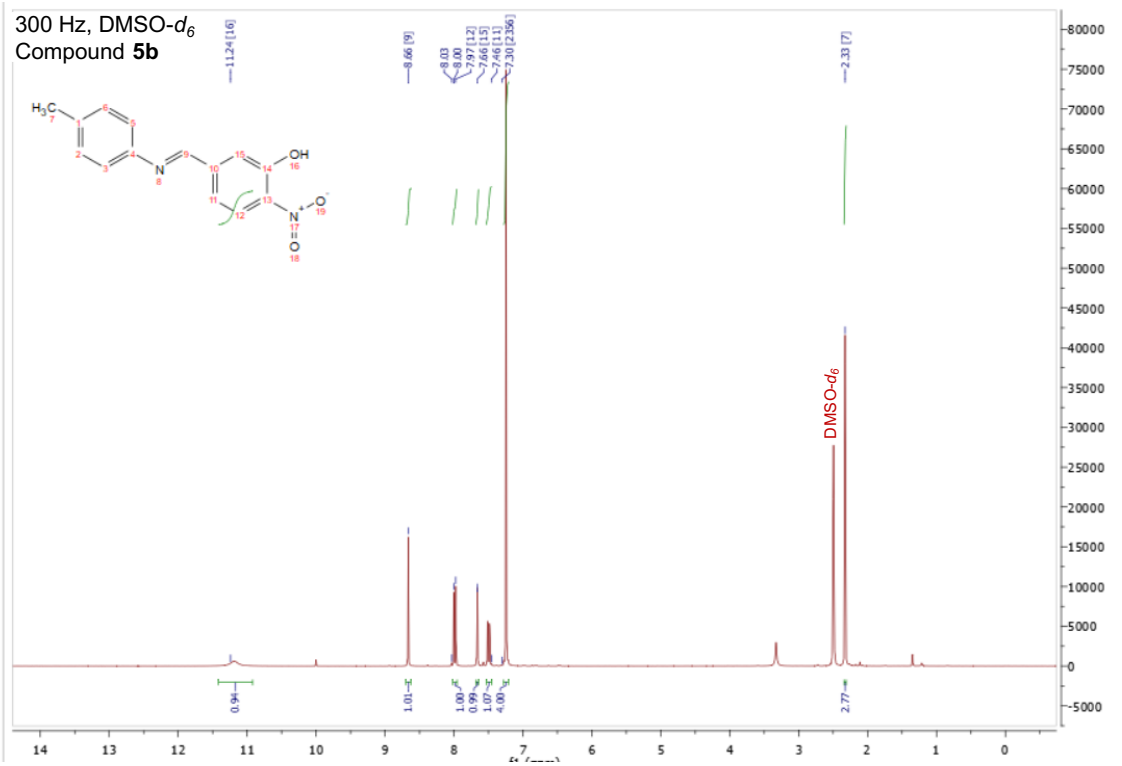


Figure S24. ^{1}H-NMR of compound **5b** (DMSO-d_6, 300 MHz).

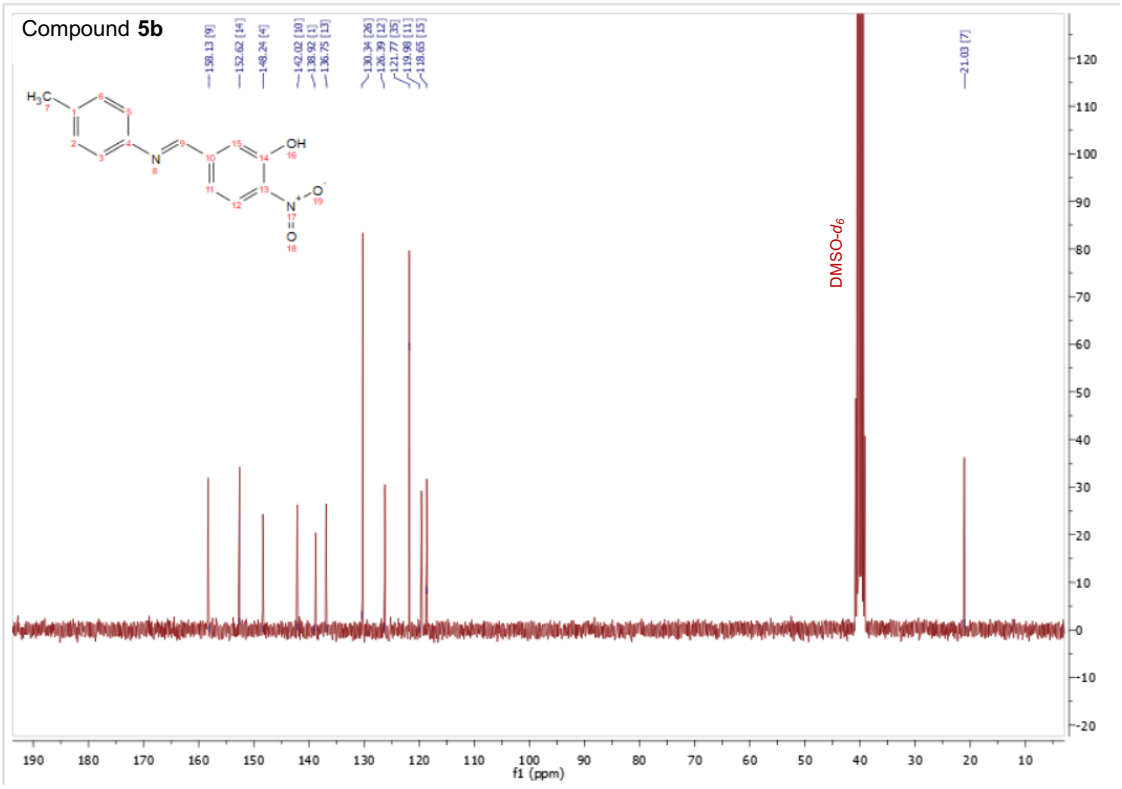


Figure S25. ^{13}C-NMR {1H} of compound **5b** (DMSO-d_6, 75 MHz).

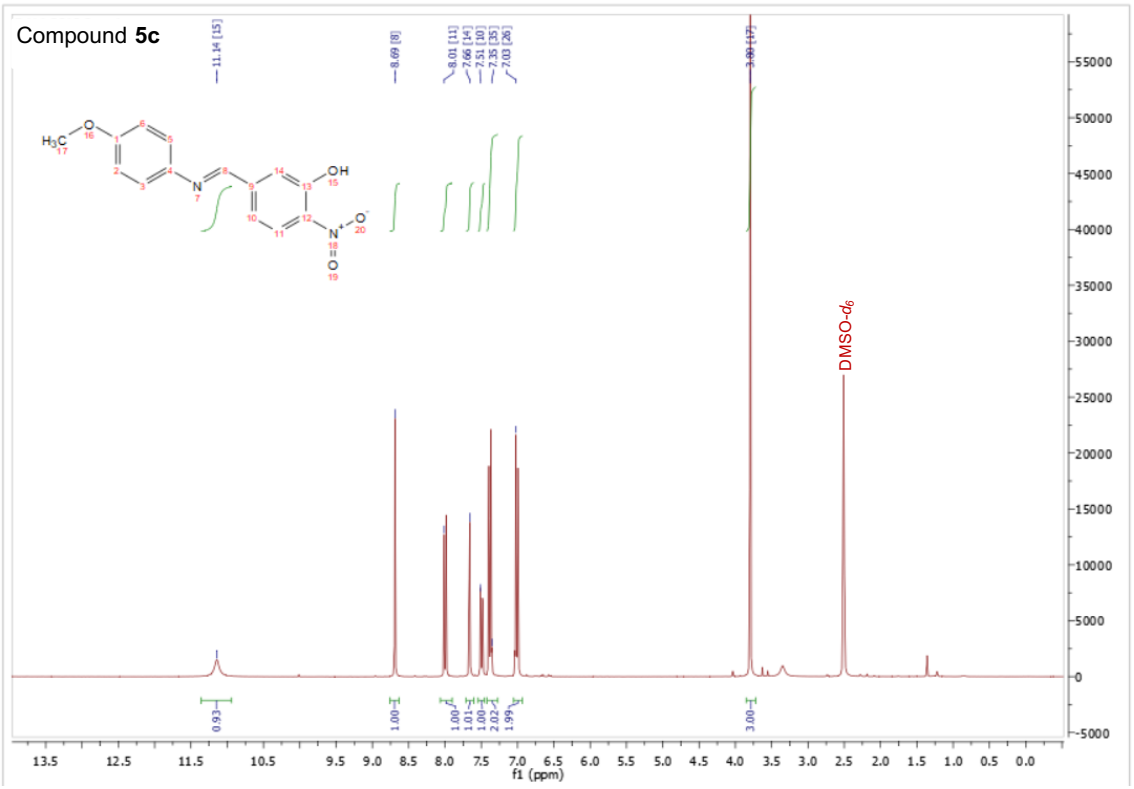


Figure S26. ^{1}H-NMR of compound **5c** (DMSO-*d*$_6$, 300 MHz).

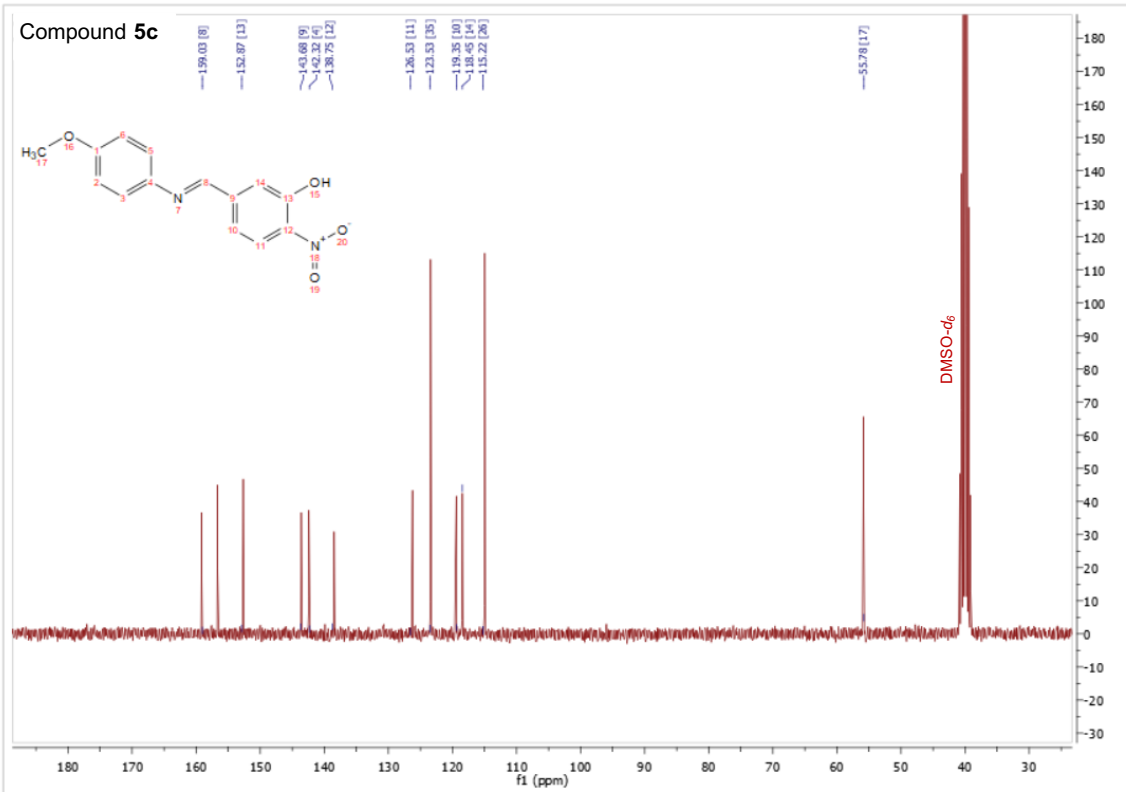


Figure S27. ^{13}C-NMR {1H} of compound **5c** (DMSO-*d*$_6$, 75 MHz).

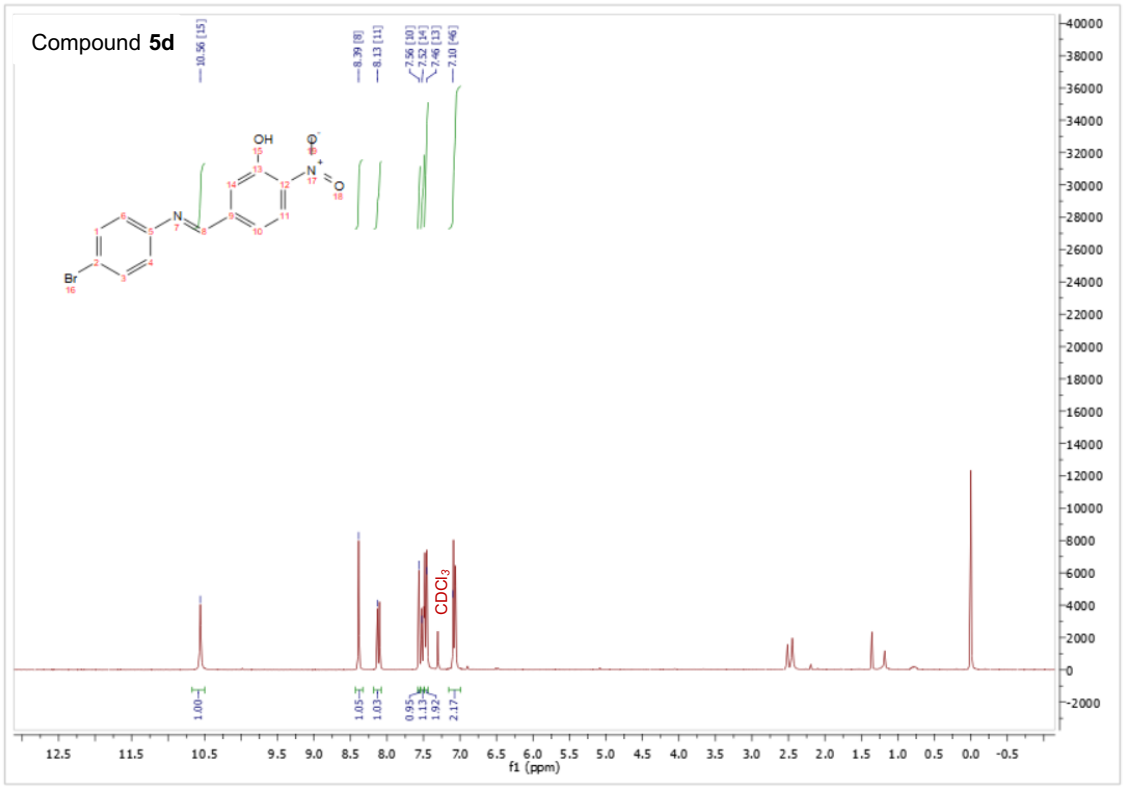


Figure S28. ^{1}H-NMR of compound **5d** ($CDCl_3$, 300 MHz).

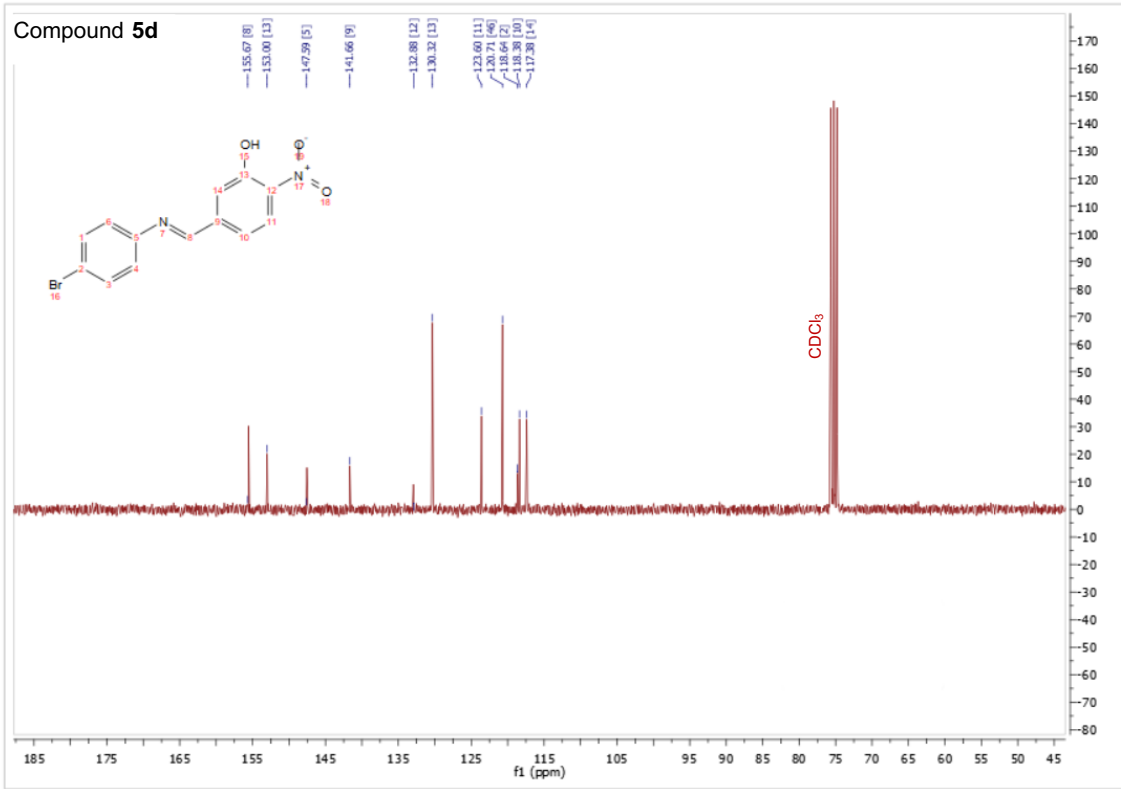


Figure S29. ^{13}C-NMR {1H} of compound **5d** ($CDCl_3$, 75 MHz).

6. KINETIC STUDY FOLLOWED BY HPLC

Table S4. Average value of the acylhydrazone 7 concentration during the time course (from 0.3 min to 360 min) of the reaction in the different conditions studied: uncatalysed and in presence of the amines **4a-4d** as catalysts. SD is the standard deviation of the three independent experiments.

	uncatalyzed: [7b] (μM)		4a: [7b] (μM)		4b: [7b] (μM)		4c: [7b] (μM)		4d: [7b] (μM)	
Time (min)	**Average**	**SD**	**Average**	**SD**	**Average**	**SD**	**Average**	**SD**	**Average**	**SD**
0,83	1,458	0,055	22,929	0,252	18,690	0,776	12,454	0,669	13,243	0,354
30	1,825	0,574	34,558	0,368	36,722	0,143	34,181	0,849	17,856	0,617
60	1,849	0,193	43,547	0,462	48,831	0,701	52,014	0,409	21,525	0,757
90	2,601	0,010	49,946	0,749	55,447	1,131	65,775	1,029	24,759	0,575
120	2,393	0,333	56,788	0,144	63,383	0,917	75,979	0,407	26,894	0,347
150	2,547	0,216	62,995	0,175	71,495	2,060	83,308	0,266	28,161	0,839
180	2,954	0,272	66,480	0,838	78,002	0,061	86,584	0,049	31,468	0,182
210	3,501	0,258	69,418	0,103	81,063	0,575	89,422	0,001	33,624	1,622
240	3,724	0,098	74,704	0,605	85,163	0,050	89,427	0,005	34,843	0,965
270	3,665	0,391	79,613	0,037	89,376	0,000	89,431	0,000	36,950	0,713
300	4,135	0,283	82,555	0,008	89,368	0,000	89,417	0,005	39,774	2,596
330	4,429	0,315	87,083	0,077	89,360	0,001	89,420	0,010	39,990	0,931
360	5,565	0,213	89,421	0,006	89,356	0,001	89,409	0,000	41,425	0,115

7. REVERSIBILITY STUDY OF DCL IN PRESENCE OF CATALYST.

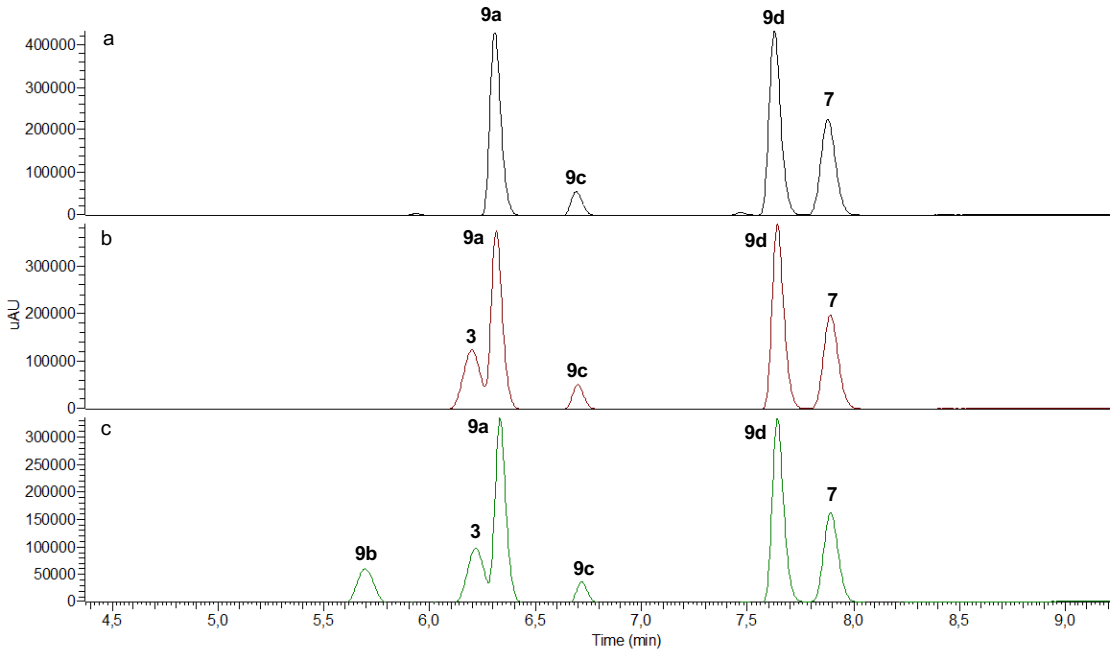


Figure S30. Chromatograms of the reversibility studies. The DCL was performed by the step-by-step addition of acylhydrazones in presence of catalyst **4c**. Firstly, a DCL made of aldehyde **1** and four acylhydrazides (**6**, **8a**, **8c**, **8d**) was set up (a). After equilibration, acylhydrazide **2** was added affording the DCL of five acylhydrazones (**3**, **7**, **9a**, **9c**, **9d**) (b), and then, acylhydrazide **8b**, affording the same result as in Fig. 6 (c).

8. DCLs CHROMATOGRAMS RELATIVE PEAK AREAS 4b AND 4c.

	4b		4c	
DCL Compounds	**RPA (%)**	**SD (%)**	**RPA (%)**	**SD (%)**
9b	8,543	0,264	8,851	0,190
3	11,979	0,180	12,243	0,392
9a	26,710	0,898	26,615	0,623
9c	3,658	0,183	3,474	0,067
9d	32,621	1,317	32,807	0,284
7	16,489	0,207	16,011	0,439

Table S5.Relative Peak Area (RPA) of the DCLs in presence of the catalysts **4b** and **4c**. Mean $\pm$ SD.