Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Enhancing Catalytic Activity of Pyridines via *Para*-Iminophosphorano Substituents

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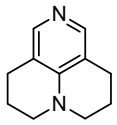
1. Experimental Details

Compounds **11a**,[1] **11b**,[1] **11c**,[2] **11d**,[2] and **12**[3] were prepared according to reported procedures. Triethylamine, dioxane, and d-chloroform were dried over calcium hydride and stored over 4A sieves in the glovebox prior to use. Acetic anhydride was distilled from magnesium turnings and stored in the glovebox prior to use. Melting points were measured on a Stanford Research Systems MPA160 melting point apparatus. ^{1}H and ^{31}P NMR spectra were recorded on an Agilent 400 MR NMR spectrometer or a Varian UNITY INOVA 300 spectrometers in $CDCl_3$. Chemical shifts were referenced internally to residual $CHCl_3$ (7.26 ppm for ^{1}H), or externally to H_3PO_4 (0.0 ppm for ^{31}P). 9-azajulolidine (**3**) was purchased from Aldrich and used as received.

2. Kinetic Measurements and Data

Samples were prepared using the amounts and concentrations described by Zipse,[4] and sealed in J. Young NMR tubes. Manipulations were carried out in an Innovative Technology glovebox under an argon atmosphere. NMR measurements were conducted on a Varian UNITY 400 MHz spectrometer or a Varian UNITY INOVA 300 MHz spectrometer. Single FIDs were collected at defined intervals (2-5 mins) until complete conversion was reached. The data array was processed using MNOVA 8.0. Conversions were determined, the data fitted, and kinetic half-lives calculated, according to the equations described by Zipse.[4–6] Every experiment was conducted at least twice and the kinetic half-lives are given with standard deviations.

10 mol % catalyst loading (Note all graphs are presented with time as the X-axis (in minutes), and % conversion on the Y axis):



$t_{1/2}$ = 12.3 ± 0.0 min

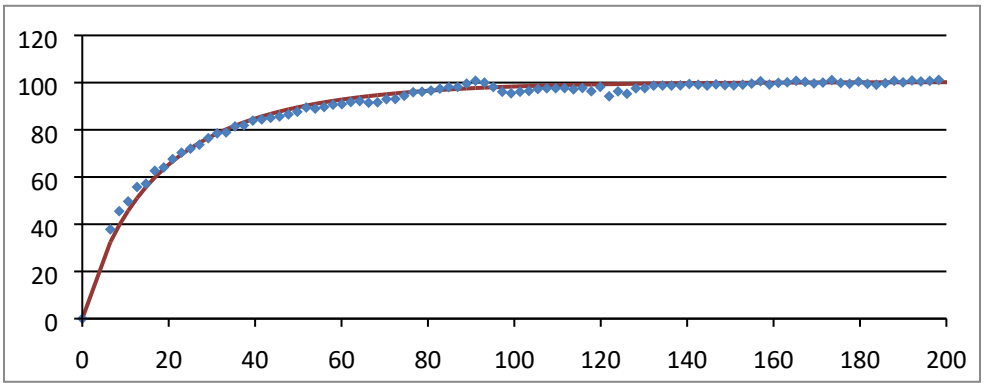
3

Run 1:

$t_{1/2}$ = 12.3 min

k = 2.75 x 10^{-3} L $mol^{-1}s^{-1}$

c = 1.00

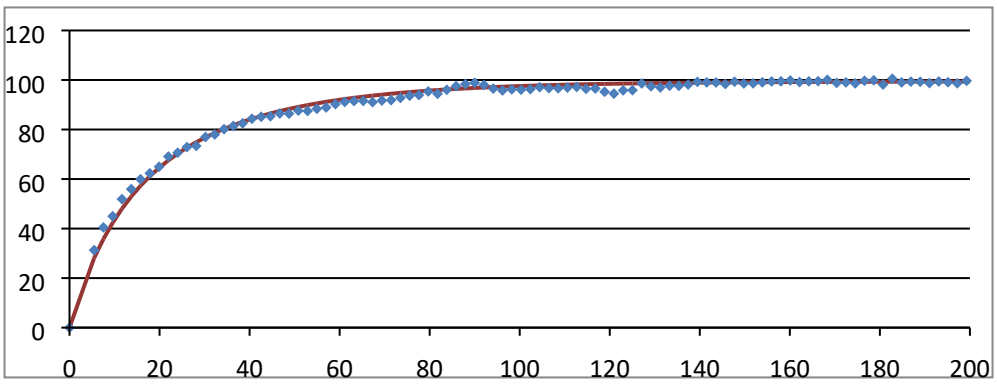


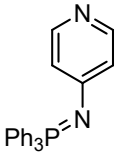
Run 2 :

$t_{1/2}$ = 12.3 min

k = 2.74 x 10^{-3} L $mol^{-1}s^{-1}$

c = 0.99





11a

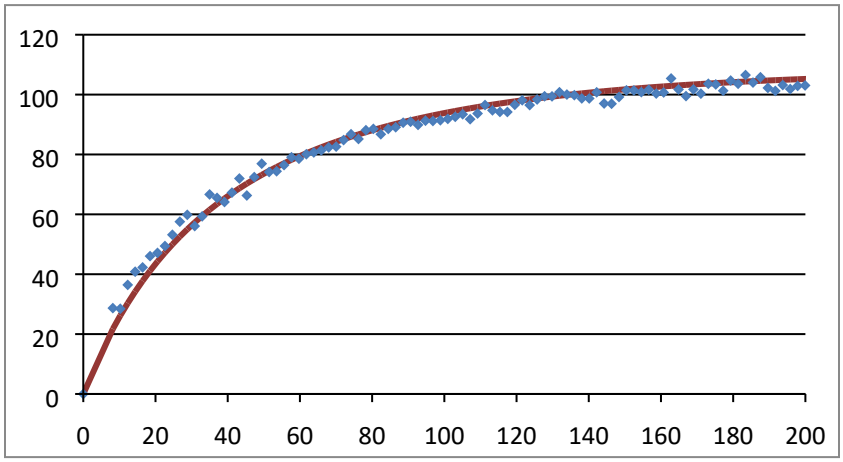
$t_{1/2}$ = 27.6 ± 0.5 min

Run 1:

$t_{1/2}$ = 28.1 min

k = 1.20 x 10^{-3} L

c = 1.08



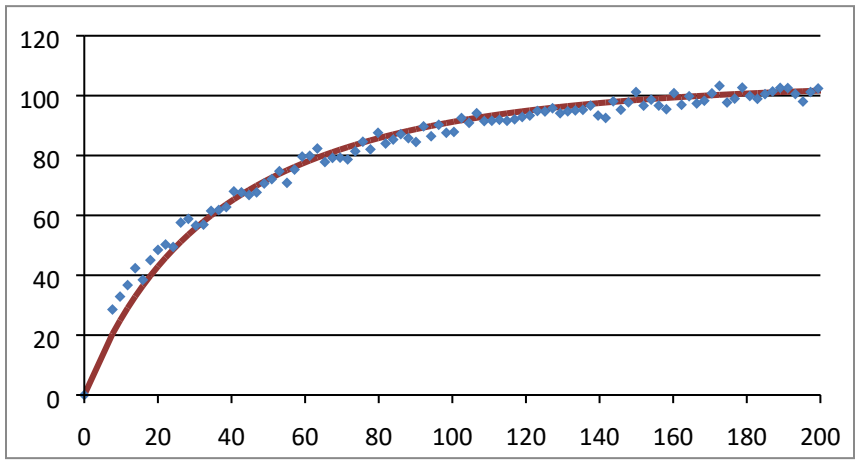
$mol^{-1}s^{-1}$

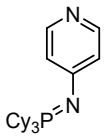
Run 2 :

$t_{1/2}$ = 27.1 min

k = 1.25 x 10^{-3} L $mol^{-1}s^{-1}$

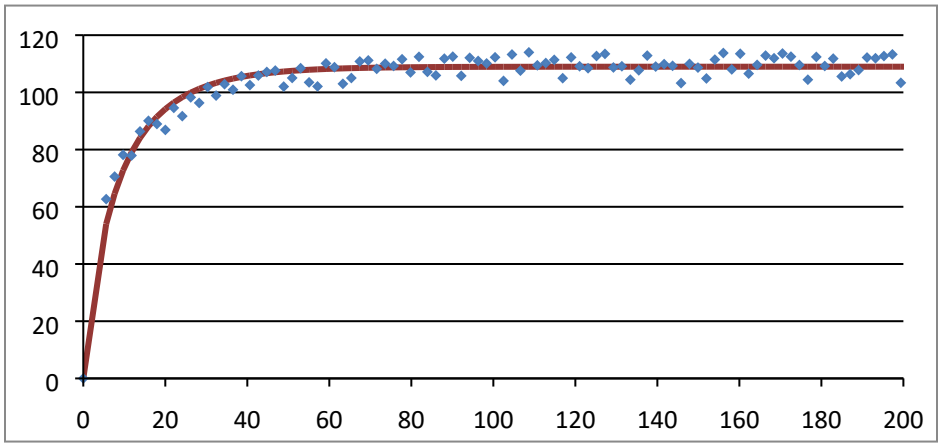
c = 1.04





11b

$t_{1/2}$ = 5.7 ± 0.1 min



Run 1:

$t_{1/2}$ = 5.7 min

k = 5.96 x 10^{-3} L $mol^{-1}s^{-1}$

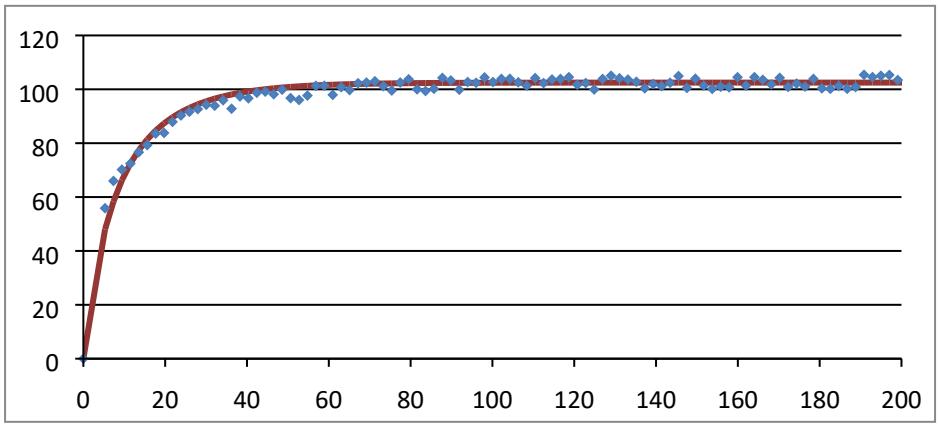
c = 1.09

Run 2:

$t_{1/2}$ = 5.9 min

k = 5.74 x 10^{-3} L $mol^{-1}s^{-1}$

c = 1.02

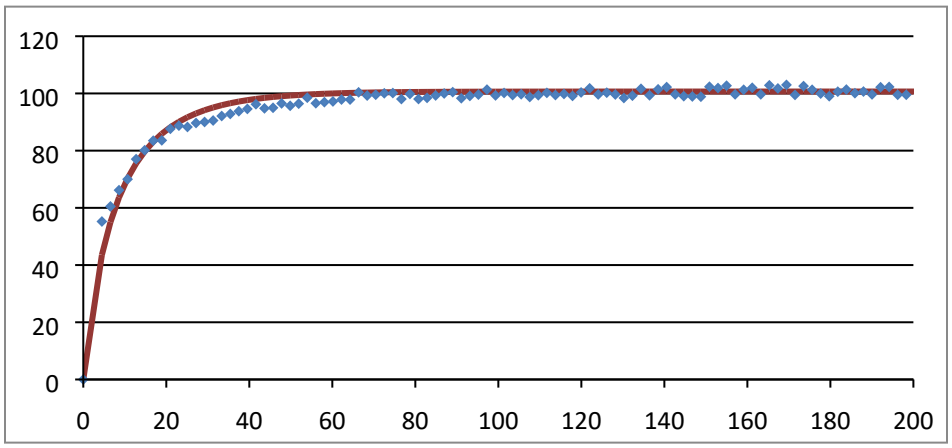


Run 3:

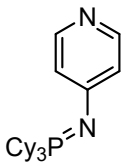
$t_{1/2}$ = 5.6 min

k = 6.00 x 10^{-3} L $mol^{-1}s^{-1}$

c = 1.01



<u>3 mol %</u> catalyst loading



11b

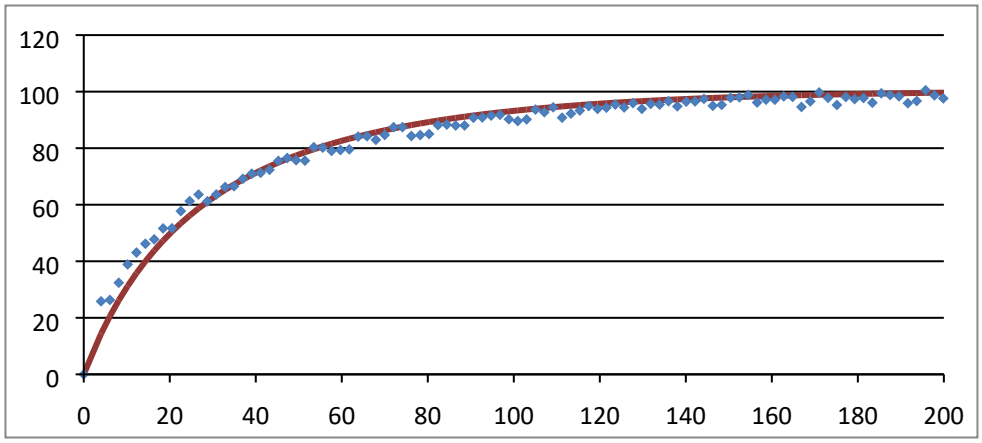
$t_{1/2}$ = 21.8 ± 1.4 min

Run 1:

$t_{1/2}$ = 20.4 min

k = 1.66 x 10^{-3} L $mol^{-1}s^{-1}$

c = 1.01

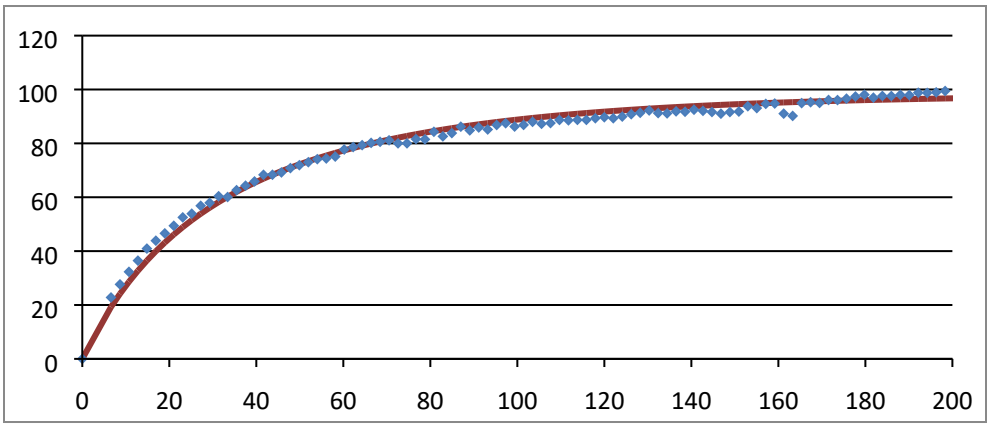


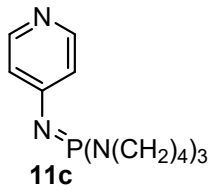
Run 2:

$t_{1/2}$ = 23.3 min

k = 1.45 x 10^{-3} L $mol^{-1}s^{-1}$

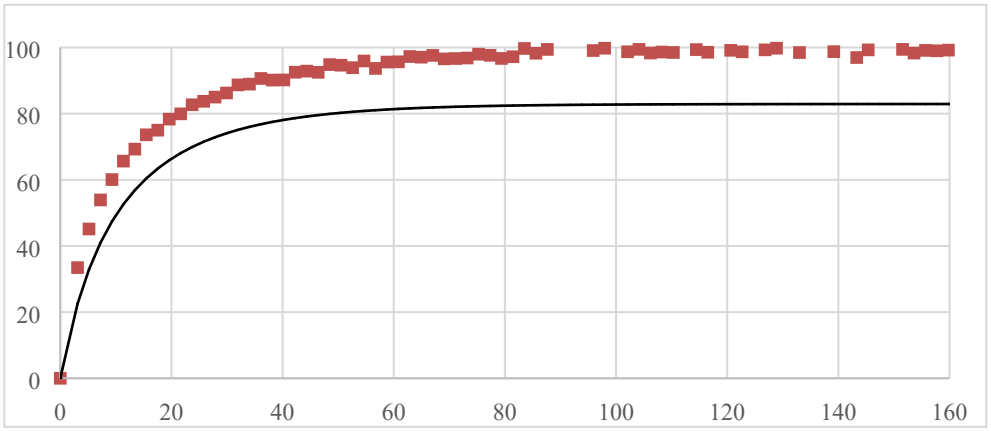
c = 0.98





11c

$t_{1/2}$ = 7.6 ± 0.3 min

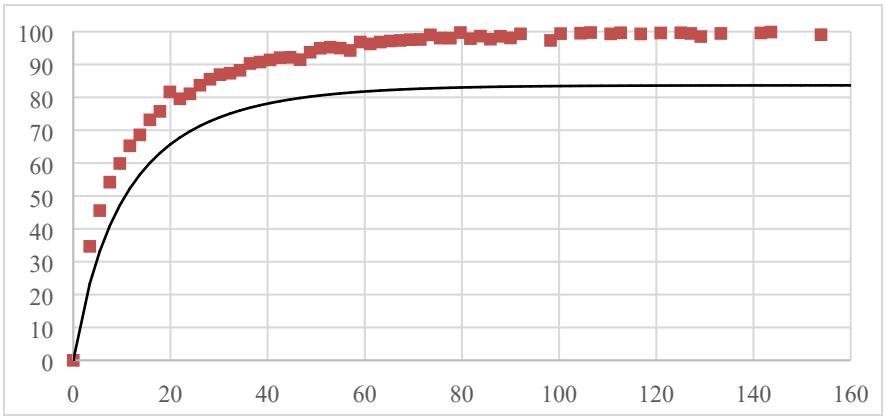


Run 1:

$t_{1/2}$ = 7.4 min

k = 4.58 x 10^{-3} L $mol^{-1}s^{-1}$

c = 1.00

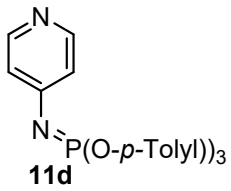


Run 2:

$t_{1/2}$ = 7.8 min

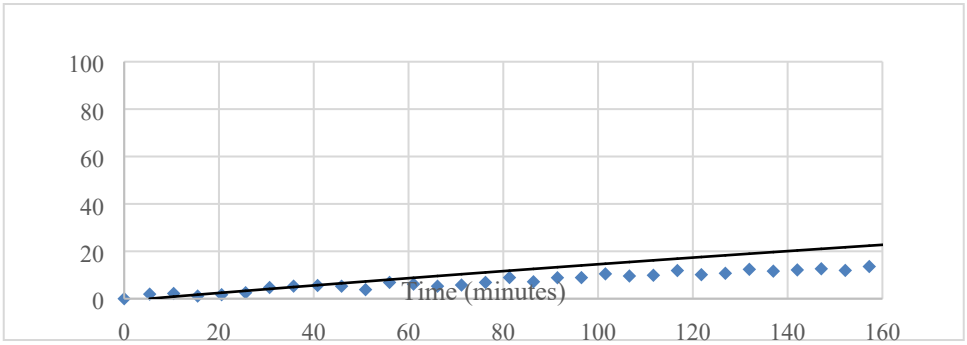
k = 4.34 x 10^{-3} L $mol^{-1}s^{-1}$

c = 1.00



11d

$t_{1/2}$ = 798.9 ± 10.2 min



Run 1:

$t_{1/2}$ = 792 min (extrapolated)

k = 4.27 x 10^{-5} L $mol^{-1}s^{-1}$

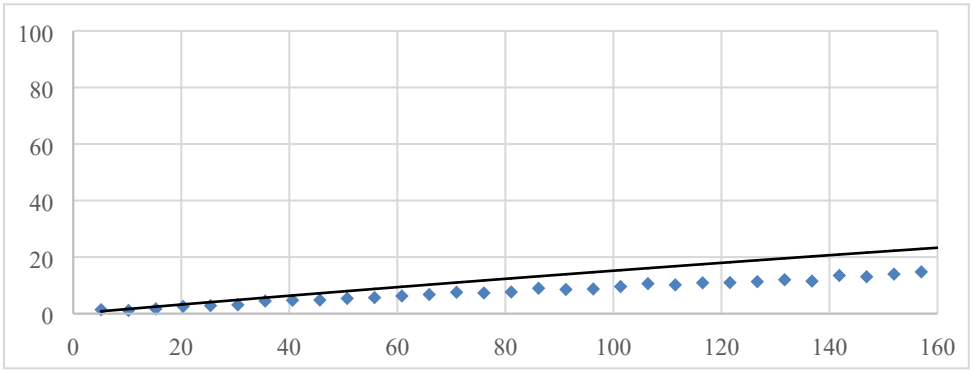
c = 0.96

Run 2:

$t_{1/2}$ = 806 min

k = 4.19 x 10^{-5} L $mol^{-1}s^{-1}$

c = 0.97



3. Supporting NMR spectra

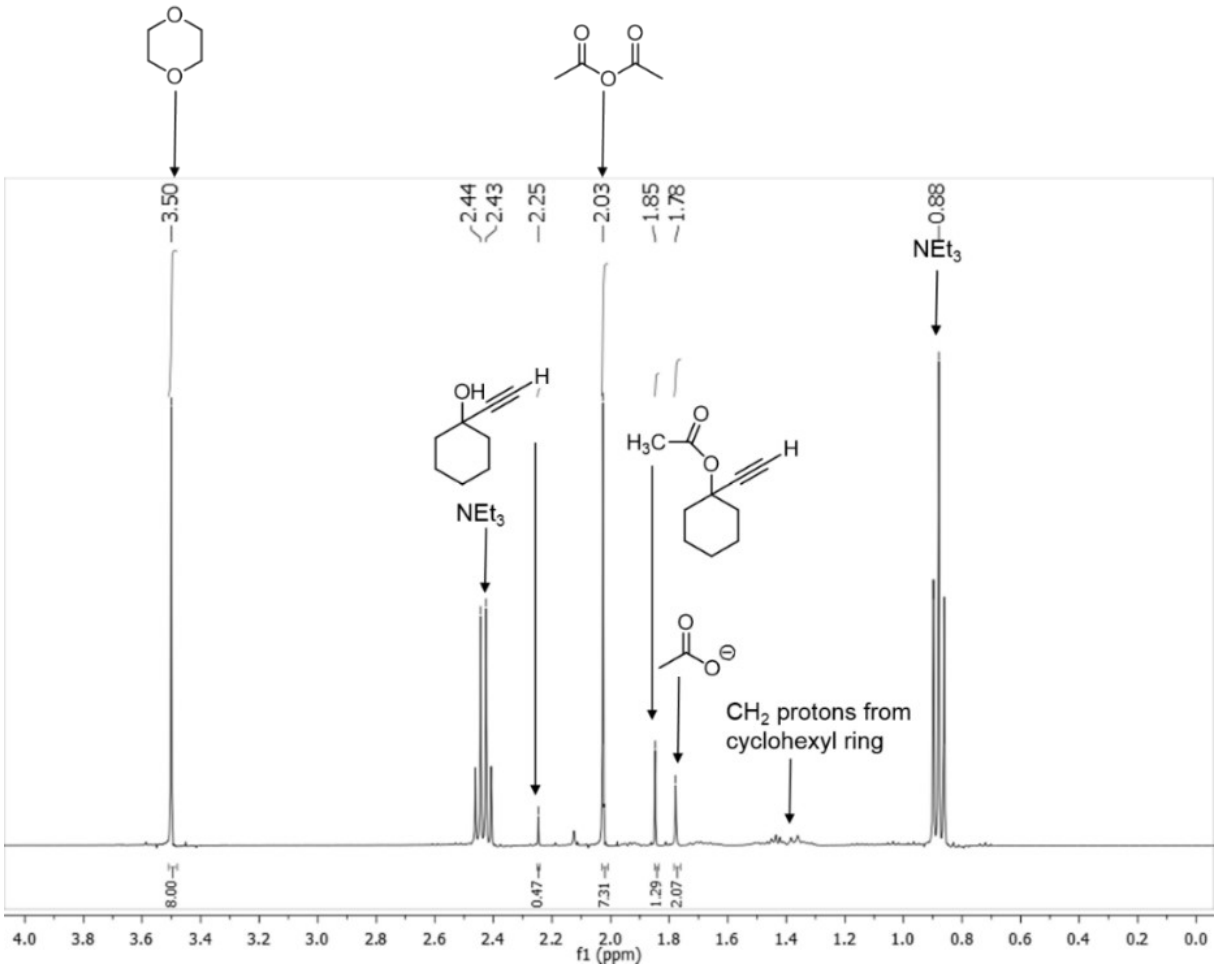


Figure S1 Representative ^{1}H NMR spectrum of the catalyzed acylation of 1-ethynyl cyclohexanol showing diagnostic signals for starting materials and products.

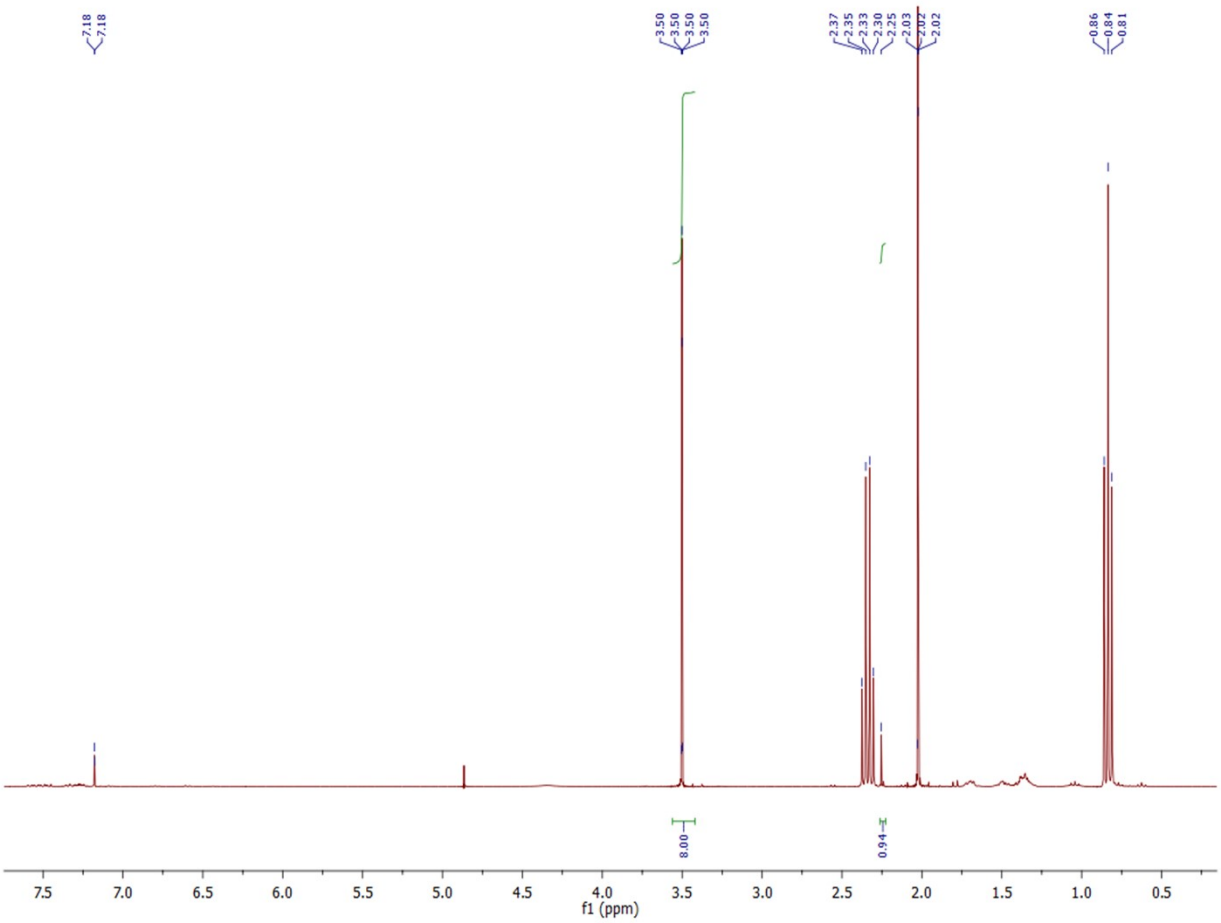


Figure S2 ^{1}H NMR spectrum of scan 1 (t = 10 minutes) of the acylation of 1-ethynyl cyclohexanol catalyzed by Ph_3PNPh (**12**), showing no conversion (see Fig S1 for reference).

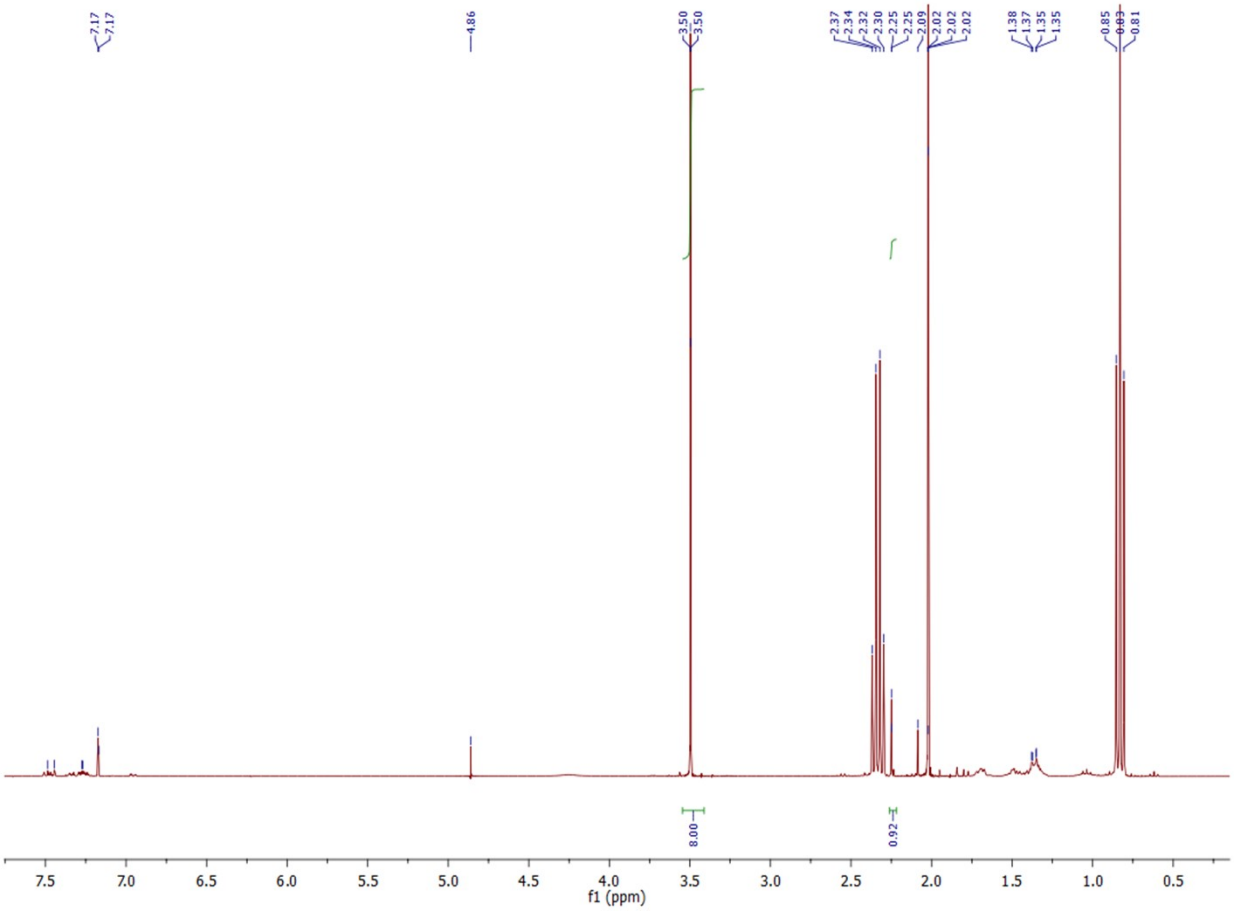


Figure S3 ^{1}H NMR spectrum of scan 300 (t = 687 minutes) of the acylation of 1-ethynyl cyclohexanol catalyzed by Ph_3PNPh (**12**), showing no conversion (see Fig S1 for reference).

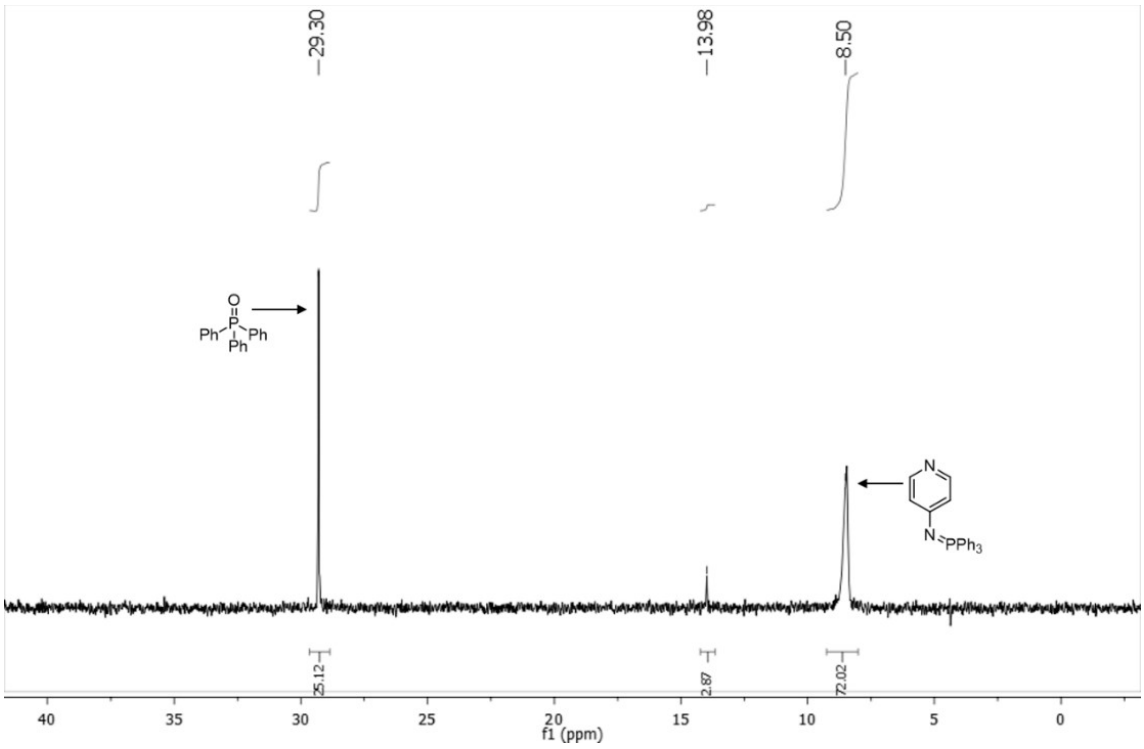


Figure S4 ^{31}P NMR spectrum 16 hours after the initiation of the catalysis with **11a** in $CDCl_3$ showings its conversion to triphenylphosphine oxide (25%) and an unidentified byproduct (3%).

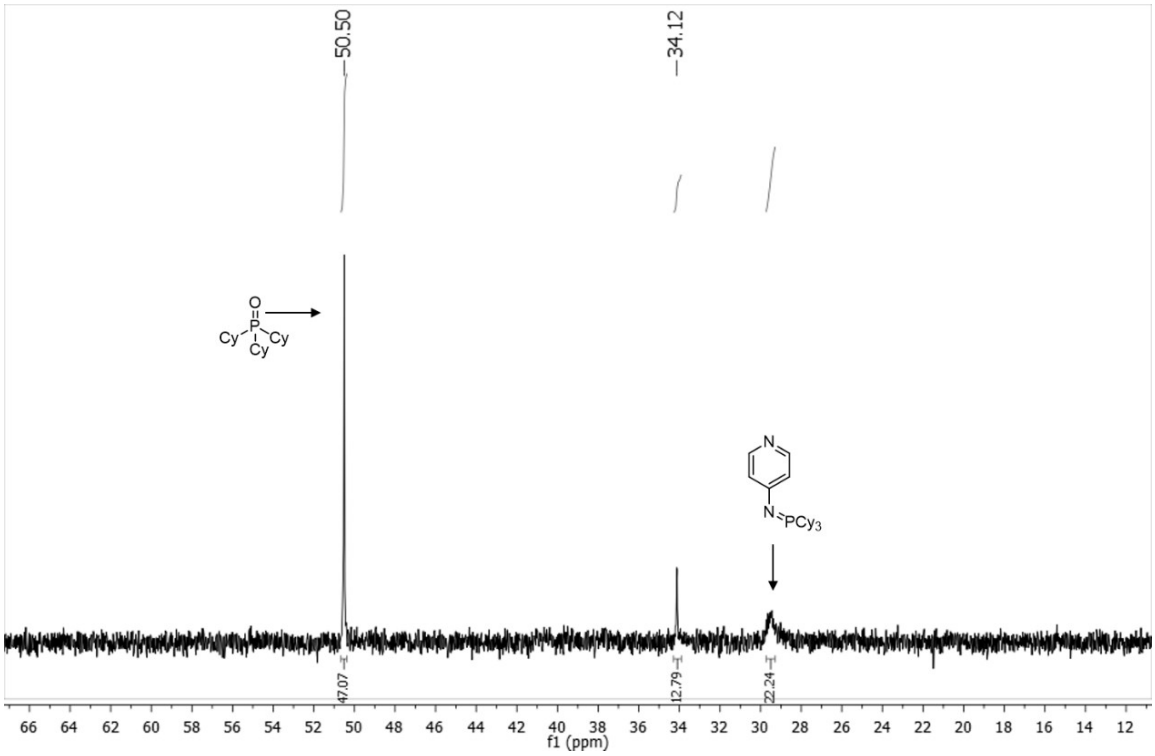


Figure S5 ^{31}P NMR spectrum 5.5 hours after the initiation of the catalysis with **11b** in $CDCl_3$ showings its conversion to tricyclohexylphosphine oxide (47%) and an unidentified byproduct (13%).

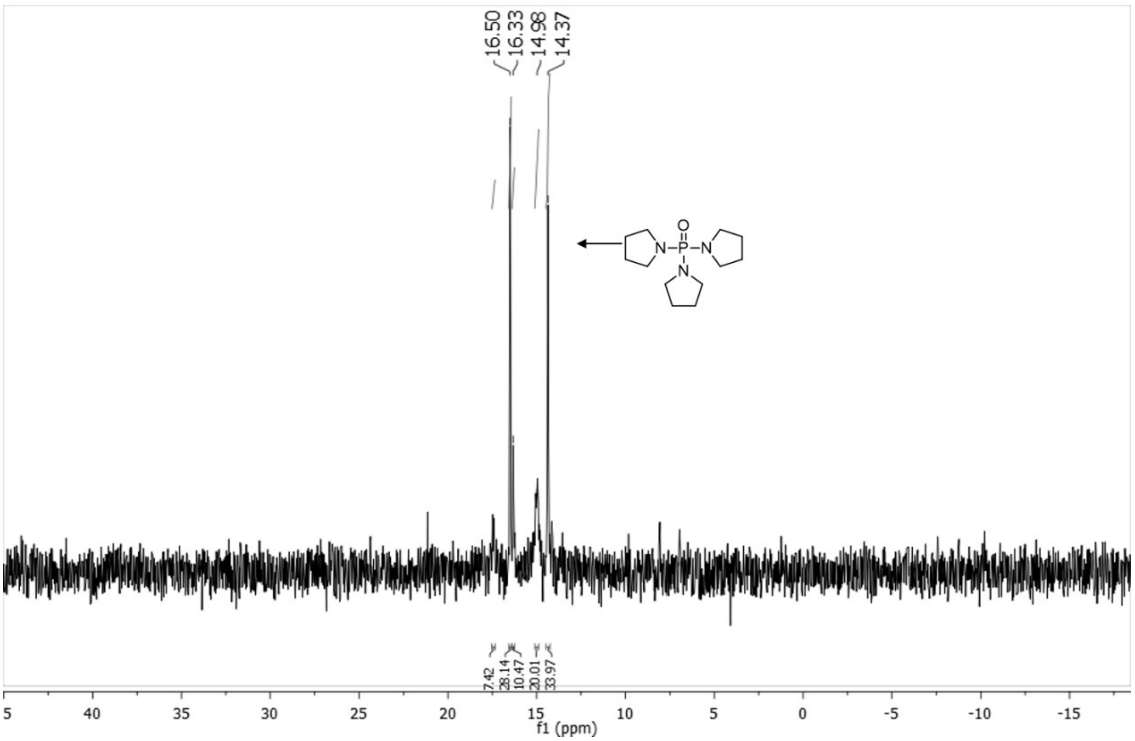


Figure S6 ^{31}P NMR spectrum 5.5 hours after the initiation of the catalysis with **11c** in $CDCl_3$ showing only 20% of **11c** remaining after 5.5 hours, with most being converted into tris(pyrrolidinyl)phosphine oxide (34%) and three other unknown species (46%).

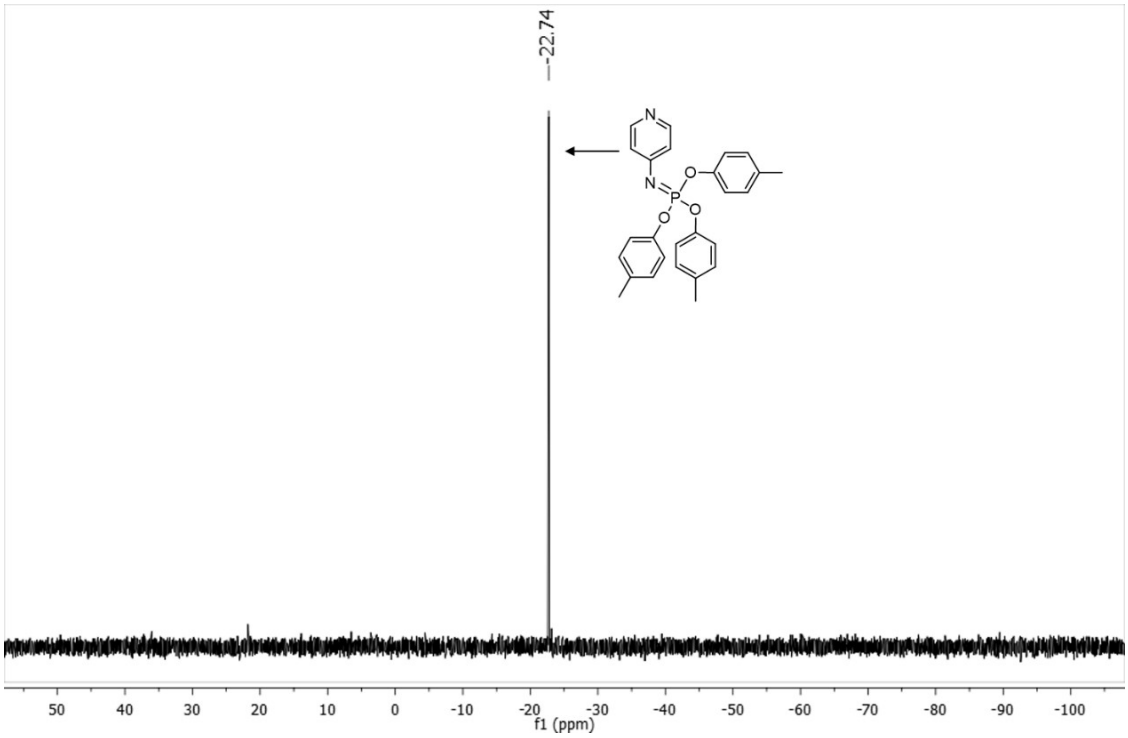


Figure S7 ^{31}P NMR spectrum 10 hours after the initiation of the catalysis with **11d** in $CDCl_3$.

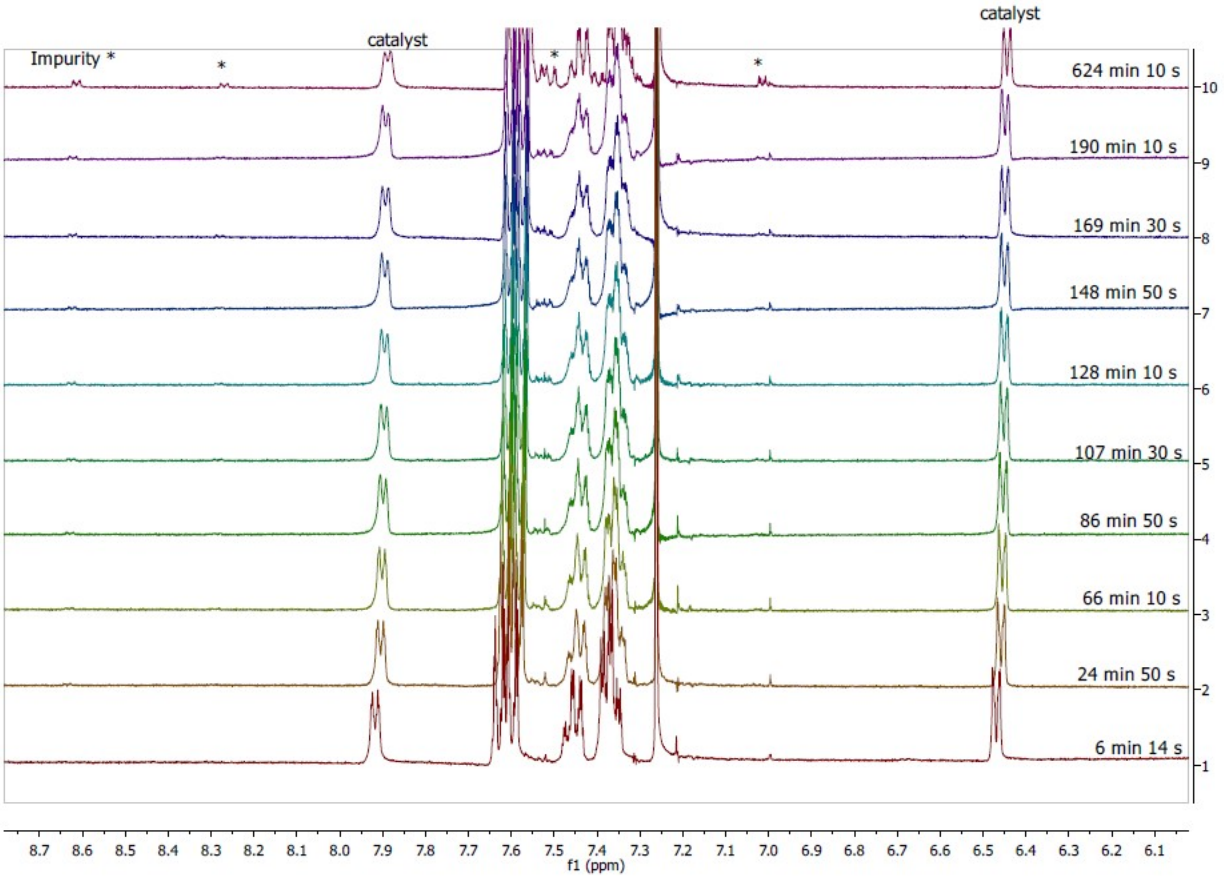


Figure S8 ^{1}H NMR spectra for the acylation of 1-ethynyl cyclohexanol catalyzed by **11a** at the indicated times. Impurities from catalyst decomposition are barely visible around 24 minutes, at which time the reaction is already at ~50% conversion. By 149 minutes the reaction is complete and the impurity peak at ~8.6 ppm has not substantially grown and is less than 1% as intense as the catalyst signal at ~7.9 ppm.

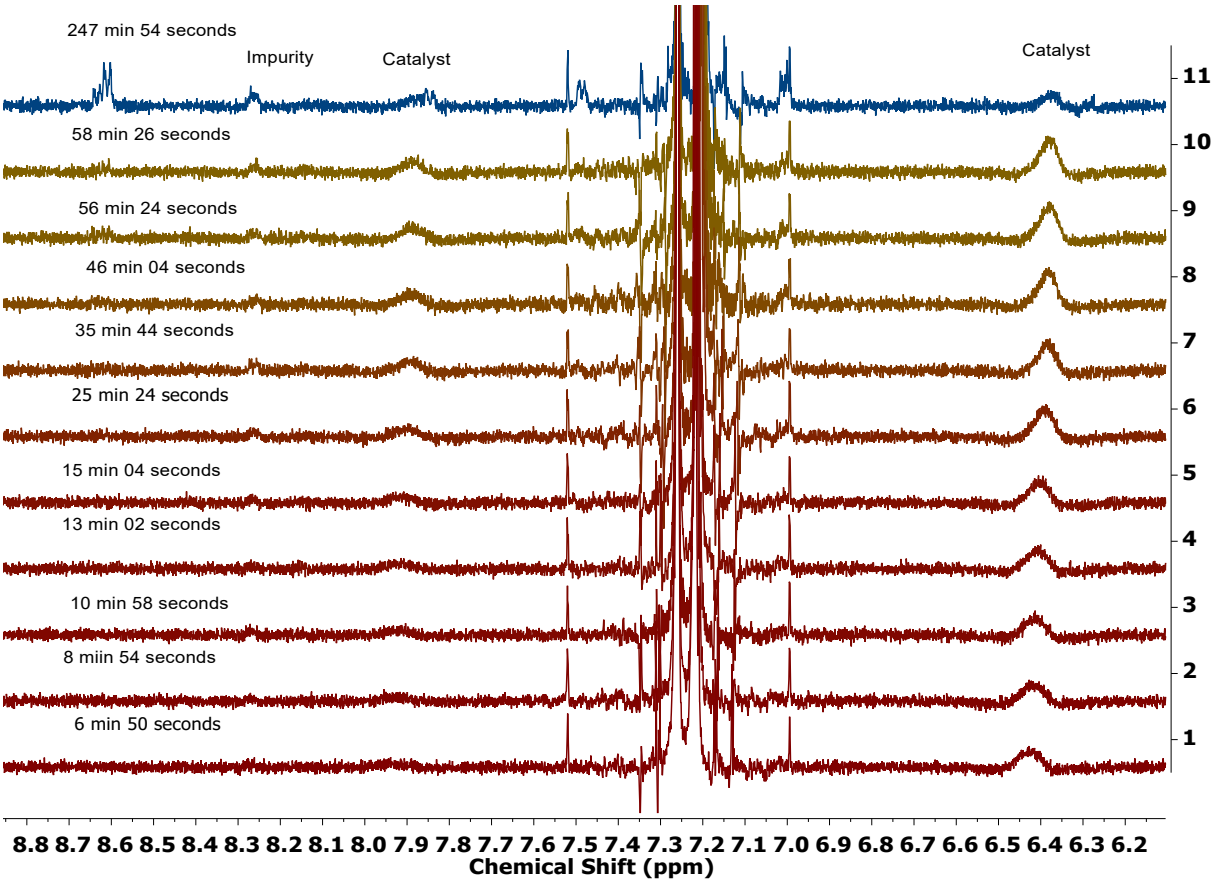


Figure S9 ^{1}H NMR spectra for the acylation of 1-ethynyl cyclohexanol catalyzed by **11b** at the indicated times. Impurities from catalyst decomposition are barely visible around 11 minutes, at which time the reaction is already at ~72% conversion. By 46 minutes the reaction is complete and the impurity peak at ~8.25 ppm has not substantially grown and is only about 1% as intense as the catalyst signal at ~6.4 ppm.

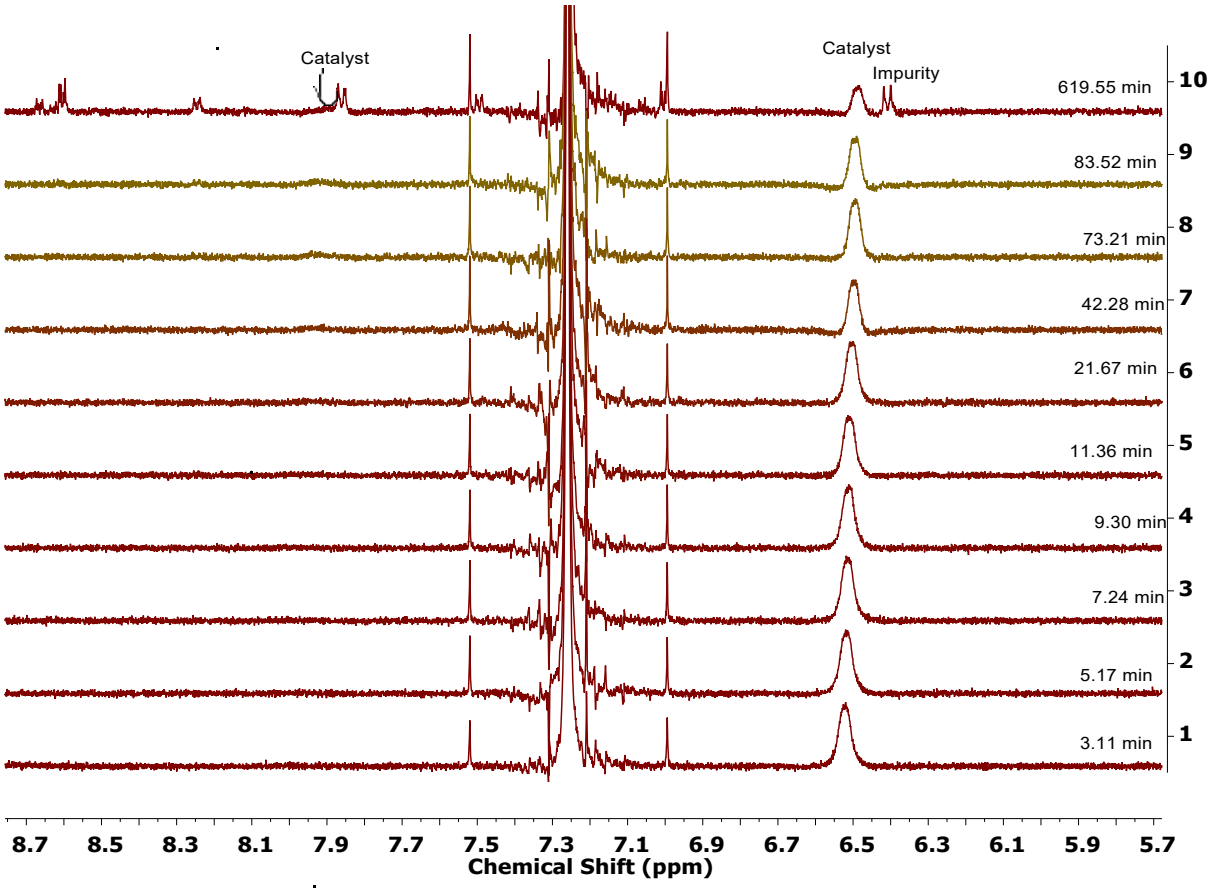


Figure S10 ^{1}H NMR spectra for the acylation of 1-ethynyl cyclohexanol catalyzed by **11c** at the indicated times. Impurities from catalyst decomposition (8.25 ppm) are barely visible around 83 minutes, at which time the reaction is already at ~99% conversion.

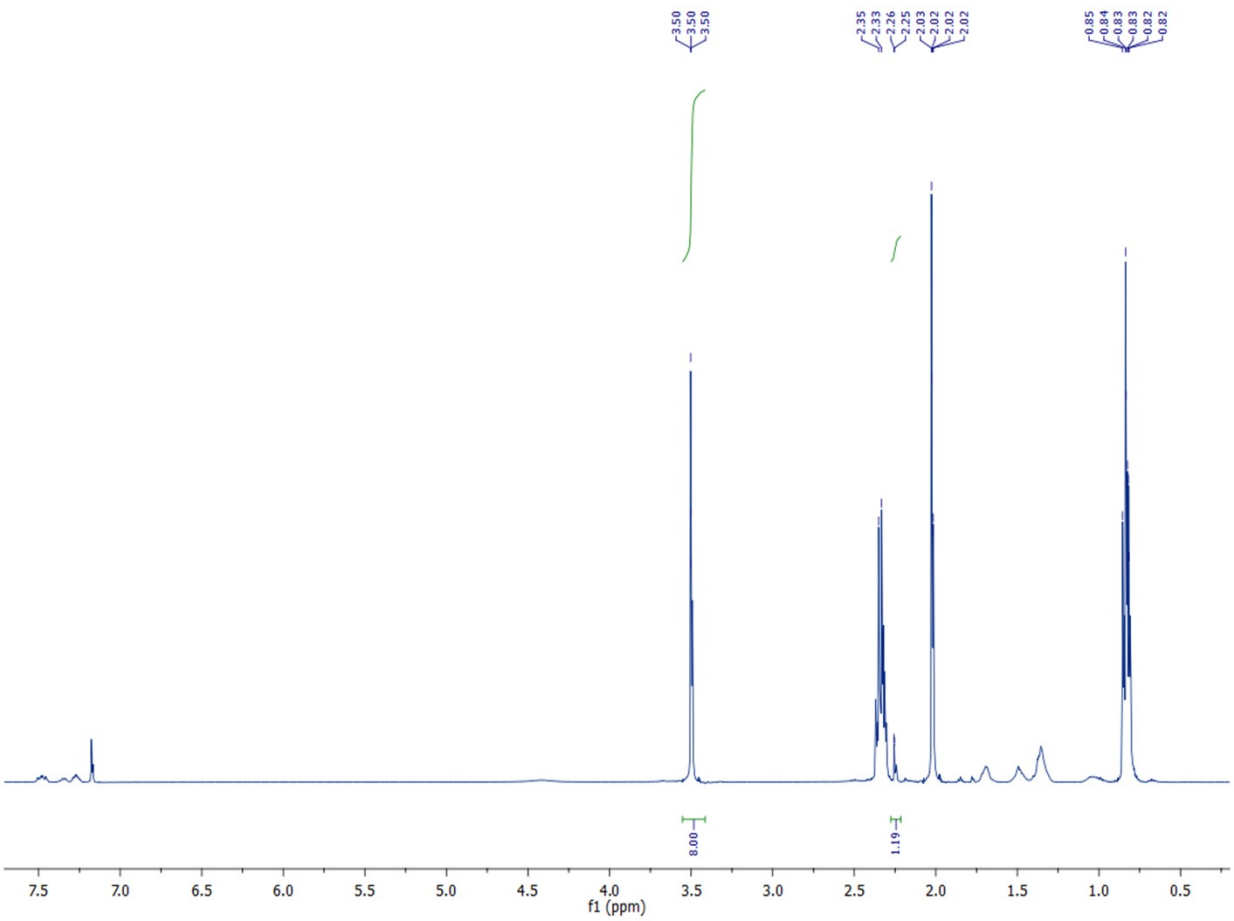


Figure S11 ^{1}H NMR spectrum of the acylation of 1-ethynyl cyclohexanol catalyzed by Ph_3PO after 15 hours, showing no conversion (see Fig S1 for reference).

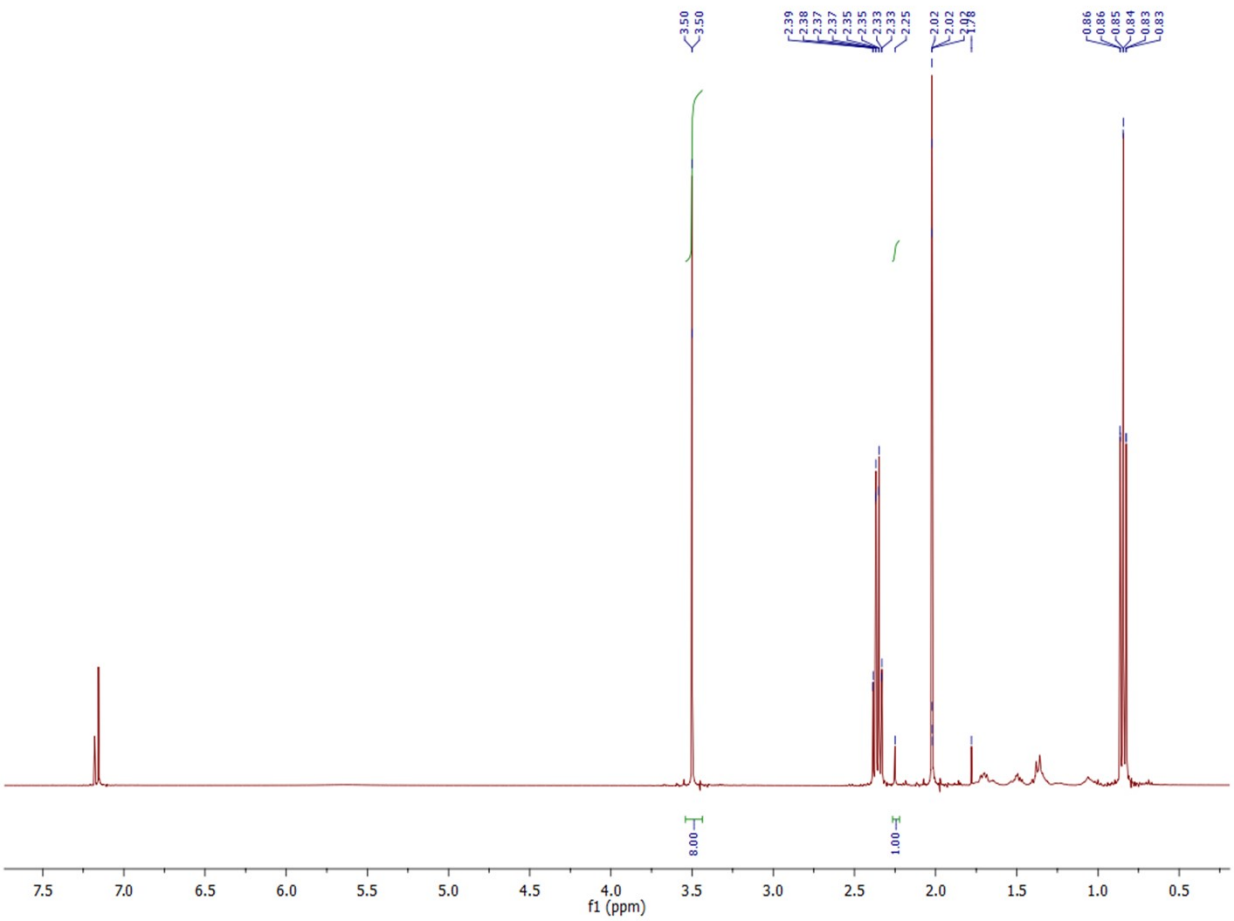


Figure S12 ^{1}H NMR spectrum of the acylation of 1-ethynyl cyclohexanol catalyzed by Ph_3PO after 21 hours, showing no conversion (see Fig S1 for reference).

4. Predicting Catalytic Activity

The linear correlation (Fig. 2, $R^2 = 0.965$) between catalytic activity [$\ln(1/t_{1/2})$] and the substituent constants (σ_p^+) of the related substituents for catalysts **1**–**3** and **11a**-**d** is expressed as:

$$\ln(1/t_{1/2}) = -5.4897*(\sigma_p^+) - 13.958$$

We have shown[2] that, for iminophosphorano substituents, σ_p^+ is correlated to the Tolman electronic parameter (TEP) of the R_3P subunit, such that:

$$\sigma_{p^+ (R3PN-)} = 0.034927*(TEP) - 74.110$$

Therefore, for new 4-iminophosphoranopyridine catalysts, we can estimate reaction half-lives via:

$$\ln(1/t_{1/2}) = -0.19174*(TEP) + 392.884$$

5. References

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2 N. A. Richard, C. K. Khor, S. M. Hetherington, S. L. Mills, A. Decken and C. A. Dyker, *Chem. Eur. J.*, 2020, **26**, 17371–17375.

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4 E. Larionov, F. Achrainer, J. Humin and H. Zipse, *ChemCatChem*, 2012, **4**, 559–566.

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6 R. Tandon, T. Unzner, T. A. Nigst, N. De Rycke, P. Mayer, B. Wendt, O. R. P. David and H. Zipse, *Chem. Eur. J.*, 2013, **19**, 6435–6442.