THE PENNSYLVANIA STATE UNIVERSITY
SCHREYER HONORS COLLEGE

SCHOOL OF SCIENCE

Synthesis and Reactivity of Aryl(alkynyl)iodonium Salts with Carboxylate Nucleophiles to Afford α-Acyloxyketones.

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SPRING 2023

A thesis
submitted in partial fulfillment
of the requirements
for a baccalaureate degree
in Chemistry
with honors in Chemistry

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ABSTRACT

The Michael-type reaction of soft nucleophiles with alkynyliodonium species with carboxylate nucleophiles is well known. The utility of these reactions is primarily limited by the moderate yields and difficulty in preparing the alkynyliodonium species themselves rather than any inherent limitations to the nucleophilic reaction itself. In the present study, a series of aliphatic and aryl alkynes were treated with 1*H*-1-hydroxy-1,2,3-benziodoxathiole 3,3-dioxide (HBI) and trifluoroacetic anhydride in acetonitrile to form the alkynyliodonium species *in situ*. This was followed by the addition of a buffered mixture of carboxylic acids and their corresponding potassium salts. The products obtained were primarily α-acyloxyketones in moderate to high yields. The reduced 2-iodobenzenesulfonic acid could be readily removed by simple liquid-liquid extraction and recycled and reused at a high rate. This series of experiments expands the current knowledge of multivalent iodine compounds and their usefulness in developing organic frameworks and applications in green chemistry.

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ACKNOWLEDGEMENTS

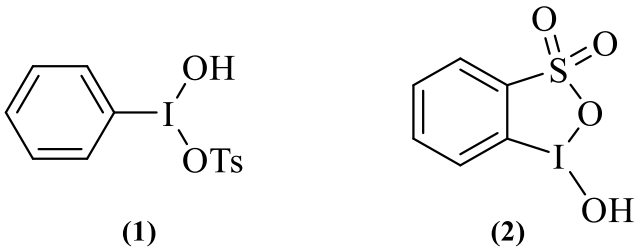
First and foremost, I would like to thank Dr. Michael Justik for all the of the advice he has given me throughout the years, especially relating to the completion of this thesis. I would also like to thank Dr. Jason Bennett for making sure this thesis was completed in a timely fashion. The Behrend chemistry faculty have also been a tremendous help throughout the years, and I'm very thankful for their support in my success and future endeavors. I would not have been able to complete this thesis without the support of my peers, who have taught me to enjoy the process and the field of chemistry. I have also been very fortunate to have a supportive family who have encouraged me throughout the years to go the extra mile and achieve all that is possible. Last but not least, I would like to thank Windsor Lundy for subjecting me to the worst nightmare imaginable. Without her, I would have never taken on this challenge, and I would have probably regretted it for the rest of my life. This process has reminded me to keep working even when everything seems impossible.

Chapter 1

Introduction

1.1 Hypervalent Iodide

Iodine, due to its large size and polarizability, is able to form stable multivalent compounds with oxidation states of III, V, and VII. These oxidation states are termed λ^3, λ^5, and λ^7, respectively. A compound with a λ^3 term will have three primary bonds with the iodine center, while a λ^5 term will have five primary bonds, and so on. Of all of the hypervalent iodine classes, the λ^3 class is most common. Within the λ^3 class, there are many fascinating compounds that have significant synthetic purposes.[1] One example is [Hydroxy(tosyloxy)iodo]benzene (HTIB), **1**. HTIB was discovered back in the 1980s by Gerald F. Koser and his colleagues. Today, the reagent is termed Koser's reagent. Koser's reagent has inspired many analogs that are capable of reacting in very similar fashions. One analog of interest is 1*H*-1-hydroxy-1,2,3-benziodoxathiole 3,3-dioxide (HBI), **2**. HBI's structure is very similar to that of HTIB and is also water soluble. The solubility of HBI allows for it to be recovered by aqueous extraction, and through reoxidation, it could be reused.[2,3] The molecular structures for Koser's reagent and HBI are shown below in Figure (1).



(1) **(2)**

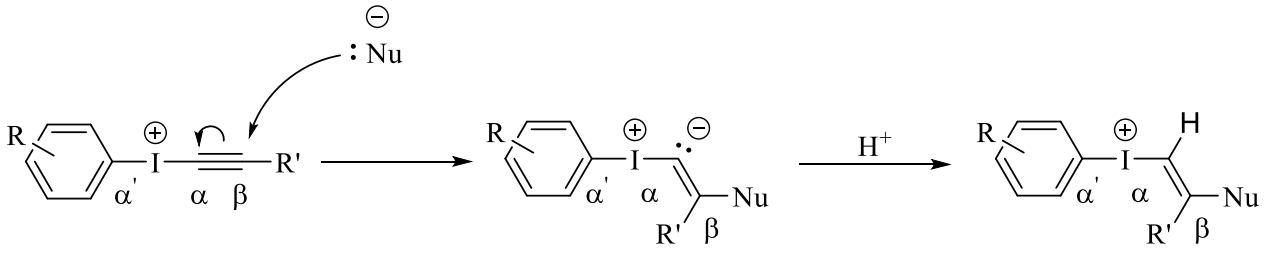
Figure 1. Molecular structures for Koser's reagent and HBI.

Another example of a subclass of hypervalent iodide compounds with a λ^3 term are aryl(alkynyl)iodonium salts. These salts are of great interest because they are selective in their reaction profiles, as well as useful intermediates that can produce highly desired organic framework molecules.[1,4]

1.2 Alkynyliodonium Species

Alkynyliodonium salts have been shown to react through Michael-type conjugative addition pathways – the general molecular structure for an alkynyliodonium salt is given in compound **3**, where R is any functional group attached ortho, para, or meta on the aryl portion, and R′ is the functional group on the acetylene portion. The α′ carbon is in the ipso position on the aryl portion, while the α and β carbons are on the acetylene portion. The strong electron-withdrawing properties of the iodonium group also allows these compounds to react through Diels-Alder and other various cycloadditions. In the case of conjugate addition, the nucleophile, Nu, will add directly to the electron-deficient β-acetylenic carbon to form an iodonium ylide, **4**. The iodonium ylide could then be protonated to form a stable alkynyliodonium salt, also known as a β-functionalized alkynyliodonium salt, **5**.[4,5] The conjugative addition scheme to produce a β-functionalized alkynyliodonium salt is shown below in Scheme 1.

Scheme 1. Conjugate addition of a nucleophile and protonation to afford a β-functionalized alkynyliodonium salt.



(3) **(4)** **(5)**

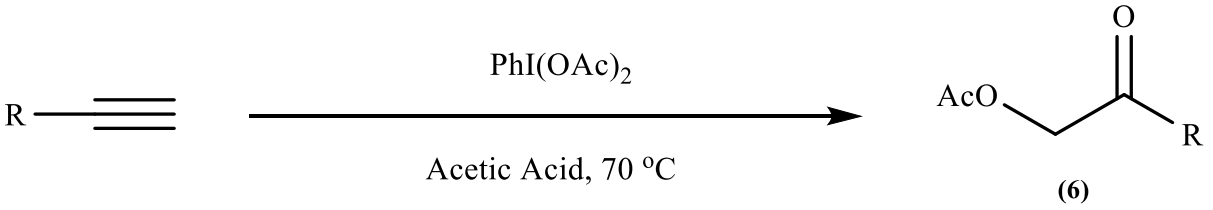
Additionally, alkynyliodonium salts also have been shown to lose the aryl iodonium portion of the molecule following the conjugate addition. The loss of the aryl iodonium species leads to the formation of a alkylidene carbene intermediate, which could undergo two different reaction pathways. The first reaction pathway is a carbene rearrangement, which is highly dependent upon the migratory aptitude of either the R′ substituent or the nucleophile. The second possible reaction pathway is a carbene insertion, which would form a cyclic product. This pathway happens if both the R′ substituent and the nucleophile have a very poor migratory aptitude.[5] These two reactions pathways were not studied within this experiment, as the primary focus was the conjugate addition and protonation product and the formation of the alkynyliodonium salts.[3]

1.3 α-Acyloxyketones and Current Synthesis

Previous research has shown that alkynyliodonium salts react with sodium or potassium salts of carboxylic acids to produce α-acyloxyketones. α-Acyloxyketones are a series of compounds that contain structural elements of many different natural products and provide significance in supplying organic frameworks used in synthetic organic chemistry. Currently, there is one widely accepted method to synthesizing α-acyloxyketones that has replaced many of the previous synthetic procedures; this method was proposed by Xue-Long Hou and his colleagues in an effort to combat the previous synthetic approaches of using metal-catalyzed insertion reactions and organometallics to promote oxidation reactions. These previous methods were not environmentally friendly or cost effective. Hou's new approach utilized (diacetoxyiodo)benzene, $PhI(OAc)_2$, in the presence of an aryl acetylene or an aliphatic terminal alkyne with acetic acid as the solvent.[5,6] The reaction took place at 70 °C and had a reaction time

of 12 hours. Scheme 2 shows the conversion of an aryl acetylene or an aliphatic terminal alkyne to an α-acyloxyketone, **6**, proposed by Hou.[6]

Scheme 2. Hou's reaction procedure to produce α-acyloxyketones.



(6)

It is important to note that this current procedure relies heavily on the purification of the final product through flash column chromatography on silica gel. The heavy reliance on chromatography often deters any industrial or large scale synthesis from taking place. Although Hou's new approach is more environmentally friendly than previous methods, the $PhI(OAc)_2$ reagent used could not be recycled.[6]

Chapter 2

Experimental Methods

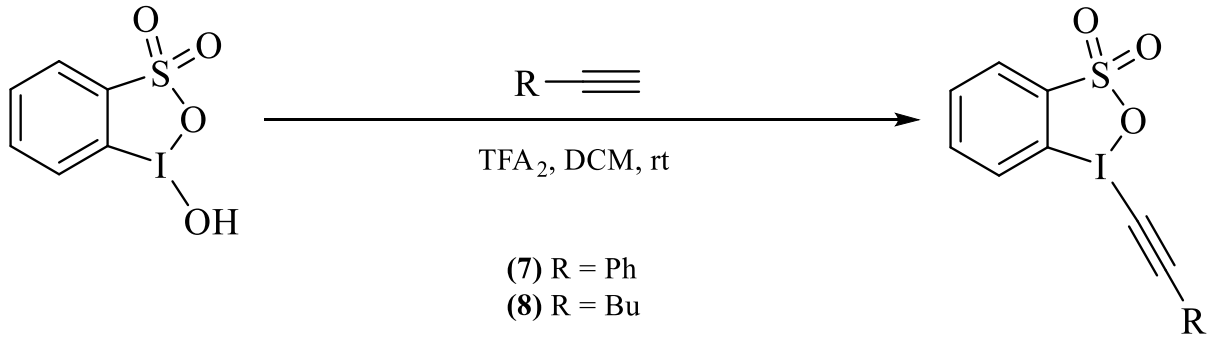
2.1 General Procedures

All reaction conditions were at atmospheric pressure and no utilization of a Schlenk apparatus was necessary. If needed, the crude α-acyloxyketone products were purified through flash chromatography using celite and silica gel. The ^{1}H NMR spectra were obtained on a Bruker 400 UltraShield spectrometer at ambient temperature. Chemical shifts were expressed as ppm downfield of internal TMS, followed by multiplicity and hydrogen count.

2.2 Isolation of Alkynyliodonium Salts

The initial approach in synthesizing α-acyloxyketones involved the isolation of the alkynyliodonium salts. To isolate the alkynyliodonium salts, HBI (1 equivalent) was added to DCM. A catalytic amount of trifluoroacetic anhydride (TFA_2, 2 equivalents) was added, followed by the corresponding alkyne (2 equivalents). The reactions took place at room temperature for 4 hours. The alkynyliodonium salts were precipitated out through the addition of diethyl ether and product formation was confirmed through ^{1}H NMR. This process was lengthy, and precipitating out the desired product was tedious. A small amount of ethyl acetate was often added to help remove the tar-like products. The synthetic scheme for the alkynyliodonium salts using HBI is shown below in Scheme 3. The two alkynes used were phenylacetylene and 1-hexyne, as these gave the best yields and were the easiest to isolate.

Scheme 3. Synthesis of alkynyliodonium salts.



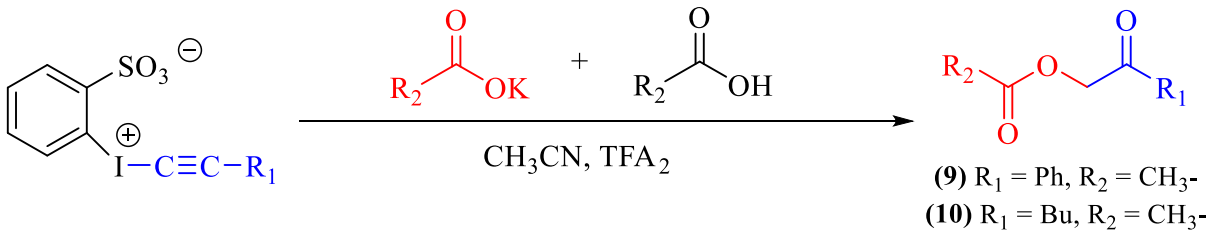
(7) R = Ph
(8) R = Bu

It was clear that the isolation of the alkynyliodonium salts posed an issue because of the difficulty in isolating the final products. For that reason, only two alkynyliodonium salts were obtained, **7** and **8**, that were used in subsequential reactions to synthesize the α-acyloxyketones.

2.3 Conversion of Alkynyliodonium Salts to α-Acyloxyketones

The isolated alkynyliodonium salts, **7** and **8** (1 equivalent), were added to a 10-mL round bottom flask and treated with the acetate nucleophile (2 equivalents) and acetic acid (2 equivalents) in acetonitrile (3 mL) as the solvent. A small amount of TFA_2 was also added (1.5 equivalents). The reactions took place at room temperature with a reaction time of 12 hours. It was observed that the reaction solution changed from a white color to a light yellow. The desired α-acyloxyketone products were obtained through aqueous extractions with ethyl acetate as the extracting solvent. Using a separatory funnel, the water layer was removed, and any ethyl acetate fractions were combined. These fractions were then washed with a 5% sodium bicarbonate solution, followed by a brine solution. Finally, the obtained organic layer was dried over sodium sulfate, and excess solvent was removed through rotary-evaporation. The synthetic scheme for conversion of the alkynyliodonium salts to α-acyloxyketones are shown below in Scheme 4.

Scheme 4. Isolation of alkynyliodonium salts and conversion to α-acyloxyketones.



(9) R_1 = Ph, R_2 = CH_3-
(10) R_1 = Bu, R_2 = CH_3-

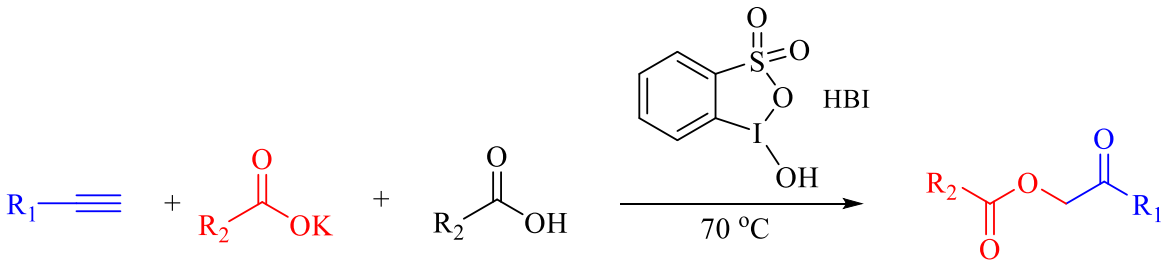
The following products, **9** and **10**, were obtained in moderate yields and were characterized through ^{1}H NMR analysis. The ^{1}H NMR spectra for product **9** and **10** in $CDCl_3$ were recorded in Appendix A as Figures 1 and 2. After reviewing the NMR spectra, both products were then purified through flash column chromatography using celite and silica gel.

2.4 A One-Pot Conversion of Alkynes to α-Acyloxyketones

From Figures 1 and 2, it was observed that there were many impurities in the final product and characterization was very difficult, despite purification through flash column chromatography. Thus, an optimized procedure was developed and titled a one-pot conversion. This procedure bypassed the isolation of the alkynyliodonium salts and generated them *in situ*. The one-pot conversion was done by adding HBI (1 equivalent) to carboxylic acid (1 mL) in a small vial with a stir bar. No acetonitrile or TFA_2 was added. The reaction was stirred for 5 minutes before the sodium or potassium carboxylate (2 equivalents) was added, followed by the addition of the aryl acetylene or aliphatic terminal alkyne (2 equivalents). The reaction was heated to 70 °C and was left to react for 12 hours. Once the reaction was completed, water was added (5 mL) and the desired product was extracted using chloroform (2 x 5 mL) in a separatory funnel. The two chloroform fractions were combined and washed with a 5 % sodium bicarbonate solution (5 mL) and a brine solution (5 mL). The obtained organic layer was then dried over sodium sulfate and the excess solvent was reduced using rotary evaporation. The synthetic

scheme for the one-pot conversion of alkynes to α-acyloxyketones is shown below in Scheme 5. This procedure was repeated for five different carboxylates with six different alkynes. The carboxylates used were acetate, propionate, chloroacetate, methoxyacetate, and trifluoroacetate. The alkynes used were phenylacetylene, 4-methylpen-1-yne, 1-hexyne, 1-octyne, 3,3-dimethylbut-1-yne, and ethynylcyclohexane.

Scheme 5. The one-pot conversion of alkynes to α-acyloxyketones.



(11) R_1 = Ph, R_2 = CH_3- **(17)** R_1 = Ph, R_2 = CH_3CH_2- **(23)** R_1 = Ph, R_2 = $ClCH_2$-
(12) R_1 = ^{i}Bu, R_2 = CH_3- **(18)** R_1 = ^{i}Bu, R_2 = CH_3CH_2- **(24)** R_1 = ^{i}Bu, R_2 = $ClCH_2$-
(13) R_1 = Bu, R_2 = CH_3- **(19)** R_1 = Bu, R_2 = CH_3CH_2- **(25)** R_1 = Bu, R_2 = $ClCH_2$-
(14) R_1 = Hx, R_2 = CH_3- **(20)** R_1 = Hx, R_2 = CH_3CH_2- **(26)** R_1 = Hx, R_2 = $ClCH_2$-
(15) R_1 = ^{t}Bu, R_2 = CH_3- **(21)** R_1 = ^{t}Bu, R_2 = CH_3CH_2- **(27)** R_1 = ^{t}Bu, R_2 = $ClCH_2$-
(16) R_1 = Cx, R_2 = CH_3- **(22)** R_1 = Cx, R_2 = CH_3CH_2- **(28)** R_1 = Cx, R_2 = $ClCH_2$-

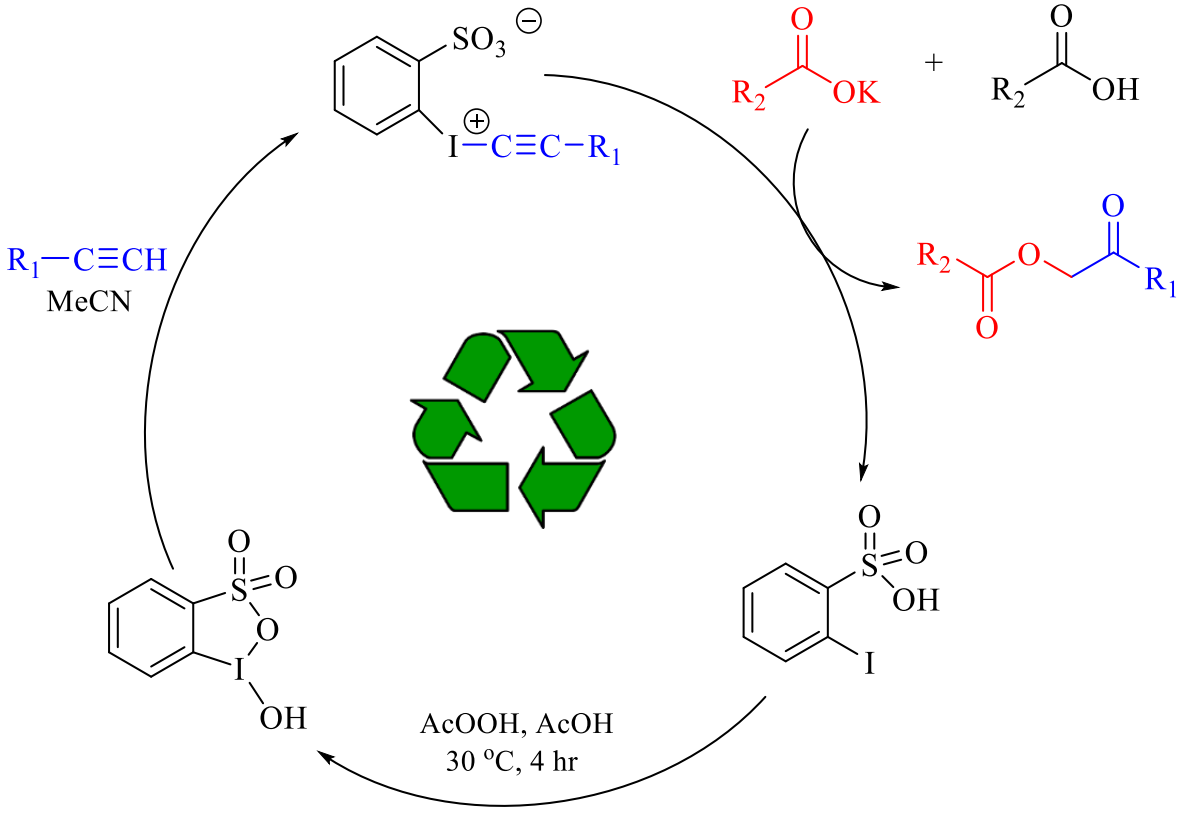
(29) R_1 = Ph, R_2 = $MeOCH_2$- **(35)** R_1 = Ph, R_2 = CF_3-
(30) R_1 = ^{i}Bu, R_2 = $MeOCH_2$- **(36)** R_1 = ^{i}Bu, R_2 = CF_3-
(31) R_1 = Bu, R_2 = $MeOCH_2$- **(37)** R_1 = Bu, R_2 = CF_3-
(32) R_1 = Hx, R_2 = $MeOCH_2$- **(38)** R_1 = Hx, R_2 = CF_3-
(33) R_1 = ^{t}Bu, R_2 = $MeOCH_2$- **(39)** R_1 = ^{t}Bu, R_2 = CF_3-
(34) R_1 = Cx, R_2 = $MeOCH_2$- **(40)** R_1 = Cx, R_2 = CF_3-

Products **11** through **40** were obtained in moderate to high yields and were characterized through ^{1}H NMR analysis. The ^{1}H NMR spectra for products **11** through **40** in $CDCl_3$ are recorded in Appendix A as Figures 4 through 33, respectively. No flash column chromatography was done on any of the final products.

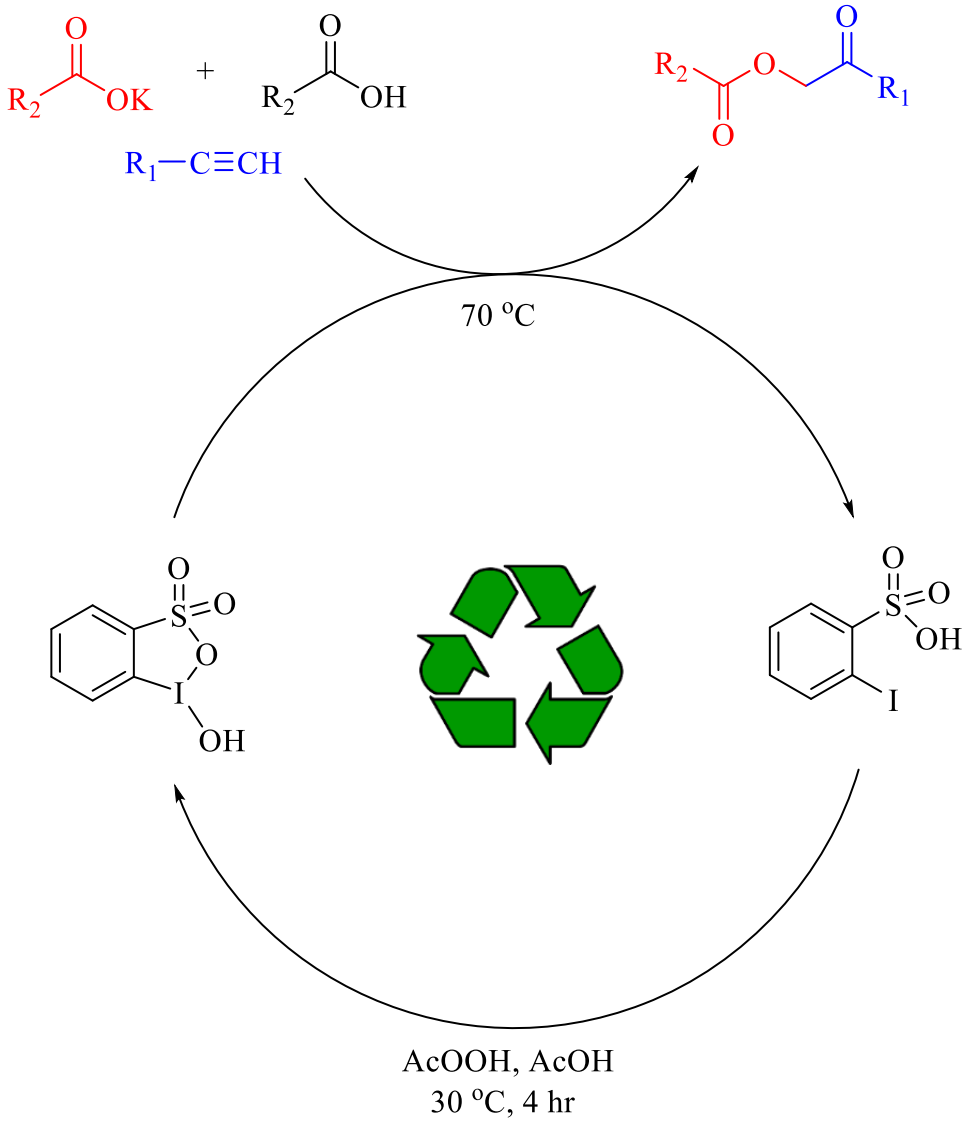
2.5 The Reoxidation of 2-Iodobenzenesulfonate

What made the two procedures within this study significant was the reusability of HBI. As the alkynyliodonium salts reacted with the carboxylate nucleophiles to produce the α-acyloxyketones, 2-iodobenzenesulfonate was produced. The 2-iodobenzenesulfonate was collected in the aqueous layers of the extraction and placed in a large petri dish to allow the excess water to evaporate. The solid obtained was dissolved in acetic acid and then treated with peracetic acid to oxidize the 2-iodobenzenesulfonate back to HBI.[2,3,7] The reusability of HBI and oxidation of 2-iodobenzenesulfonate is shown below in Schemes 6 and 7. Scheme 6 shows the oxidation for the isolation of the alkynyliodonium salt method, while Scheme 7 shows the oxidation for the one-pot conversion method.

Scheme 6. Isolation of alkynyliodonium salts and conversion to α-acyloxyketones, followed by the oxidation of 2-iodobenzenesulfonate.



Scheme 7. The one-pot conversion of alkynes to α-acyloxyketones, followed by the oxidation of 2-iodobenzenesulfonate.



Chapter 3

Results and Discussion

3.1 Initial Procedure of Isolating the Alkynyliodonium Salts

One of the most interesting parts of this experiment was the development of the procedure. Initially, the alkynyliodonium salts were synthesized and isolated. It was quickly realized that this process was time intensive and posed many issues in terms of isolating the more complex alkynyliodonium salts, as well as the obtaining pure products. Only the phenyl and butyl alkynyliodonium salts were able to be produced in significant yields to be able to be used in subsequential reactions. Completing a series of alkynyliodonium salts with the six alkynes studied in this experiment would have been a very difficult and ineffective method in synthesizing the desired α-acyloxyketones.

3.2 Conversion of Alkynyliodonium Salts to α-Acyloxyketones

When analyzing Figures 2 and 3, it was observed that the desired α-acyloxyketones products were synthesized in moderate yields through the conversion of the isolated alkynyliodonium salts. What made this method less ideal was the impurities observed in the ^{1}H NMR spectra in Figures 2 and 3. The defining peak that confirmed the presence of the desired α-acyloxyketones, products **9** and **10**, was the methylene peaks. The methylene peak appeared in the range of 4.5 to 6.0 ppm, depending on the product. The crude products were subjected to two to three rounds of flash column chromatography to remove the majority of the impurities. It was clear that this procedure was time intensive and difficult to obtain purified α-acyloxyketones. What made this procedure more ideal than the previous synthetic approaches was the use of the recyclable reagent, HBI. The oxidation of 2-iodobenzenesulfonate back to HBI was able to be done in yields close to 90%. This has large potential in green chemistry because the starting

material is reusable and only excess solvent and carboxylate are going to waste. This method is far more environmentally friendly than previous synthetic approaches, especially those that rely on the use of organometallics.

3.3 A One-Pot Conversion of Alkynes to α-Acyloxyketones

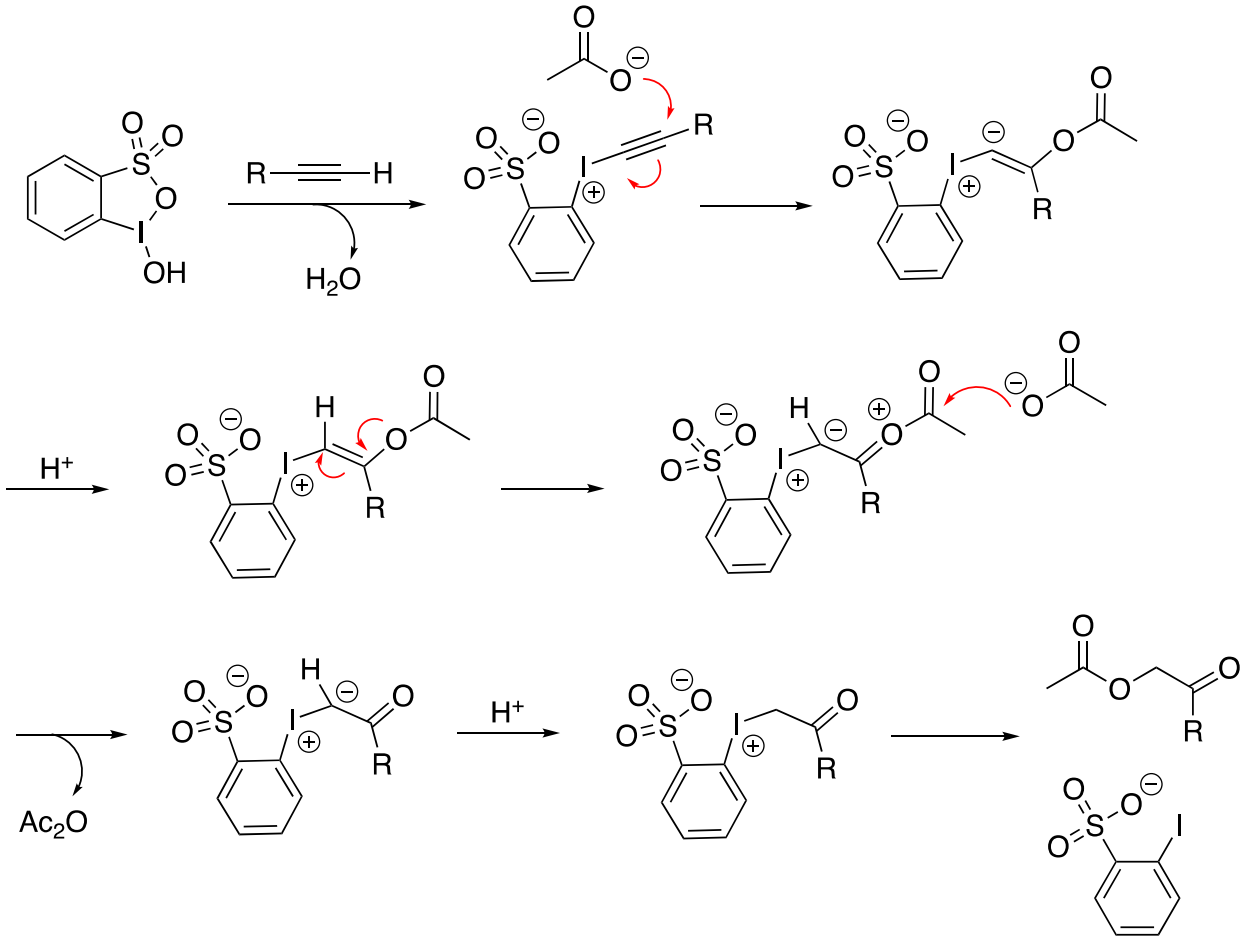
The one-pot conversion method was the optimized procedure developed within this study. From Figures 4 and 6, it was observed that products **11** and **12** were far purer than the previous method's products, **9** and **10**. What made this procedure more ideal than the previous procedure was the lack of chromatography. The NMR spectra shown in Figures 4 and 6 for products **11** and **12**, respectively, were obtained without chromatography. It is important to note that all of the products obtained were amber colored oils. The aqueous layers obtained from the reactions were collected in a petri dish and the excess water was allowed to evaporate, leaving behind residual 2-iodobenzenesulfonate, which was oxidized back to HBI in yields close to 90%. Using this optimized procedure, the yields for products **11** through **40** are recorded in Table 1, and ^{1}NMR characterizations are presented in Appendix A.

Table 1. Percent yields for the one-pot conversion of alkynes to α-acyloxyketones.

Nucleophile R_1 =	Alkynyliodonium Salt R_2 =					
	Ph	^{i}Bu	Bu	Hx	^{t}Bu	Cx
CH_3-	89	62	76	78	74	81
CH_3CH_2-	75	85	79	77	70	74
$ClCH_2$-	44	56	55	52	43	48
CH_3OCH_2-	75	42	57	42	39	42
CF_3-	84	43	60	59	44	58

When analyzing the yields obtained, it was observed that aliphatic nucleophiles, the acetate, and propionates, were afforded in the highest percent yields when compared to the substituted nucleophiles – the chloroacetates, methoxyacetates, and trifluoroacetates. With the yields and ^{1}H NMR characterization completed; a possible mechanism was proposed. The mechanism was adopted from the literature and was initially proposed by Xue-Long Hou and his colleagues.[6] Within the proposed mechanism, the nucleophile is the acetate anion, and the alkyne is any of the ones examined within this study: phenylacetylene, 4-methylpen-1-yne, 1-hexyne, 1-octyne, 3,3-dimethylbut-1-yne, or ethynylcyclohexane. The proposed mechanism for the synthesis of α-acyloxyketones is listed below as Scheme 8.

Scheme 8. Proposed mechanism for the one-pot conversion of alkynes to α-acyloxyketones.



The first step in the proposed mechanism for the one-pot conversion of alkynes to α-acyloxyketones was the formation of the alkynyliodonium salt. The alkynyliodonium salt was then able to undergo conjugate addition with a carboxylate nucleophile to form the iodonium ylide. Through protonation, the iodonium ylide is turned into a β-functionalized alkynyliodonium salt. This salt then tautomerizes, and the carbonyl carbon of the carboxylate is attacked by another carboxylate nucleophile to form the anhydride of the carboxylate. Finally, another carboxylate undergoes a substitution reaction and displaces the 2-iodobenzenesulfonate group to produce the desired α-acyloxyketone and residual 2-iodobenzenesulfonate. The proposed mechanism supports the experimental observations and results obtained in this study.

Chapter 4

Conclusion

A series of aliphatic and aryl alkynes were treated with 1*H*-1-hydroxy-1,2,3-benziodoxathiole 3,3-dioxide (HBI) and trifluoroacetic anhydride in acetonitrile to form the alkynyliodonium species *in situ*. This was followed by the addition of a buffered mixture of carboxylic acids and their corresponding potassium salts. Two procedures were developed and tested to ultimately lead to the optimized procedure of a one-pot conversion of alkynes to α-acyloxyketones. The products obtained were primarily α-acyloxyketones in moderate to high yields and analyzed through ^{1}H NMR. The reduced 2-iodobenzenesulfonic acid was removed by aqueous extraction , recycled, and reused at a high rate. This series of experiments expands the current knowledge of reusable hypervalent iodine compounds and their usefulness in developing organic frameworks. This study also challenges the current and widely accepted method in synthesizing α-acyloxyketones. The major achievements within this two year study was the development of a one-pot method that was able to produce α-acyloxyketones without the need for intense purification of chromatography, as well as applications in green chemistry and the use of a reusable reagent that is able to revert back to the starting material in high yields.

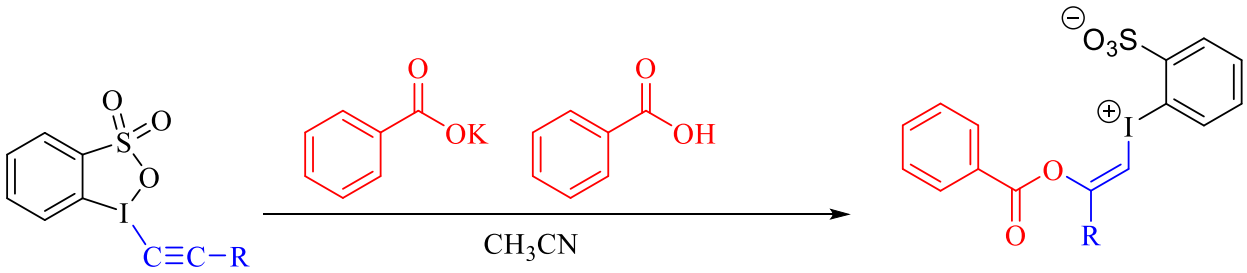
Chapter 5

Future Studies

Although a series of α-acyloxyketones was successfully synthesized in moderate to high yields, there was one set examined that was more difficult than the others in isolating. The trifluoroacetate series posed many issues throughout the course of the experiment and the ^{1}H NMR spectra obtained showed some impurities. It was also very difficult to pick out which peaks corresponded to which protons on each molecule for products **35** through **40**. Current and future studies are aimed at better understanding the trifluoroacetate series and how to obtain purer products. Some possible methods include adding a catalytic amount of trifluoracetic anhydride, as well as increasing the reaction time.

Future studies such as examining how a series of benzoate could afford a vinyliodonium salt, **41**. Vinyliodonium salts have not previously been observed in the treatment of carboxylates with alkynyliodonium salts and has been hypothesized as a possible product when treated with benzoates. Scheme 9 shows the reaction of alkynyliodonium salts with potassium benzoate and benzoic acid to afford a vinyliodonium salt.[2]

Scheme 9. Alkynyliodonium salt treated with potassium benzoate and benzoic acid to produce a vinyliodonium salt.



(41)

Appendix A

Figures and ^{1}H NMR Spectra Analysis

Isolation Method

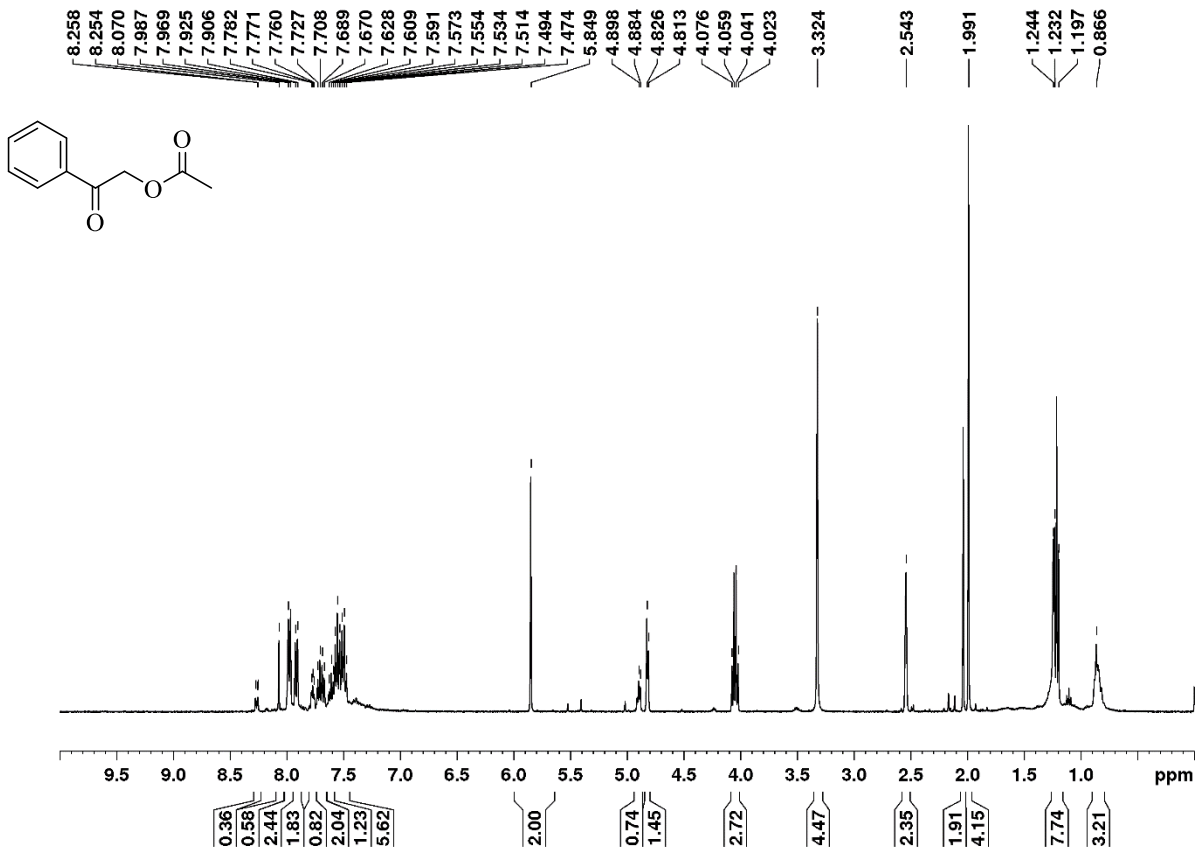


Figure 2. ^{1}H NMR spectrum for product 9 in $CDCl_3$ - isolating the alkynyliodonium salt before conversion. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - α-acetoxy acetophenone (9), 80% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.99 (s, 3H), 5.85 (s, 2H), 7.47-7.49 (m, 2H), 7.51-8.07 (m, 1H), 8.25 (d, 2H)

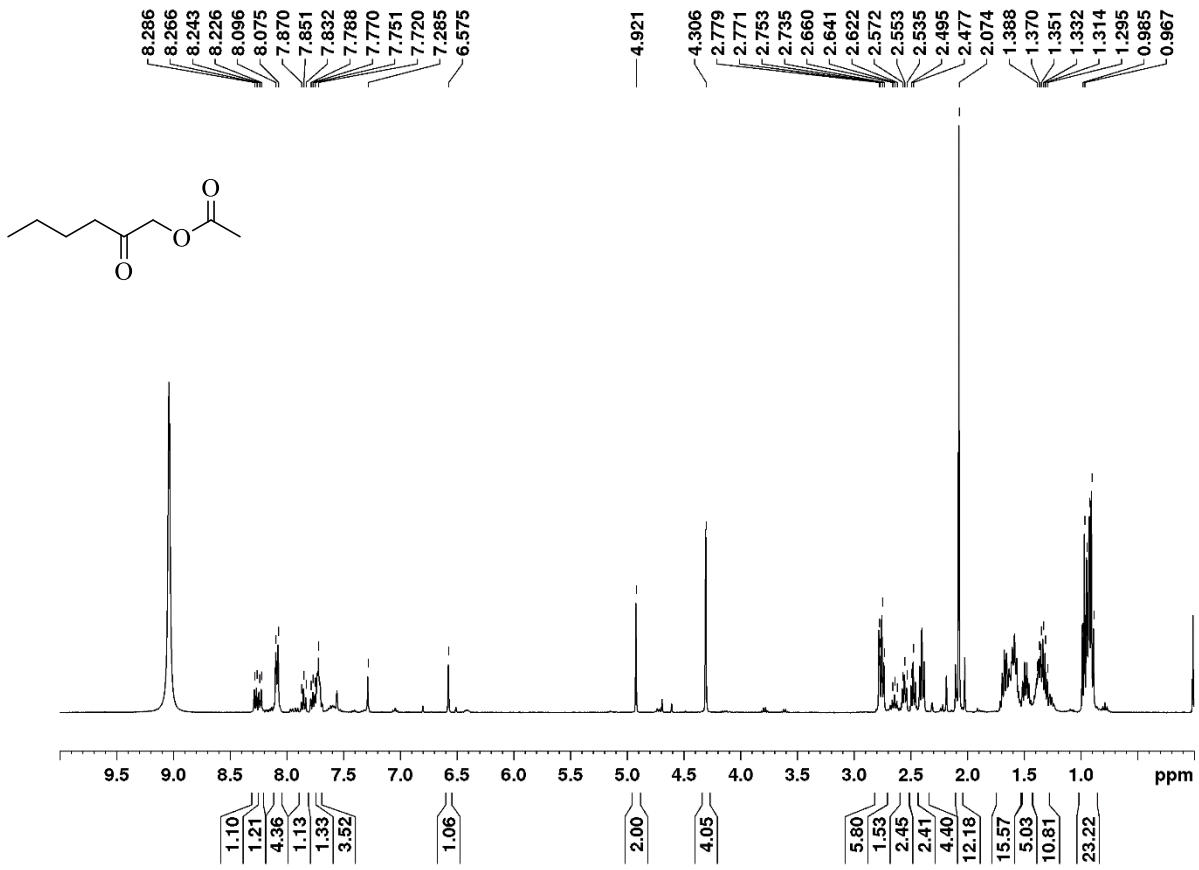


Figure 3. ^{1}H NMR spectrum for product 10 in $CDCl_3$ – isolating the alkynyliodonium salt before conversion. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxohexyl acetate (10), 83% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, 3H), 1.30-1.39 (m, 2H), 1.50-1.62 (m, 2H), 2.07 (s, 3H), 2.50 (t, 2H), 4.92 (s, 2H).

One-pot Method - Acetates

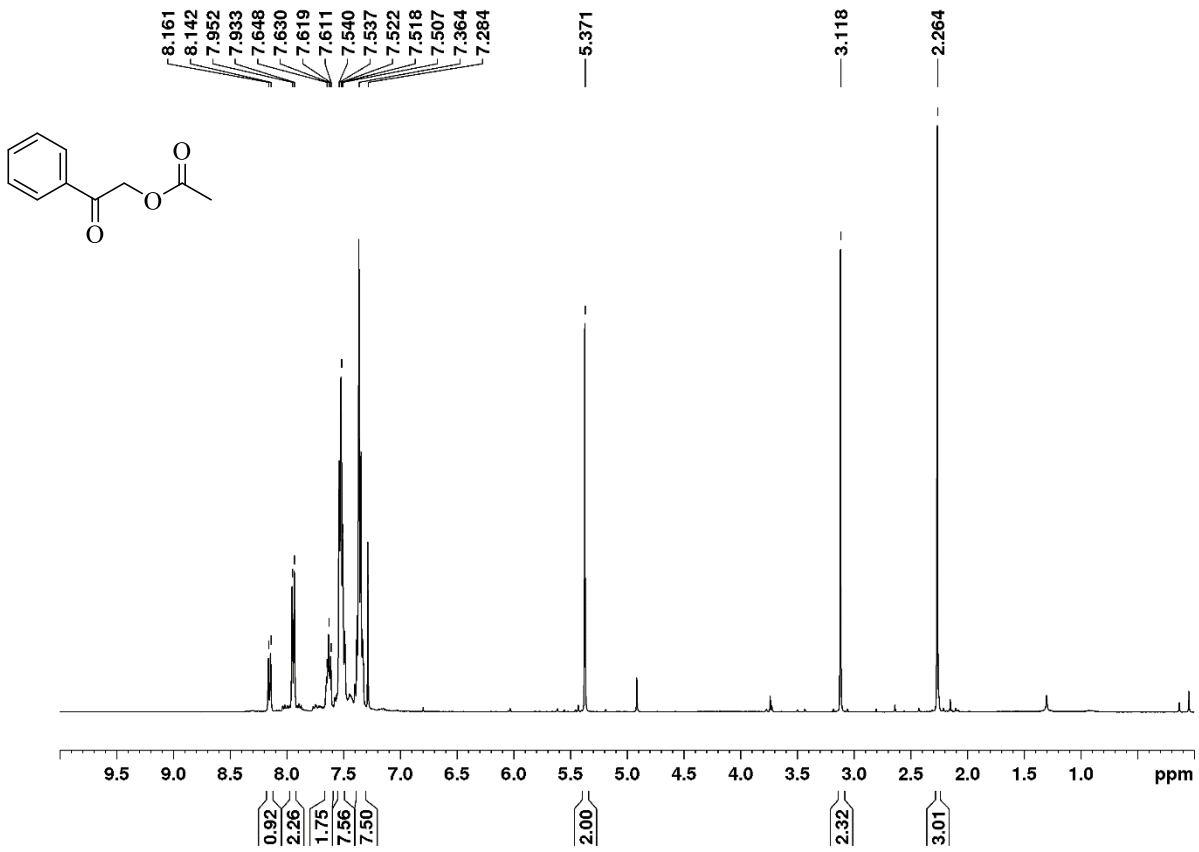


Figure 4. ^{1}H NMR spectrum for product 11 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - α-acetoxy acetophenone (11), 89% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 5.37 (s, 2H), 7.36-7.50 (m, 2H), 7.52-7.95 (m, 1H), 8.16 (d, 2H)

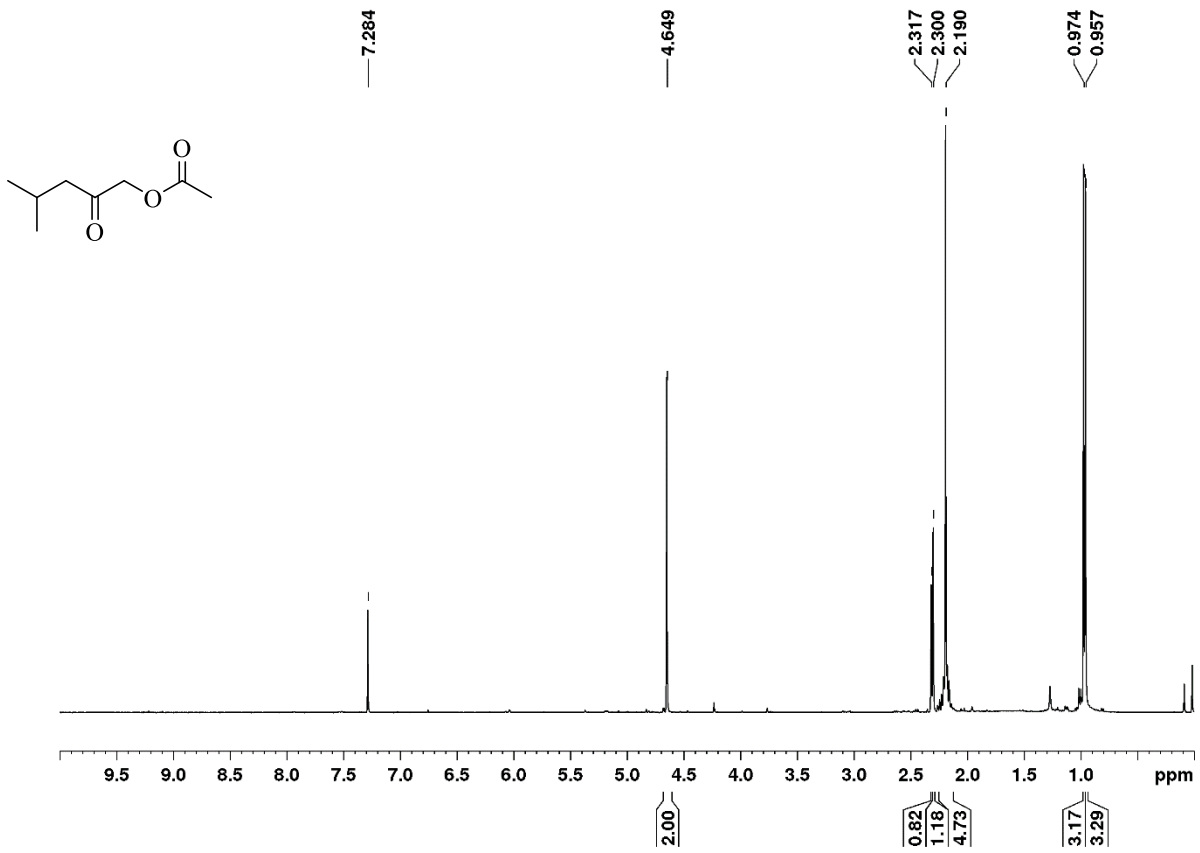


Figure 5. ^{1}H NMR spectrum for product 12 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 4-methyl-2-oxopentyl acetate (12), 62% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (s, 6H), 1.99 (m, 1H – methine - very small peak), 2.19 (s, 3H), 2.31 (d, 2H), 4.65 (s, 3H).

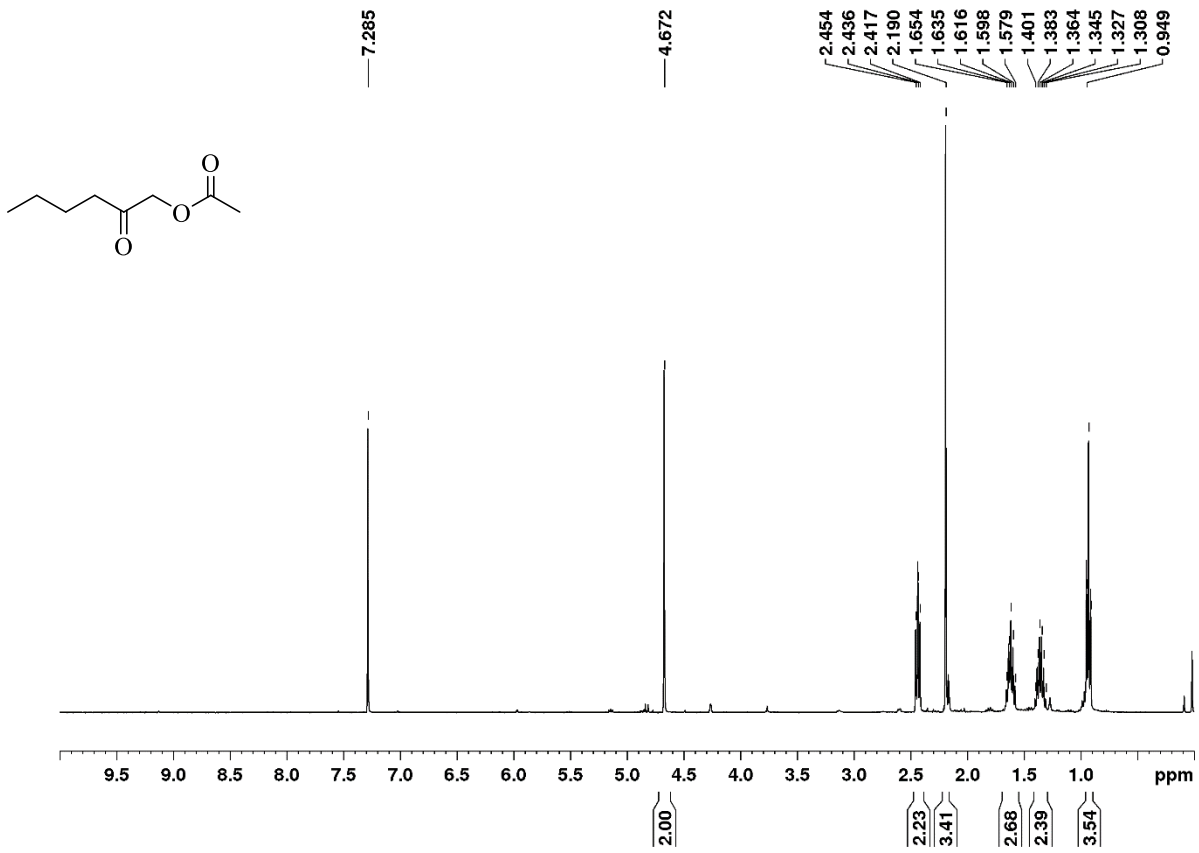


Figure 6. ^{1}H NMR spectrum for product 13 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxohexyl acetate (13), 76% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (t, 3H), 1.35 (m, 2H), 1.58 (m, 2H), 2.19 (s, 3H), 2.44 (t, 2H), 4.67 (s, 2H).

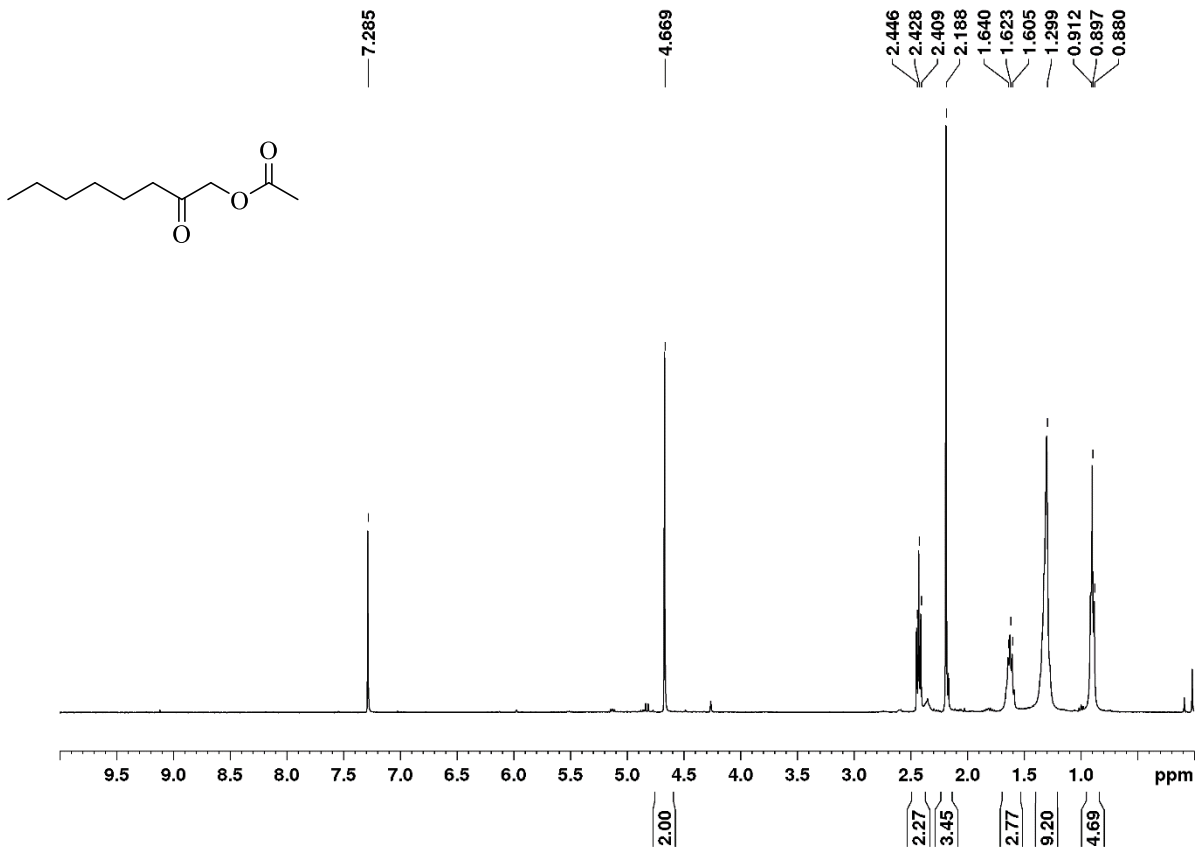


Figure 7. ^{1}H NMR spectrum for product 14 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxooctyl acetate (14), 78% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H), 1.30 (m, 6H), 1.61 (m, 2H), 2.19 (s, 3H), 2.43 (t, 2H), 4.67 (s, 2H).

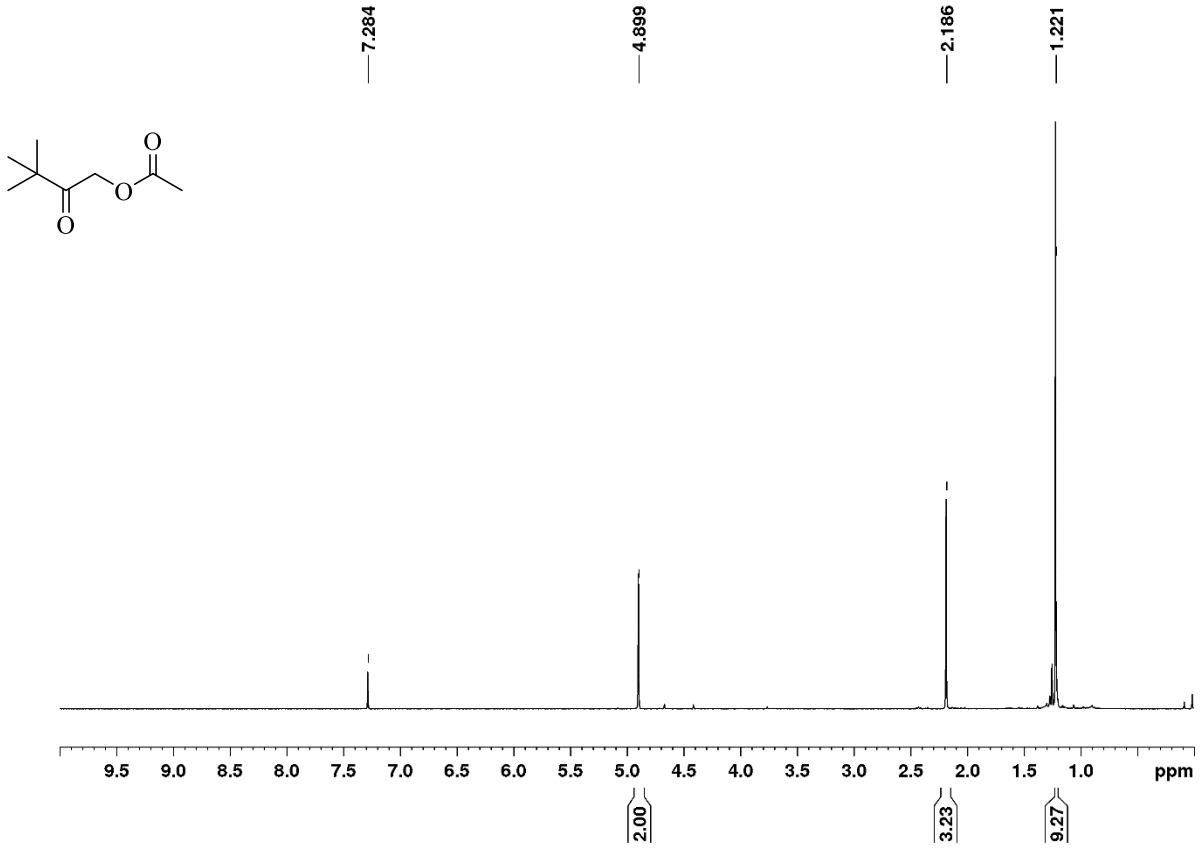


Figure 8. ^{1}H NMR spectrum for product 15 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 3,3-dimethyl-2-oxobutyl acetate (15), 74% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (s, 9H), 2.19 (s, 3H), 4.90 (s, 2H).

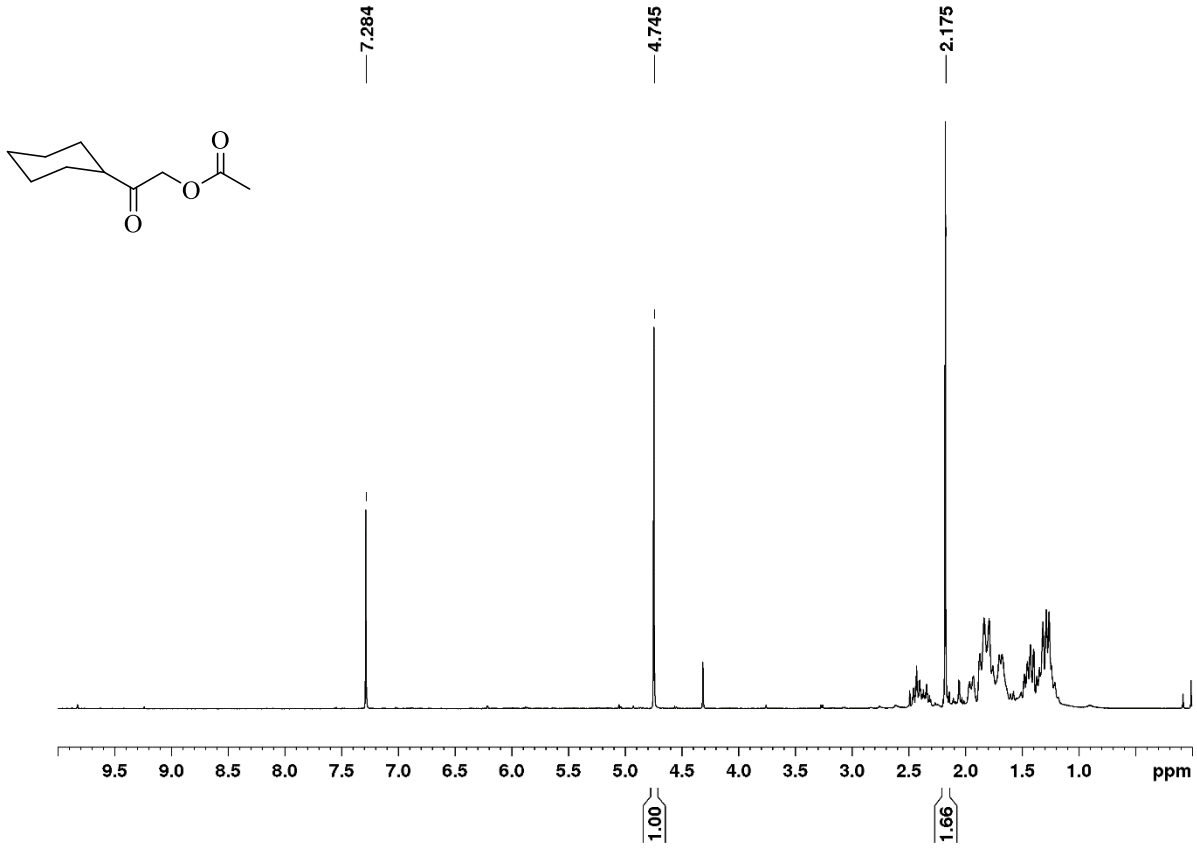


Figure 9. ^{1}H NMR spectrum for product 16 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-cyclohexyl-2-oxoethyl acetate (16), 81% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32-1.98 (m, Cx group, 10H), 2.18 (s, 3H), 4.75 (s, 2H).

One-pot Method - Propionates

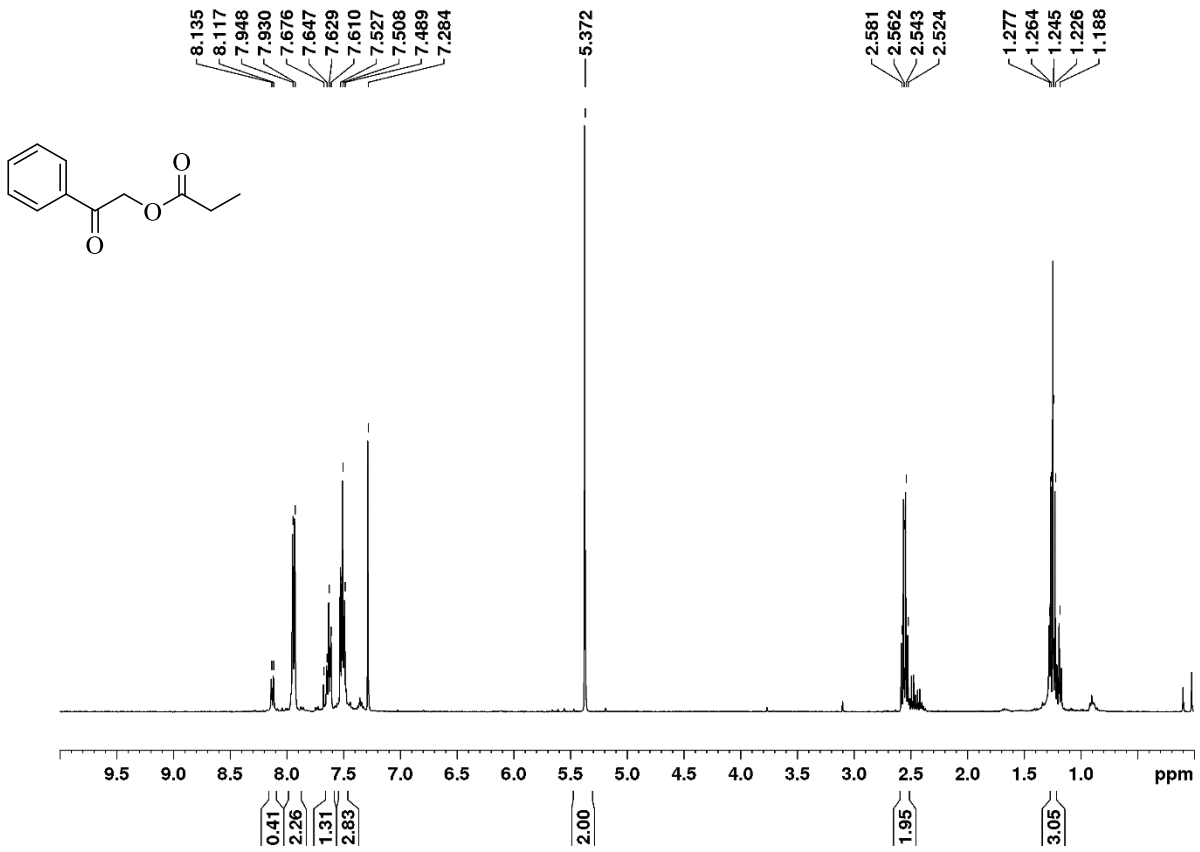


Figure 10. ^{1}H NMR spectrum for product 17 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxo-2-phenylethyl propionate (17), 75% yield.

^{1}H NMR (400 MHz, $CDCl_3$): 1.26 (t, 3H), 2.54 (q, 2H), 5.37 (s, 2H), 7.28-8.14 (m, Ph group, 5H).

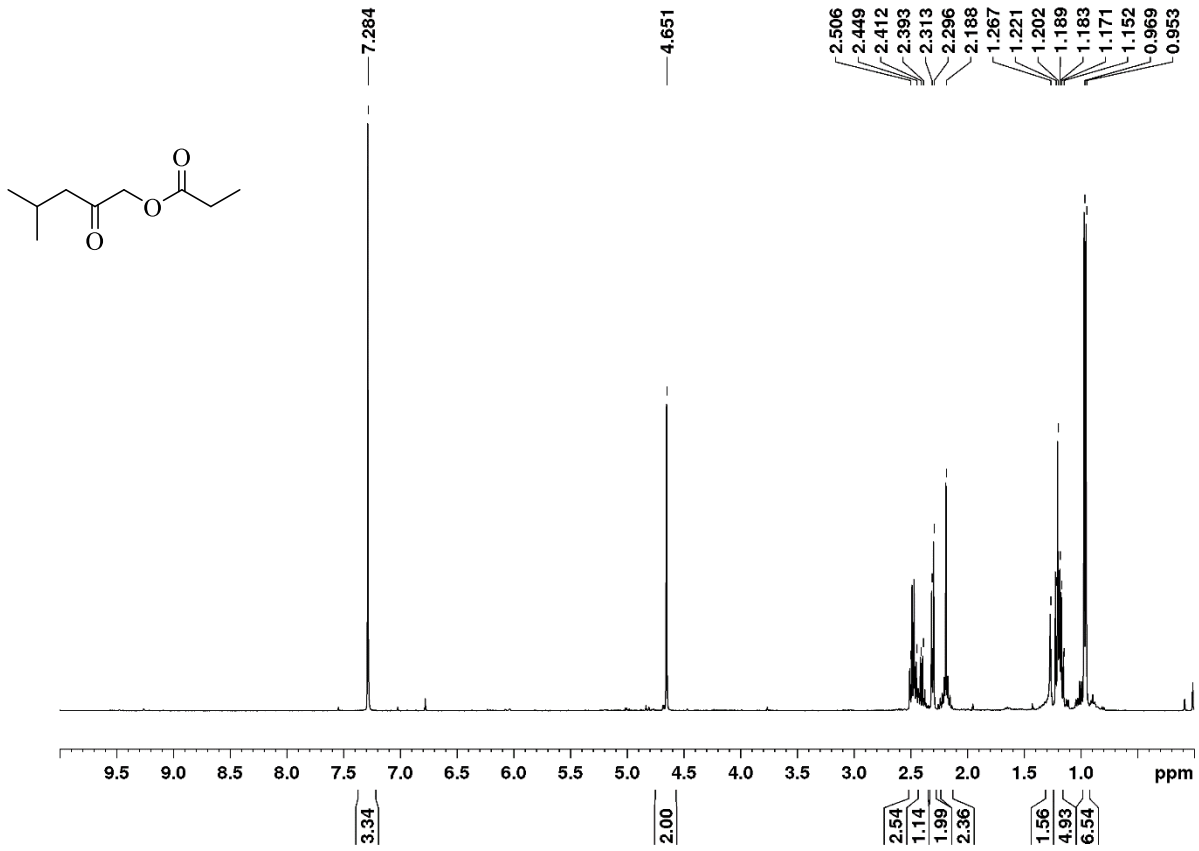


Figure 11. ^{1}H NMR spectrum for product 18 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 4-methyl-2-oxopentyl propionate (18), 85% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (d, 6H), 1.22 (t, 3H), 2.19 (m, 1H), 2.31-2.51 (m, 4H),

4.65 (s, 2H).

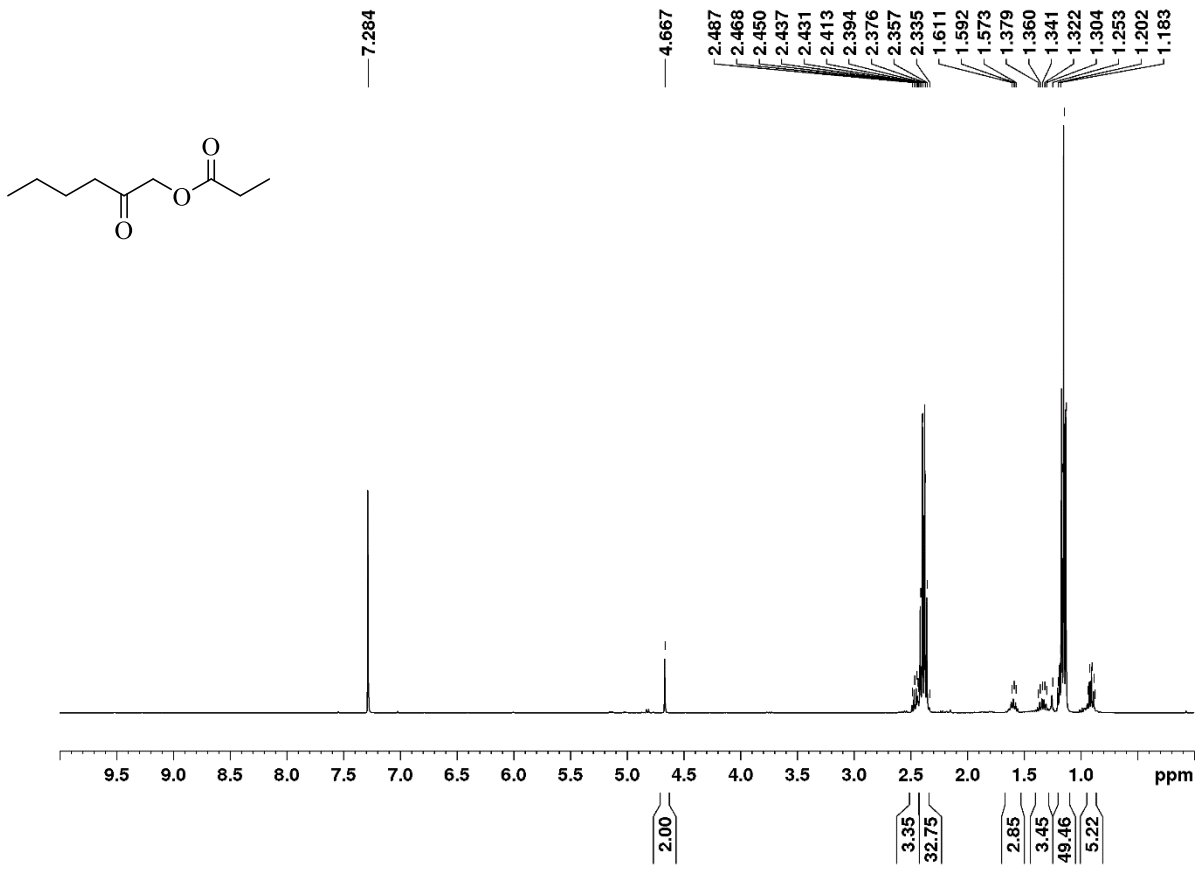


Figure 12. ^{1}H NMR spectrum for product 19 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxohexyl propionate (19), 79% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, 3H), 1.22 (t, 3H), 1.37 (m, 2H), 1.59 (m, 2H), 2.34-2.49 (m, 4H), 4.67 (s, 2H).

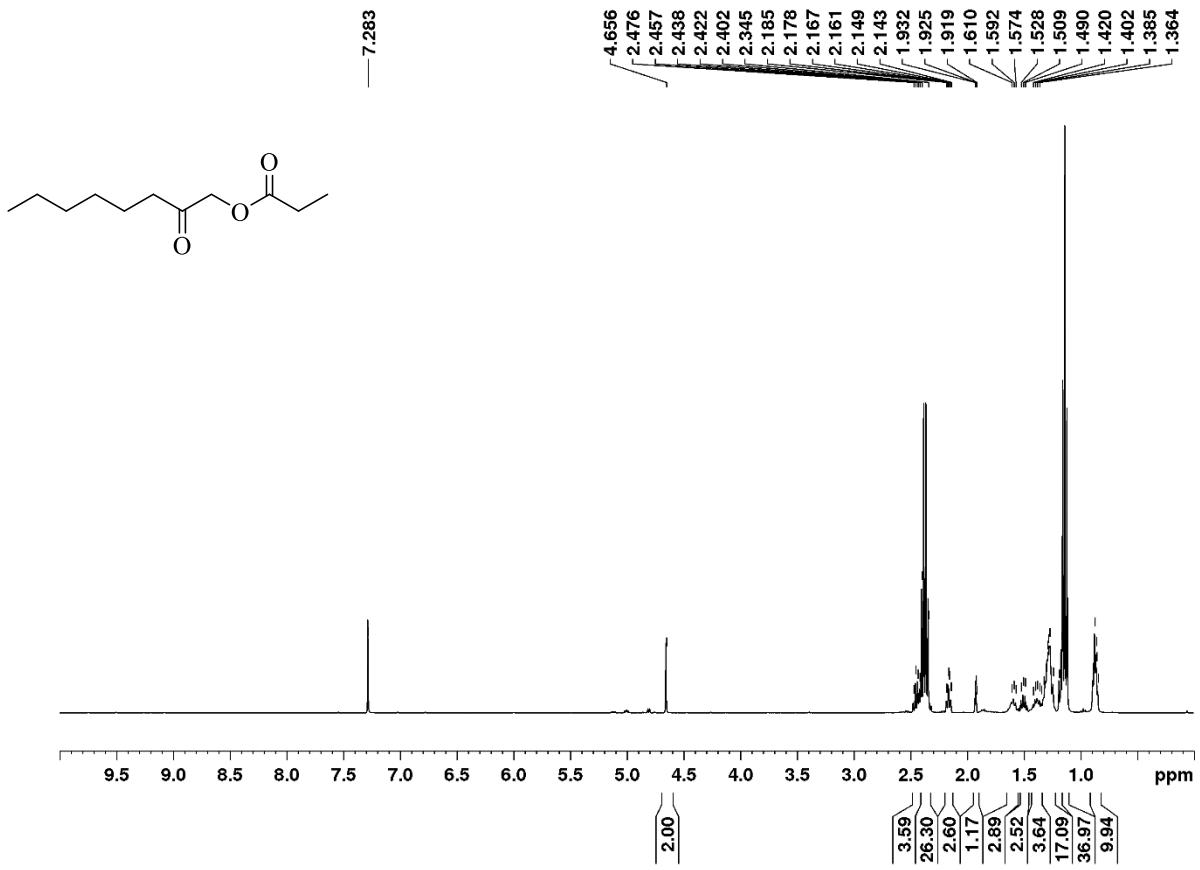


Figure 13. ^{1}H NMR spectrum for product 20 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxooctyl propionate (20), 77% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H), 1.21 (s, 3H), 1.40 (m, 6H), 1.58 (m, 2H), 2.46 (m, 4H), 4.66 (s, 2H).

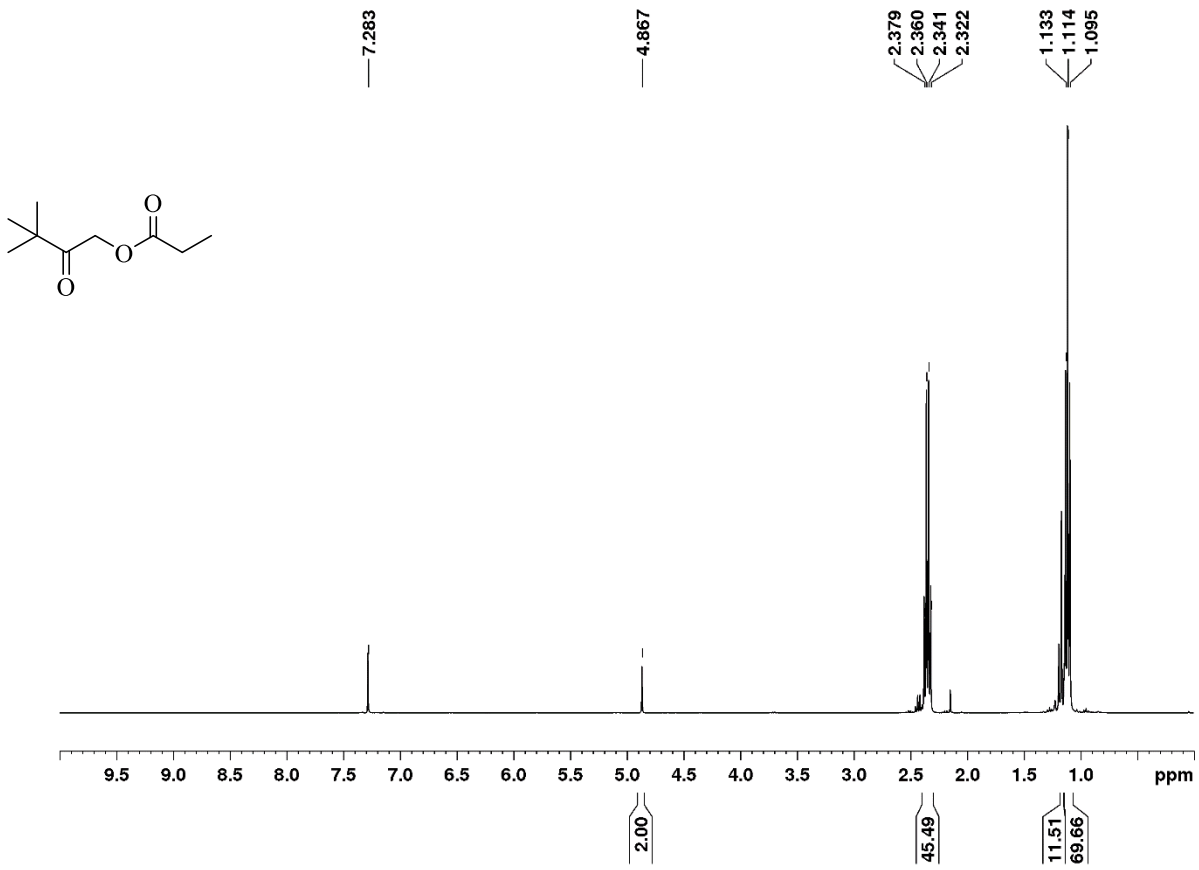


Figure 14. ^{1}H NMR spectrum for product 21 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 3,3-dimethyl-2-oxobutyl propionate (21), 70% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.12 (m, 12H), 2.36 (m, 2H), 4.87 (s, 2H)

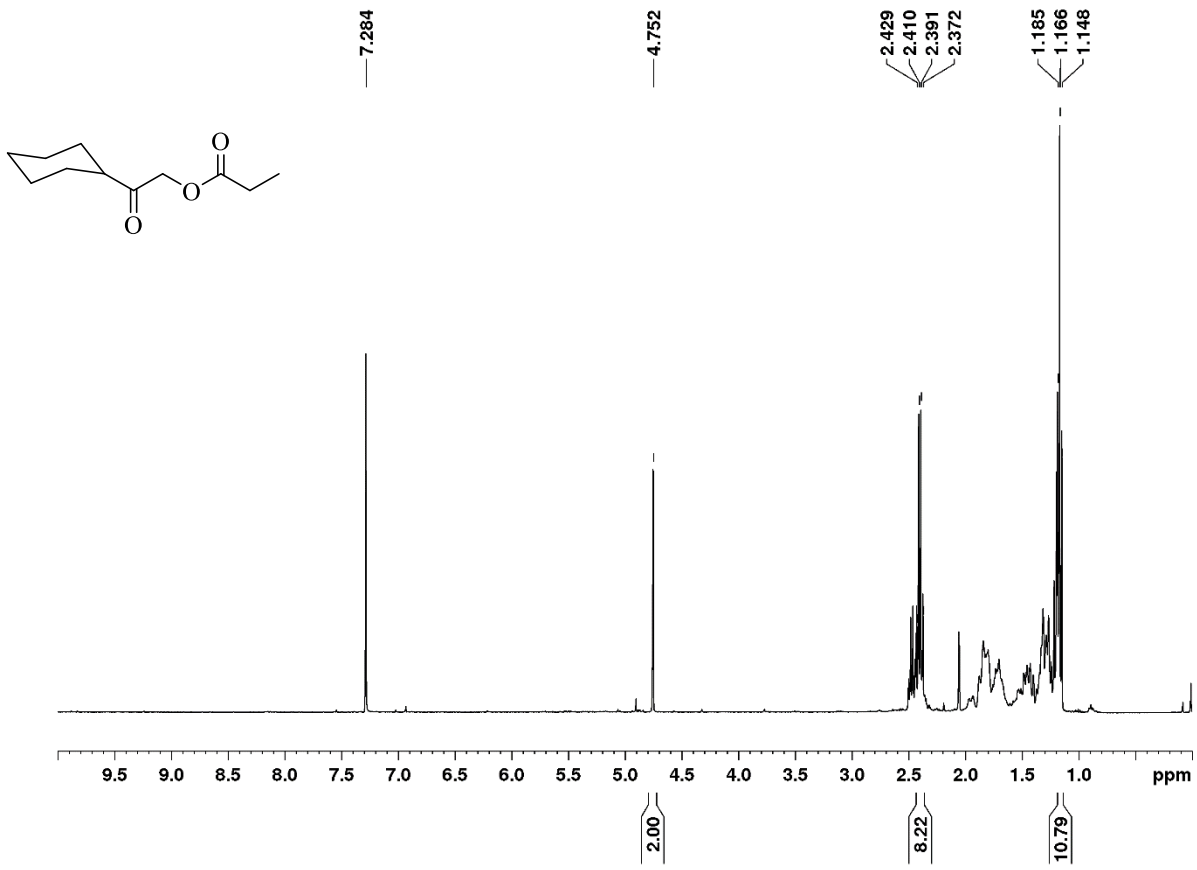


Figure 15. ^{1}H NMR spectrum for product 22 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-cyclohexyl-2-oxoethyl propionate (22), 74% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32-1.88 (m, Cx group, 10H and CH_3), 2.42 (m, 2H), 4.75 (s, 2H)

One-pot Method - Chloroacetates

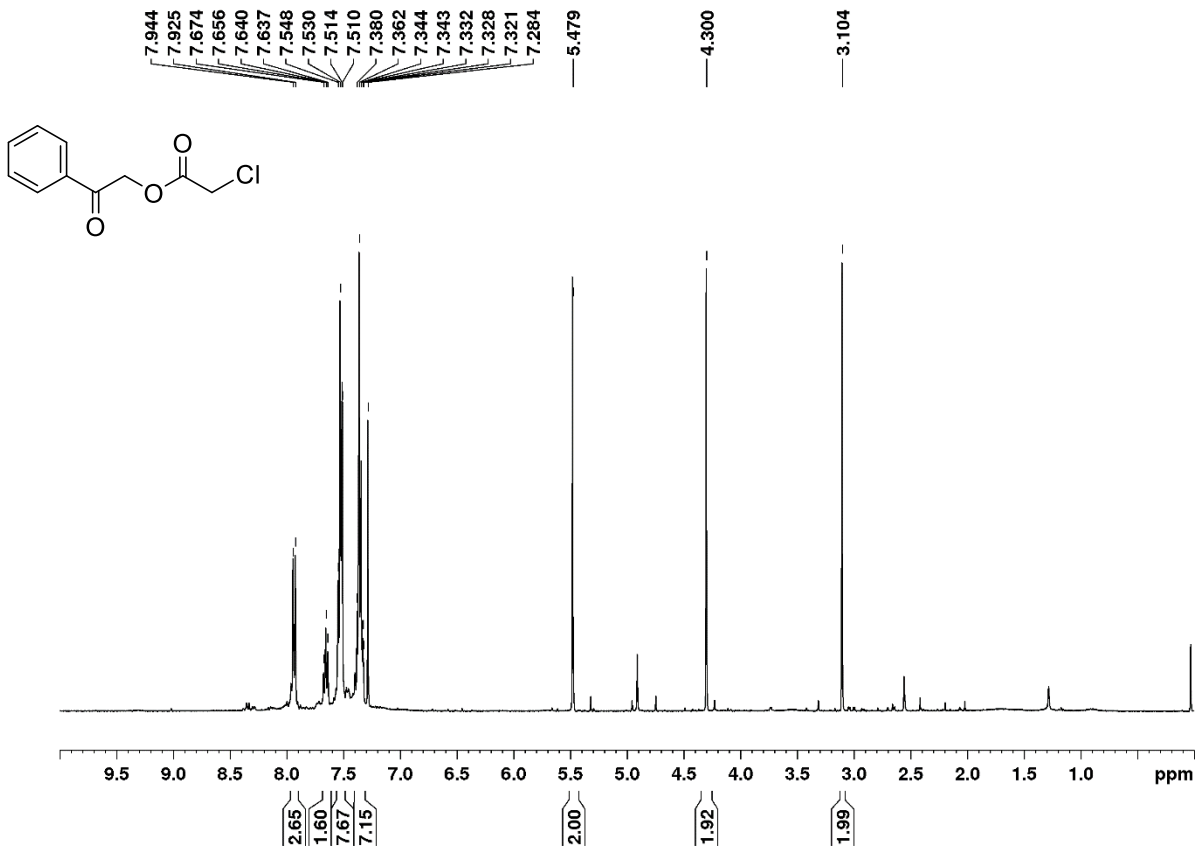


Figure 16. ^{1}H NMR spectrum for product 23 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxo-2-phenylethyl chloroacetate (23), 44% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30 (s, 2H), 5.48 (s, 2H) 7.28-7.94 (m, Ph group, 5H).

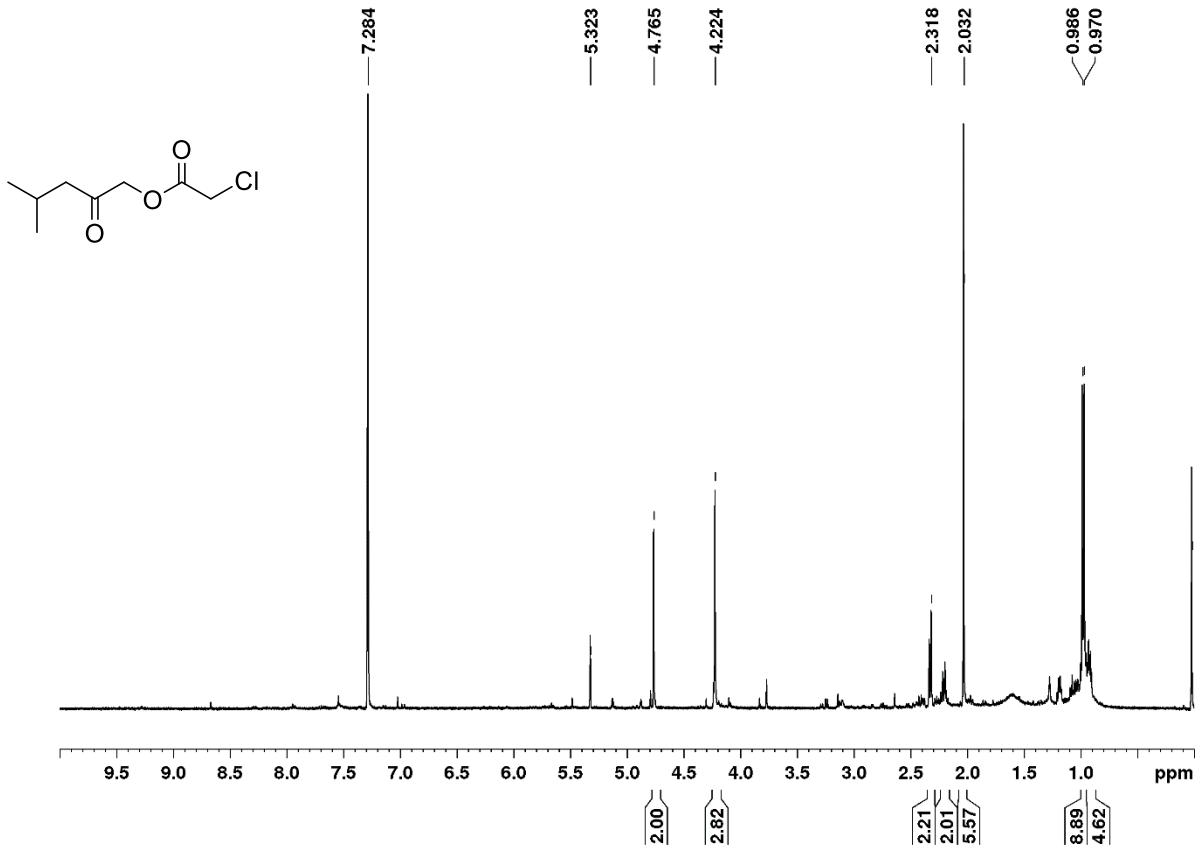


Figure 17. ^{1}H NMR spectrum for product 24 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 4-methyl-2-oxopentyl chloroacetate (24), 56% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (d, 6H), 2.03 (m, 1H), 2.32 (d, 2H), 4.22 (s, 2H), 4.76 (s, 2H).

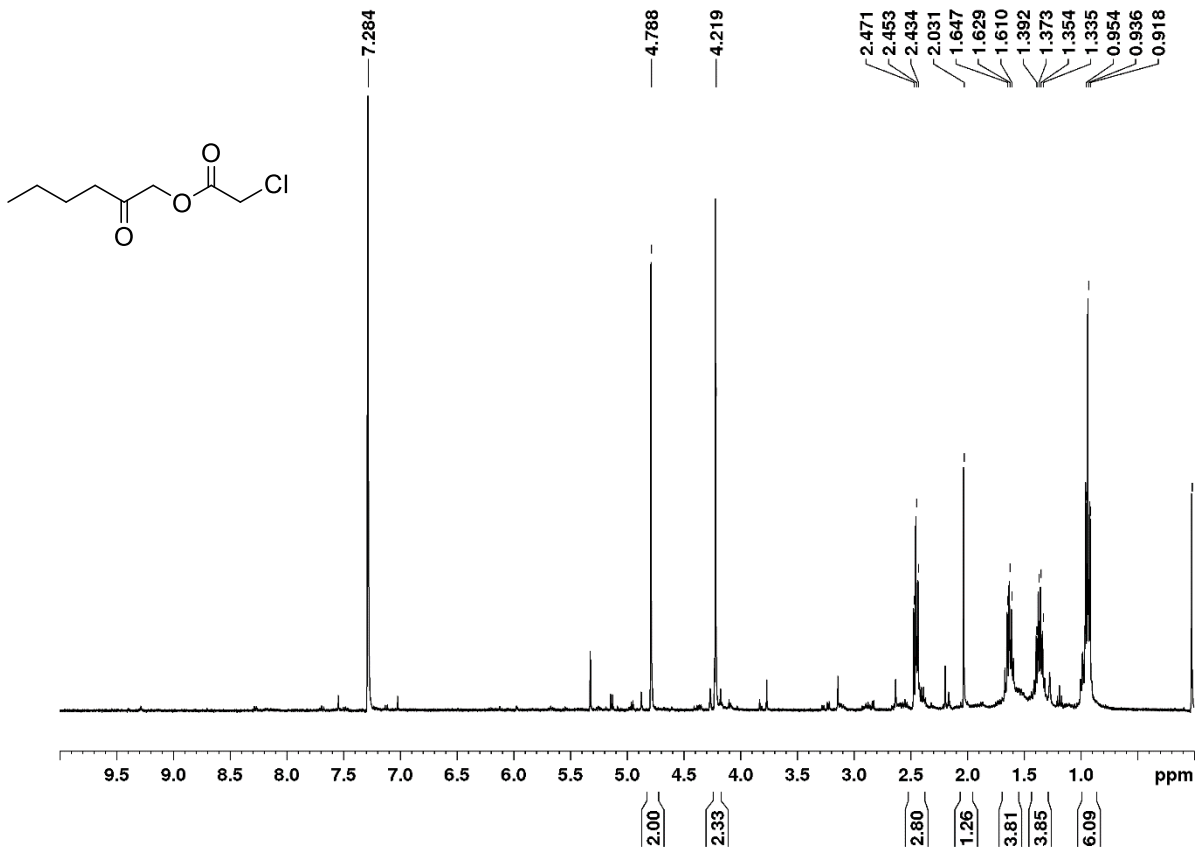


Figure 18. ^{1}H NMR spectrum for product 25 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxohexyl chloroacetate (25), 55% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (t, 3H), 1.37 (m, 2H), 1.61 (m, 2H), 2.46 (t, 2H), 4.22 (s, 2H), 4.79 (s, 2H).

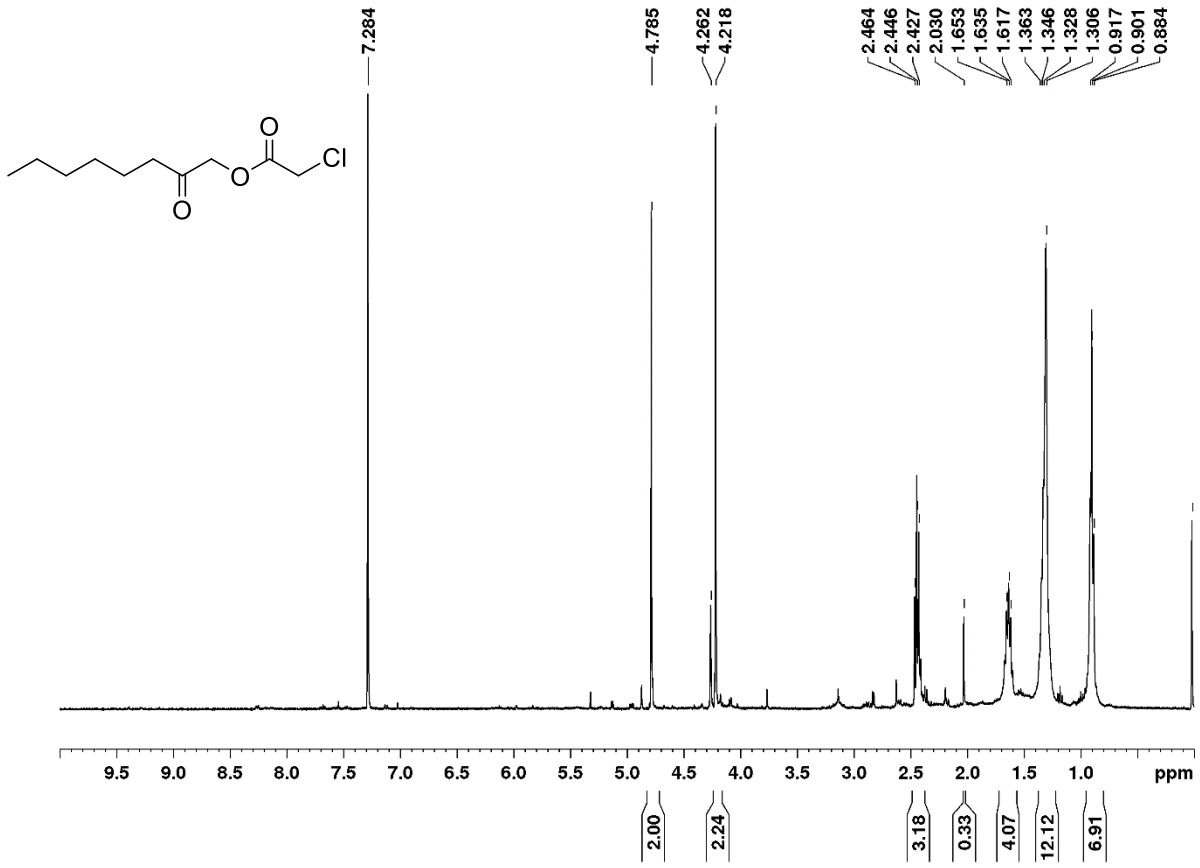


Figure 19. ^{1}H NMR spectrum for product 26 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxooctyl chloroacetate (26), 52% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H), 1.33 (m, 6H), 1.62 (m, 2H), 2.45 (m, 2H), 4.21 (s, 2H), 4.79 (s, 2H).

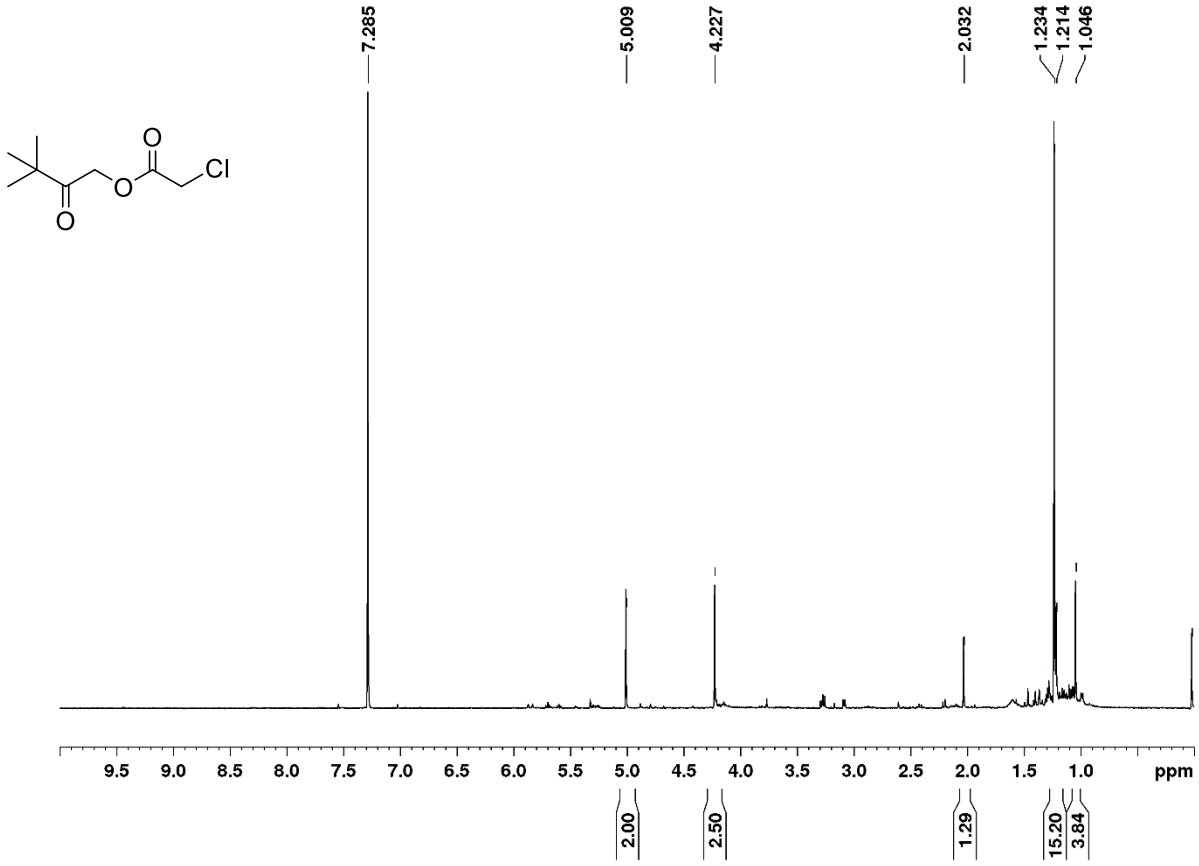


Figure 20. ^{1}H NMR spectrum for product 27 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 3,3-dimethyl-2-oxobutyl chloroacetate (27), 43% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (s, 9H), 4.23 (s, 2H), 5.01 (s, 2H).

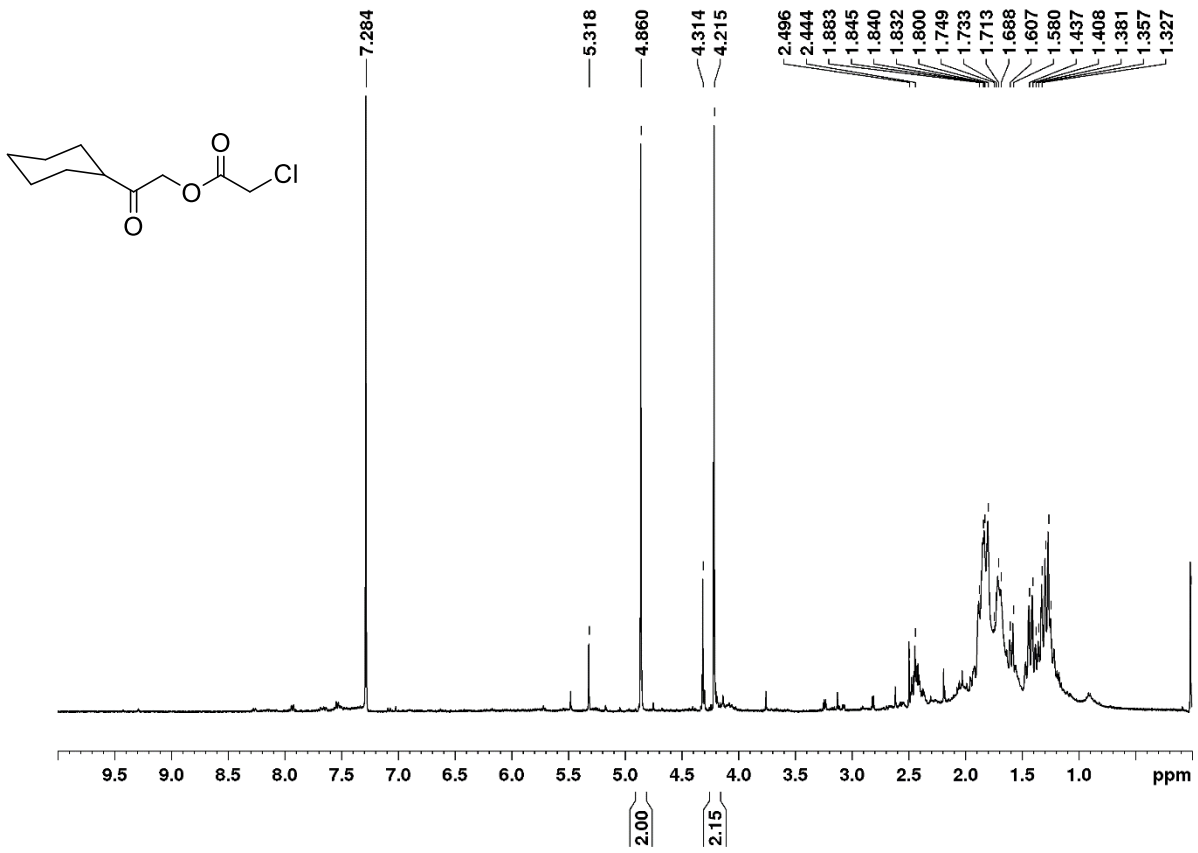


Figure 21. ^{1}H NMR spectrum for product 28 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-cyclohexyl-2-oxoethyl chloroacetate (28), 48% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32-1.88 (m, Cx group, 10H), 4.21 (s, 2H), 4.86 (s, 2H).

One-pot Method - Methoxyacetates

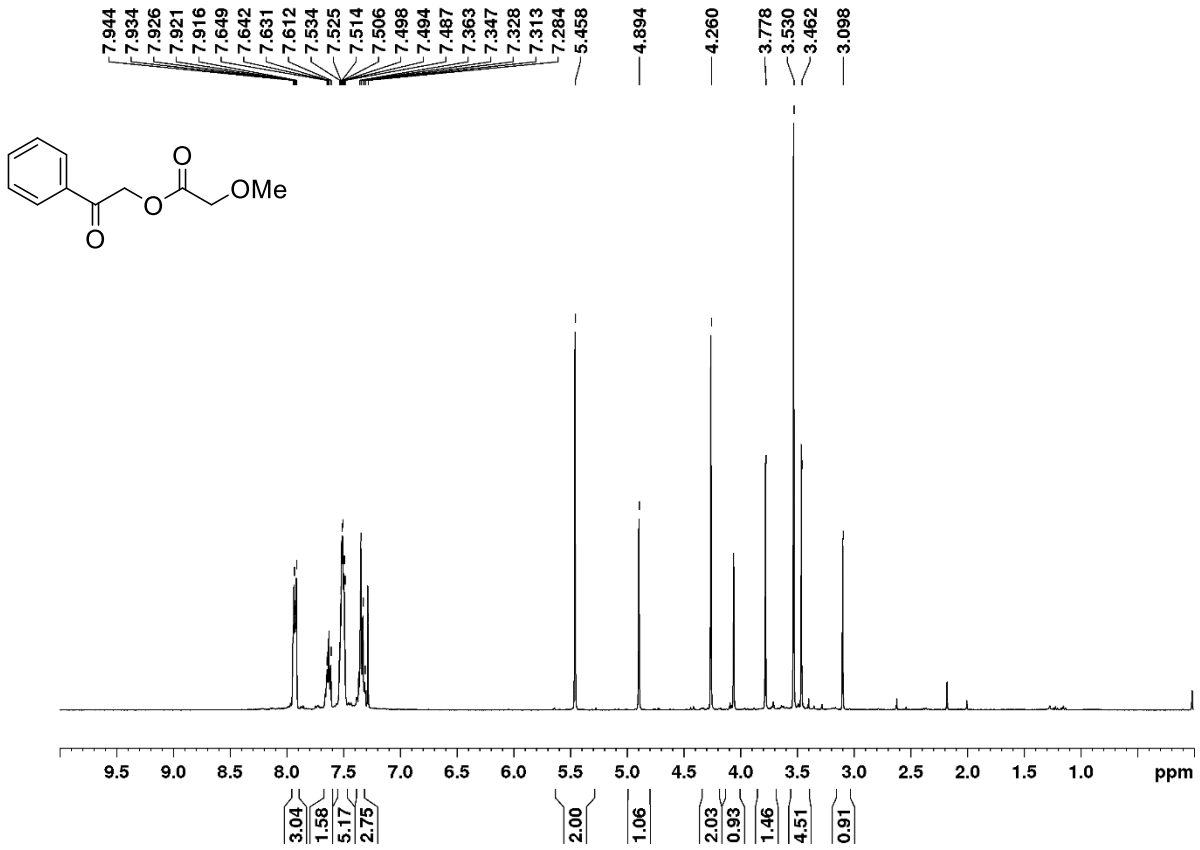


Figure 22. ^{1}H NMR spectrum for product 29 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxo-2-phenylethyl methoxyacetate (29), 75% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.53 (s, 3H), 4.26 (s, 2H), 5.46 (s, 2H) 7.28-8.01 (m, Ph group, 5H).

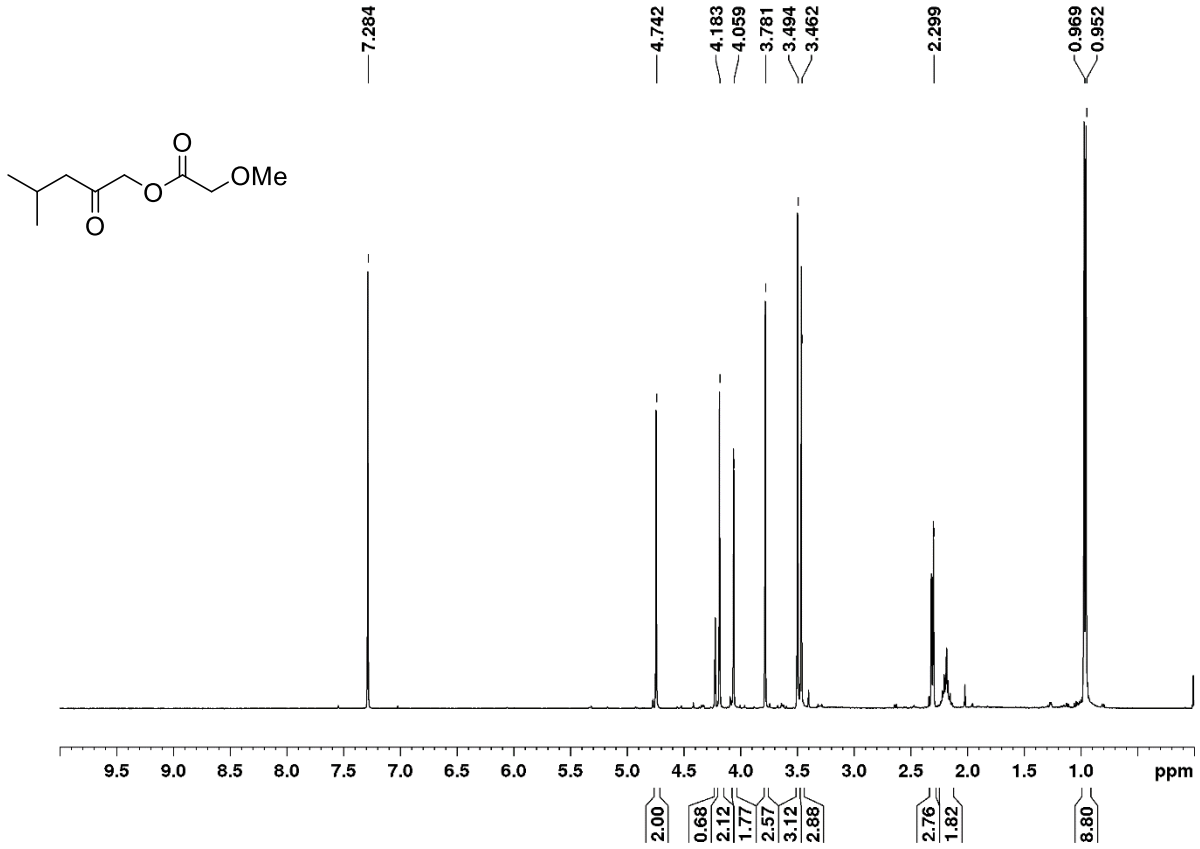


Figure 23. ^{1}H NMR spectrum for product 30 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 4-methyl-2-oxopentyl methoxyacetate (30), 42% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (d, 6H), 1.99 (m, 1H), 2.38 (d, 2H), 3.47 (s, 3H), 4.25 (s, 2H), 4.74 (s, 2H)

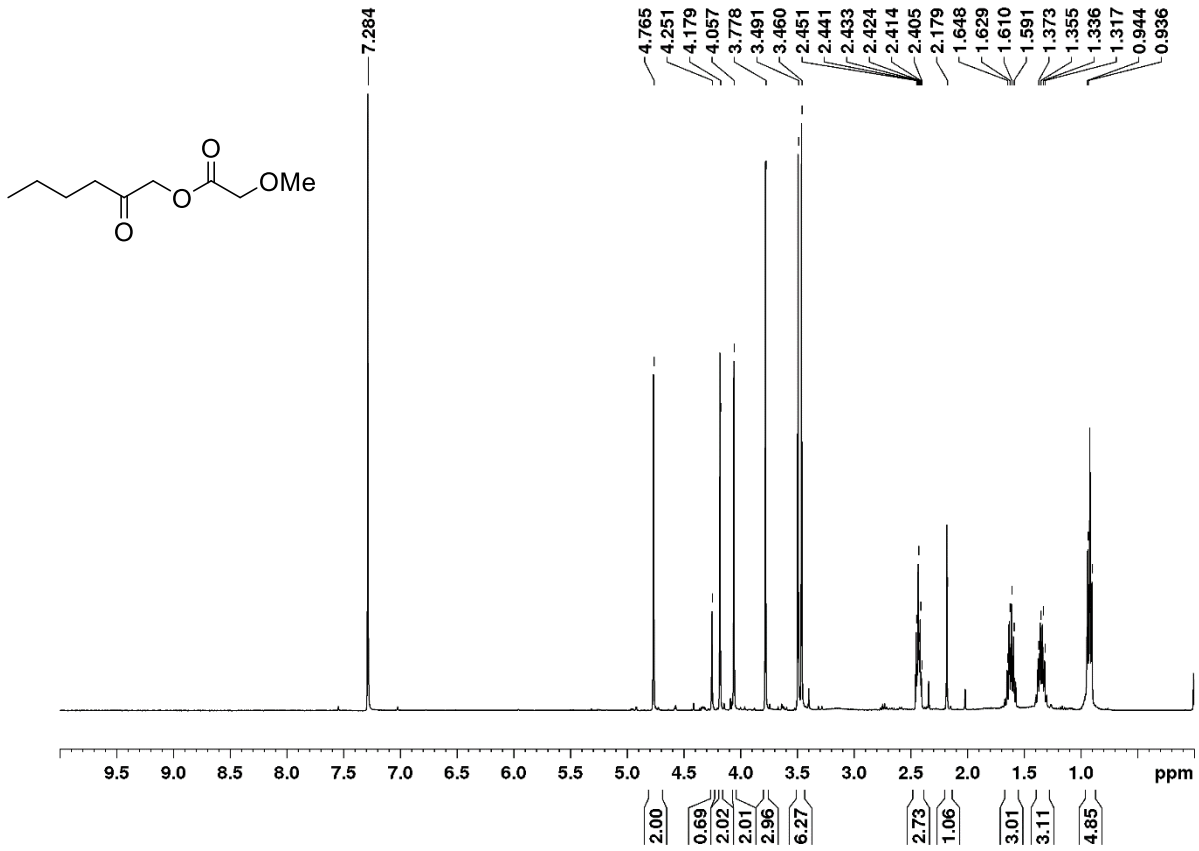


Figure 24. ^{1}H NMR spectrum for product 31 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxohexyl methoxyacetate (31), 57% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (t, 3H), 1.30-1.39 (m, 2H), 1.50-1.62 (m, 2H), 2.42 (t, 2H), 3.47 (s, 3H), 4.25 (s, 2H), 4.76 (s, 2H).

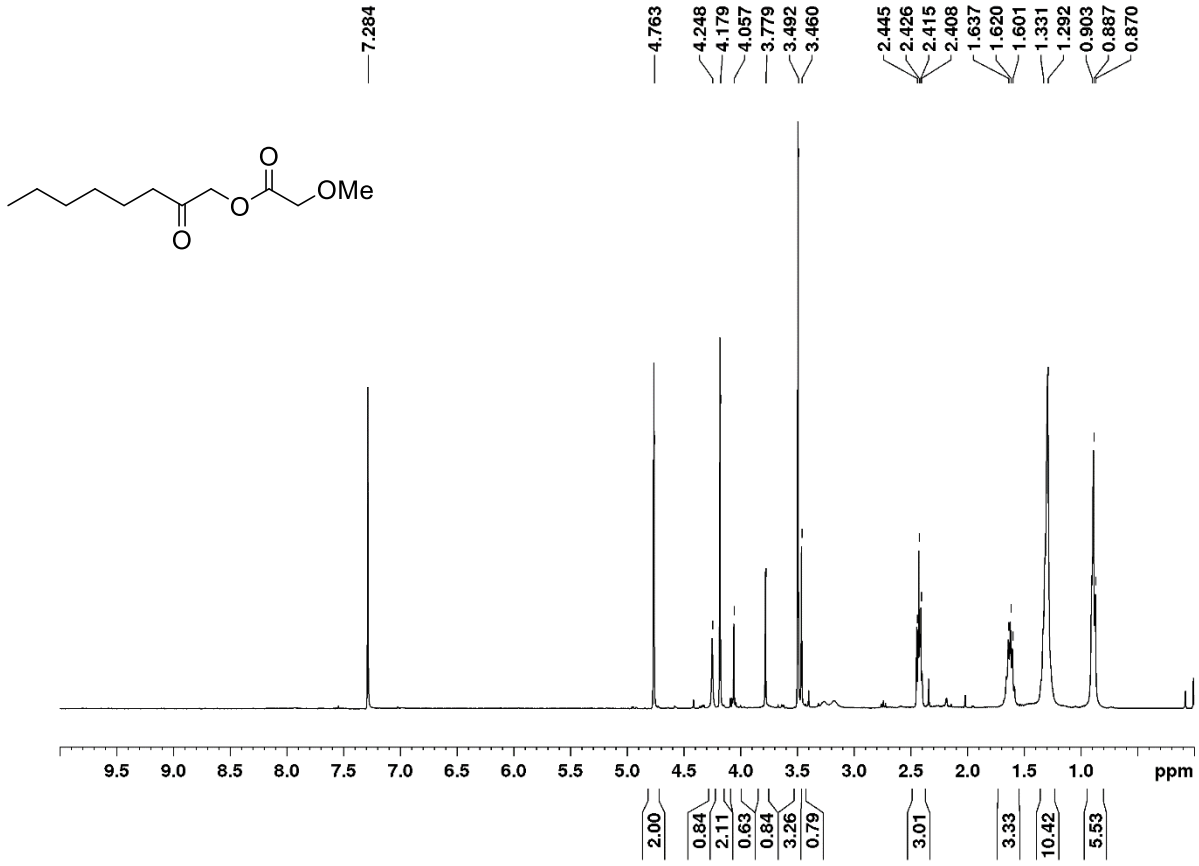


Figure 25. ^{1}H NMR spectrum for product 32 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxooctyl methoxyacetate (32), 42% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, 3H), 1.31 (m, 6H), 1.61 (m, 2H), 2.43 (t, 2H), 3.47 (s, 3H), 4.25 (s, 2H), 4.76 (s, 2H).

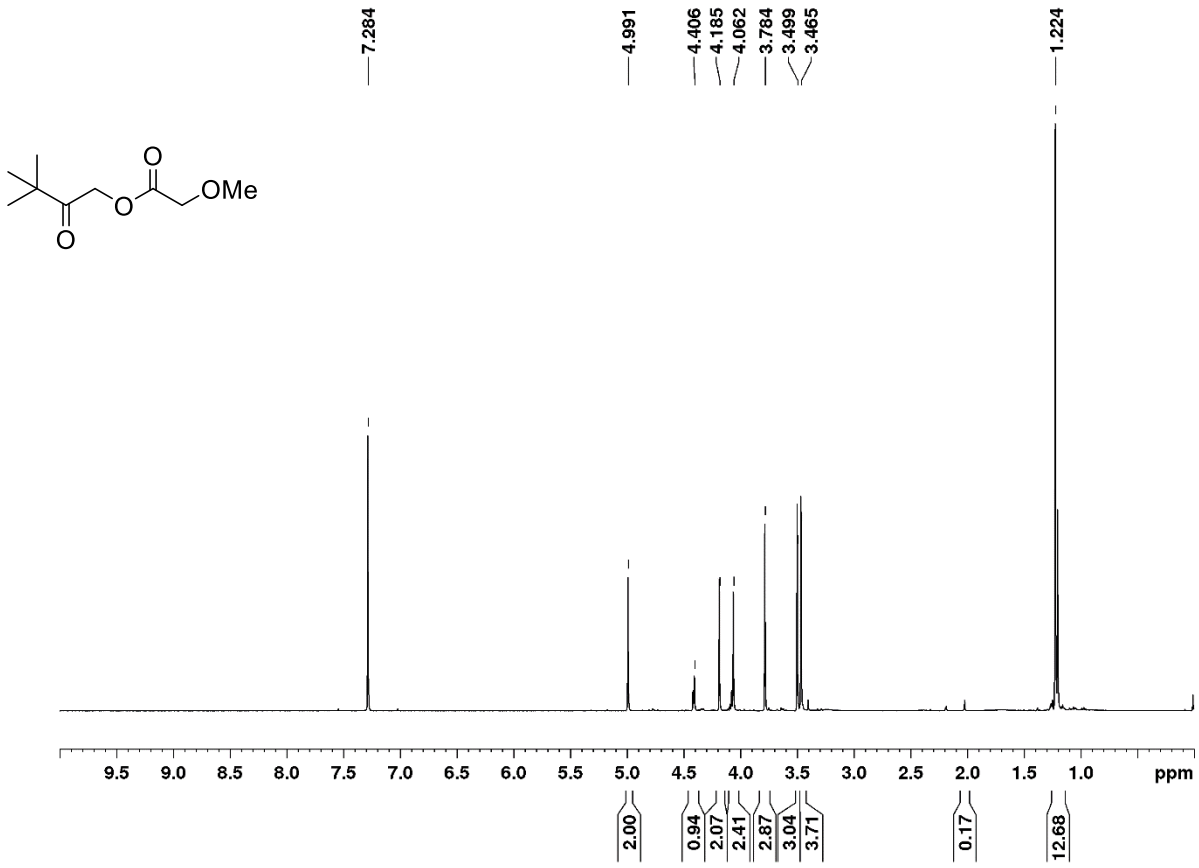


Figure 26. ^{1}H NMR spectrum for product 33 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 3,3-dimethyl-2-oxobutyl methoxyacetate (33), 39% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (s, 9H), 3.49 (s, 3H), 4.40 (s, 2H), 4.99 (s, 2H).

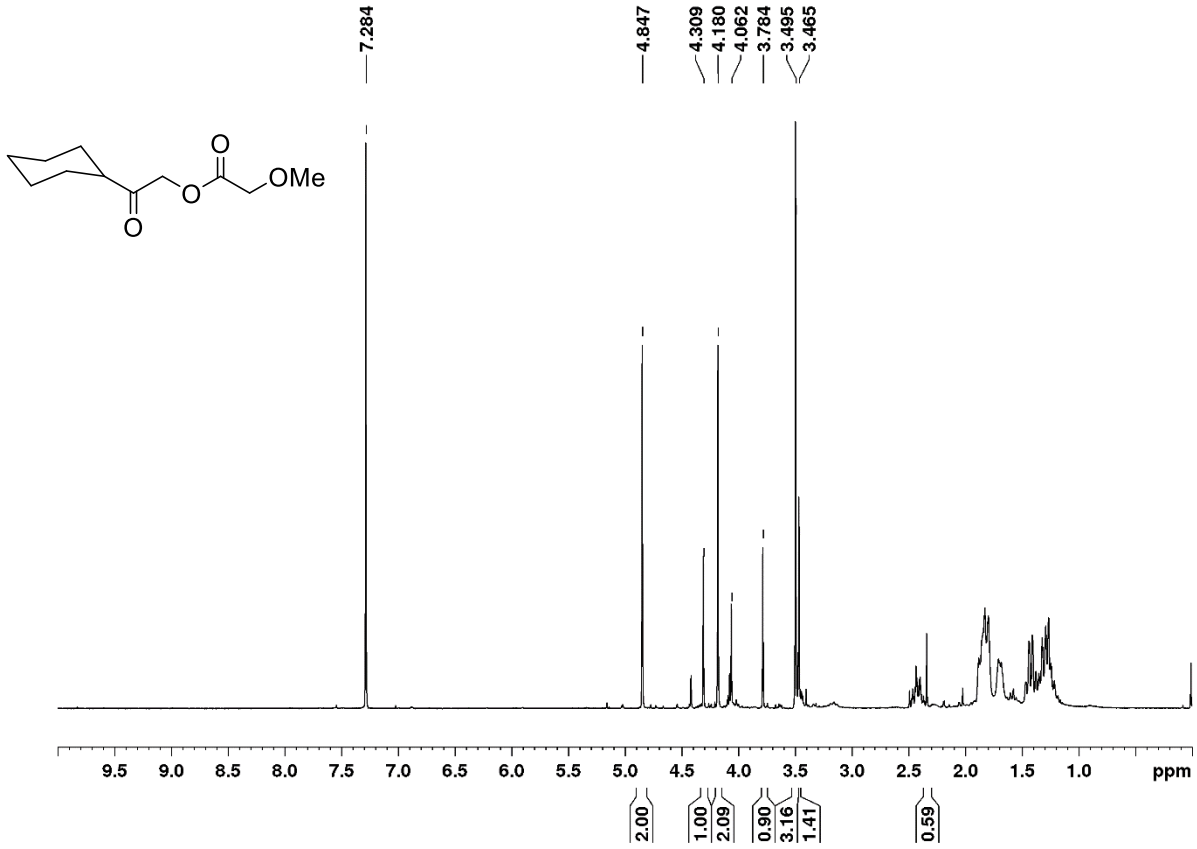


Figure 27. ^{1}H NMR spectrum for product 34 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-cyclohexyl-2-oxoethyl methoxyacetate (34), 42% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00-2.00 (m, Cx group, 10H), 3.50 (s, 3H), 4.30 (s, 2H), 4.85 (s, 2H).

One-pot Method - Trifluoroacetates

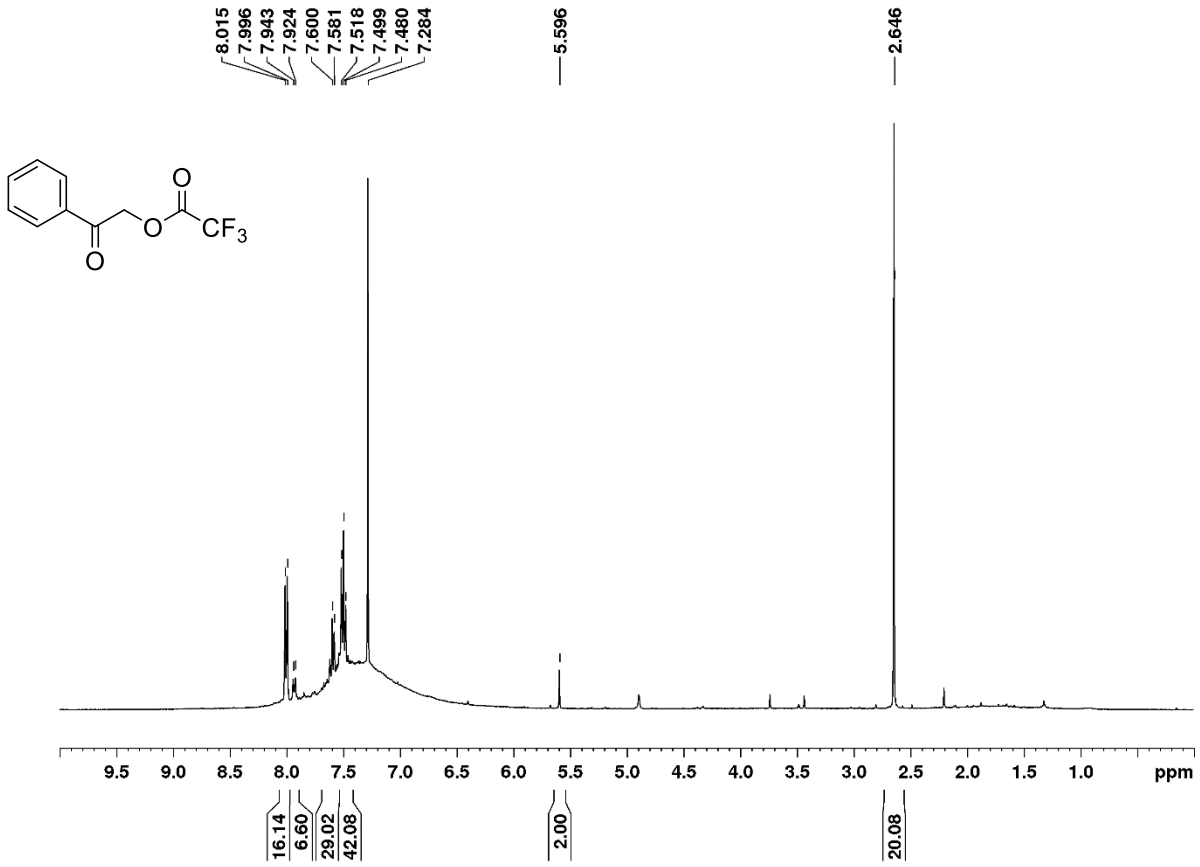


Figure 28. ^{1}H NMR spectrum for product 35 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxo-2-phenylethyl trifluoroacetate (35), 84% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.60 (s, 2H) 7.28-8.01 (m, Ph group, 5H).

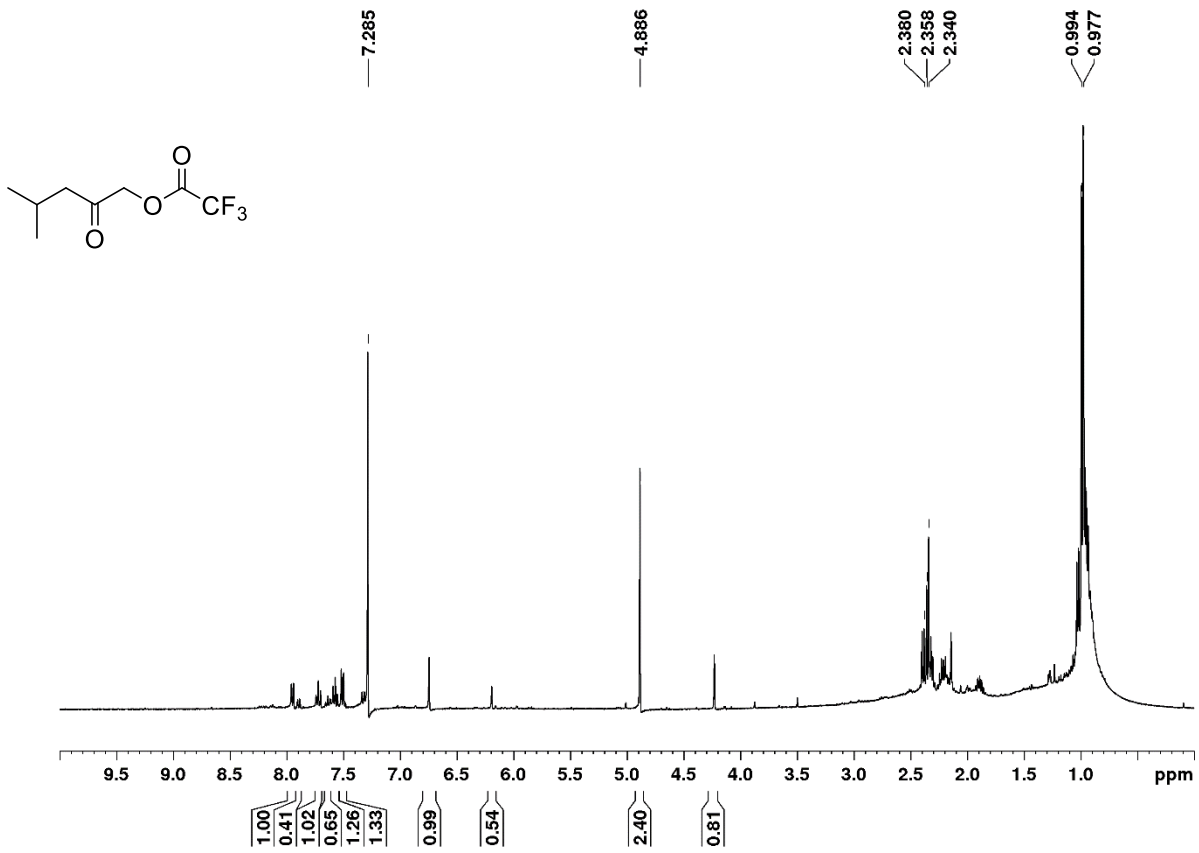


Figure 29. ^{1}H NMR spectrum for product 36 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 4-methyl-2-oxopentyl trifluoroacetate (36), 43% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (d, 6H), 1.99 (m, 1H), 2.38 (d, 2H), 4.89 (s, 2H)

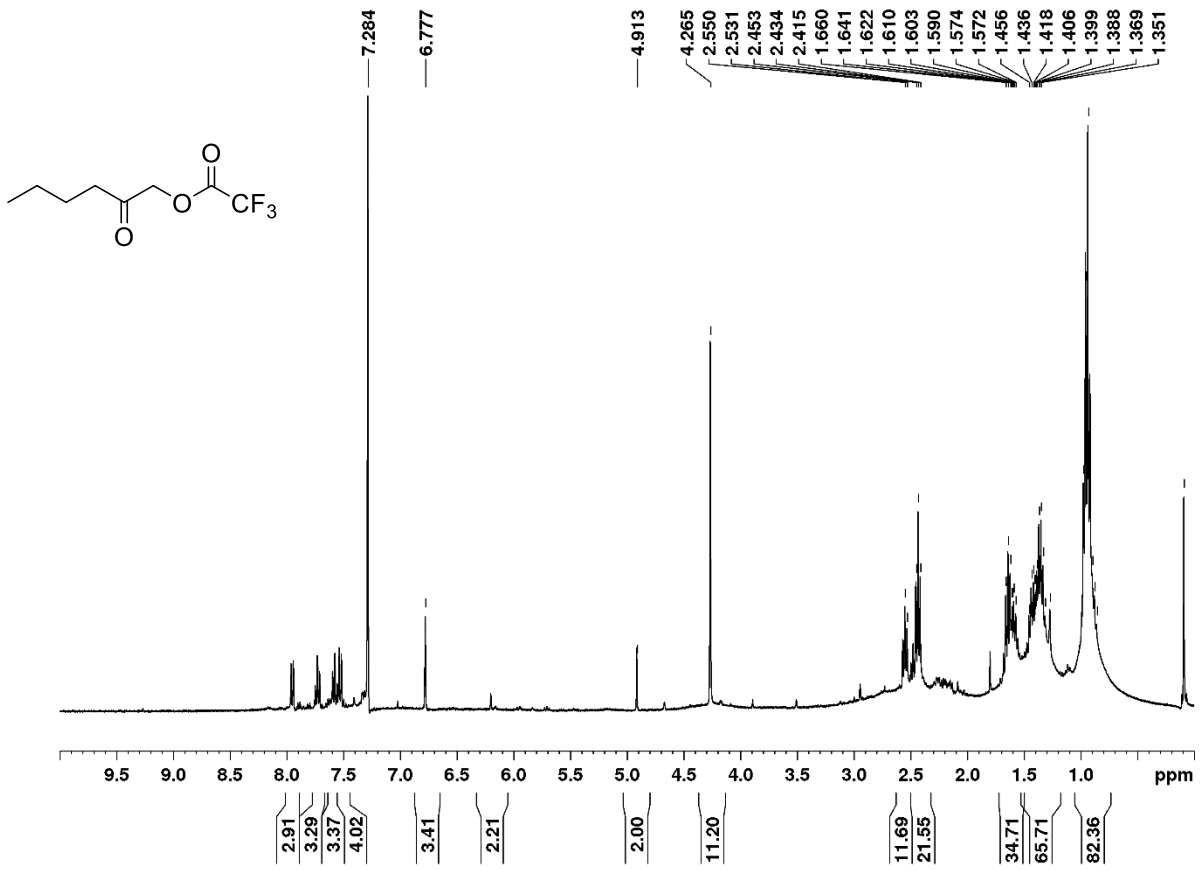


Figure 30. ^{1}H NMR spectrum for product 37 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxohexyl trifluoroacetate (37), 60% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, 3H), 1.38 (m, 2H), 1.58 (m, 2H), 2.45 (t, 2H), 4.91 (s, 2H).

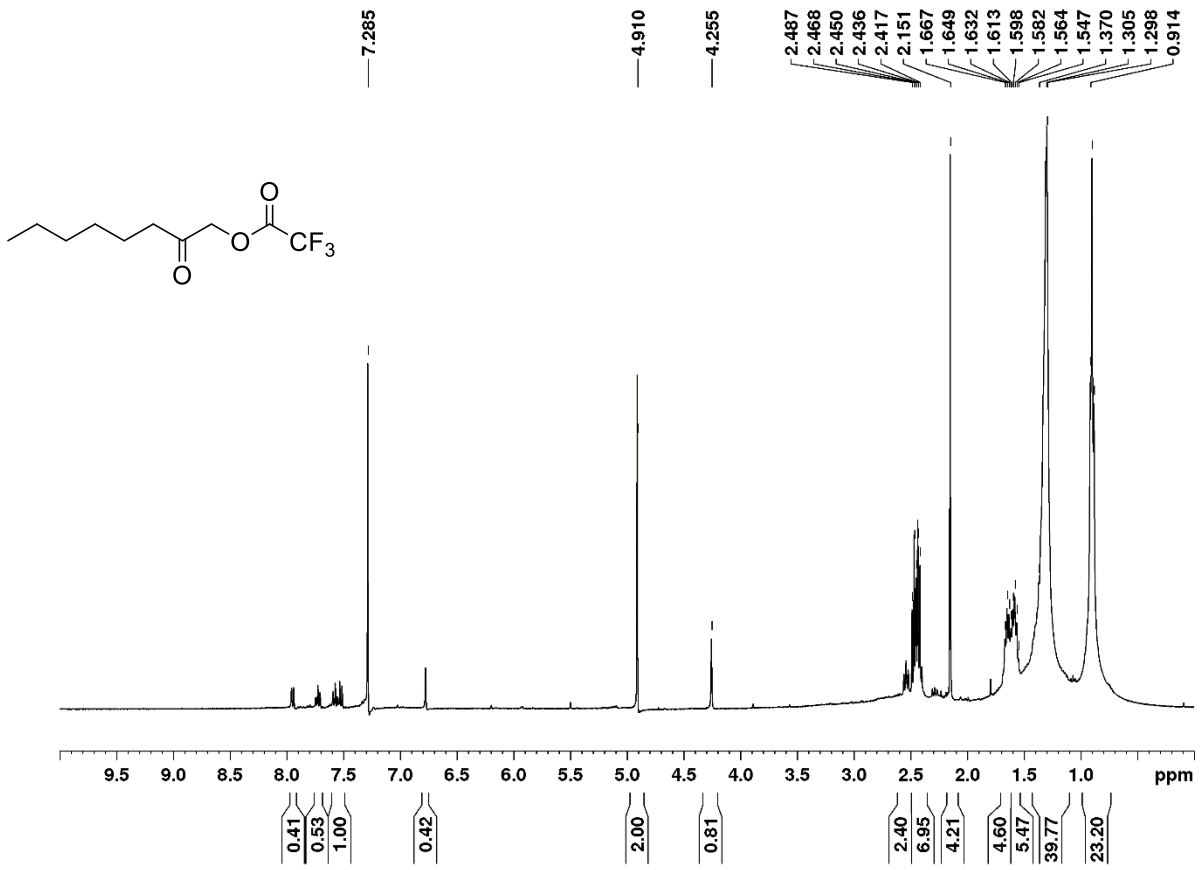


Figure 31. ^{1}H NMR spectrum for product 38 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-oxooctyl trifluoroacetate (38), 59% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, 3H), 1.31 (m, 6H), 1.55 (m, 2H), 2.45 (m, 2H), 4.91 (s, 2H)

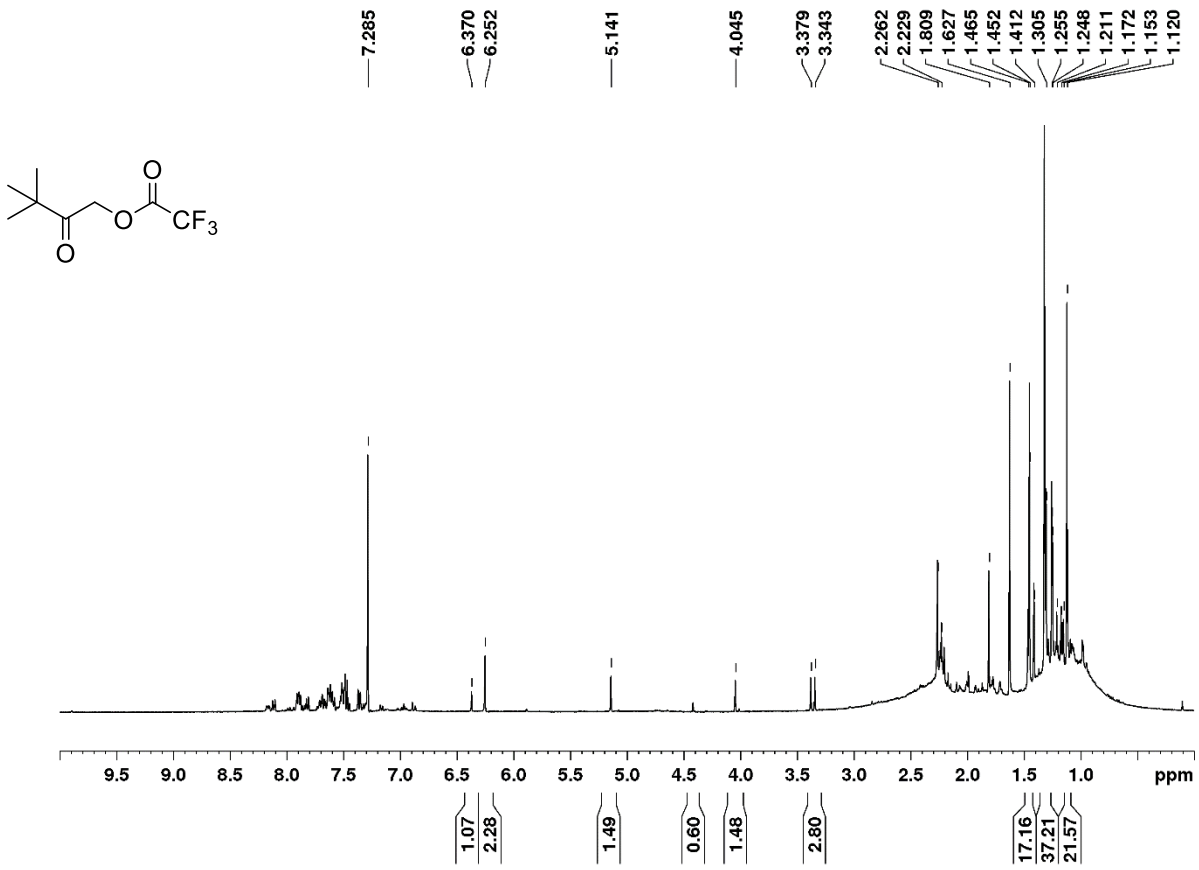


Figure 32. ^{1}H NMR spectrum for product 39 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 3,3-dimethyl-2-oxobutyl trifluoroacetate (39), 44% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (s, 9H), 5.14 (s, 2H)

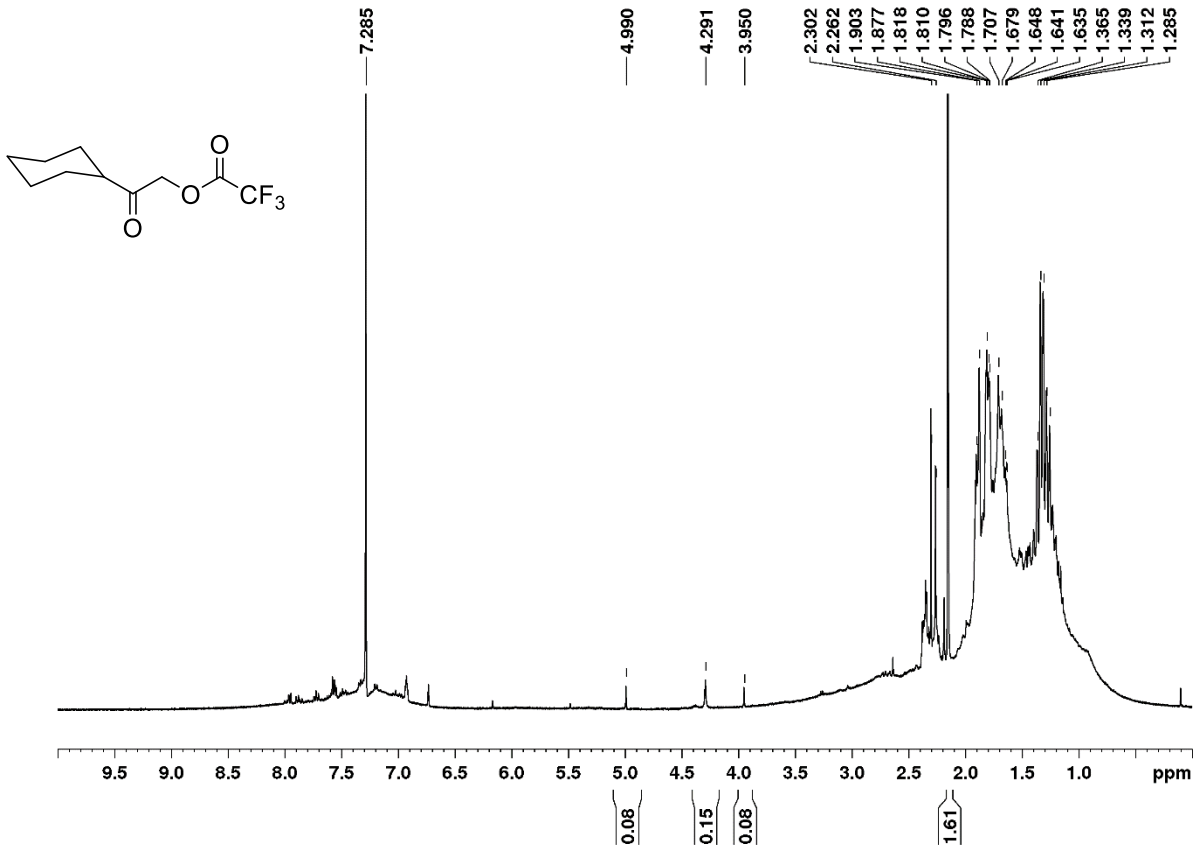


Figure 33. ^{1}H NMR spectrum for product 40 in $CDCl_3$ – one-pot conversion of alkynes to α-acyloxyketones. 400 MHz Bruker UltraShield spectrometer.

^{1}H NMR Analysis - 2-cyclohexyl-2-oxoethyl trifluoroacetate (40), 58% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29-2.30 (m, Cx group, 10H), 4.99 (s, 2H).

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CURRICULUM VITAE

Joshua Fardo

The Pennsylvania State University, Erie, The Behrend College. 4701 College Drive, Erie, PA, 16563
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Education

Penn State Erie, The Behrend College Graduation: May 2023

Chemistry, Bachelor of Science, ACS-Approved

Clinical Work Experience

Genesis Medical Associates: Northern Area Family Medicine Summer 2020 and 2021

- Assisted the nursing staff and physicians in filing patient records.
- Obtained a strong understanding of the innerworkings of an independent primary care group.
- Screened patients for COVID-19 during the pandemic.

Genesis Chiropractic & Rehabilitation Summer 2021

- Administered transcutaneous electrical nerve stimulation, interferential current, ultrasound, and traction therapies to patients.
- Developed interpersonal relationship and communication skills working with a diverse patient base.

Work Experience

Hearing Officer - Academic Integrity (AI) Student Representative Spring 2021

- Serve as a voluntary student representative in charge of reviewing cases of academic integrity or student misconduct.

Learning Recourse Center – Peer Tutor Spring 2020 - Present

- Provide tutoring and exam prep services for students taking classes at Penn State Behrend.

Learning Assistant, Chemistry, Chemical Principles I Fall 2020 - Spring 2021

- Assisted chemistry professors and students during recitation inside and outside of the classroom.
- Served as a role model and an available source for success in chemistry.
- Conducted weekly chapter-based review sessions and exam prep sessions.

Leadership | Involvement

Science Ambassador | Penn State Behrend Spring 2021-Present

- Encourage interest in the STEM field and science to various age groups.
- Spark enthusiasm in the School of Science through volunteer work.
- Build interpersonal relations through the Outreach Committee within Science Ambassadors.

Lion Ambassadors | Penn State Behrend Spring 2020-Present

- Bingo Committee Head - Hosted Midnight Bingo Events and request funding through SAF.
- Service Committee - Volunteer throughout the Behrend and Erie Community | +100 Hours.
- Social Committee Head - Organize social events for the Behrend community to help with recruitment and interpersonal relations within Lion Ambassadors.

Honors and Academic Awards

The Eric A. and Josephine S. Walker Award — Spring 2022

- This award recognizes a student whose outstanding qualities of character, scholarship, leadership, and citizenship have been directed into student programs and services. Scholarship and service to the college are the primary criteria for selection.

The Evan Pugh Scholar Award – Junior — Spring 2022

- The Evan Pugh scholars are those juniors and seniors who are in the upper 0.5 percent of their respective classes and have completed at least 48 graded Penn State credits at the end of the fall semester of the academic year in which the award is given.

Schreyer's Honors College Student — May 2021 – Present

Behrend Honors Certificate — May 2021

Penn State Behrend Dean's List — Dean's List All Semesters

The President Sparks Award — Spring 2021

- This award is presented annually to those undergraduate degree candidates who have earned a 4.0 (A) cumulative grade-point average based on at least 36 graded Penn State credits completed by the end of the fall semester of the academic year in which the award is given.

The President Walker Award — Spring 2020

- This award is presented annually to undergraduate degree candidates and degree-seeking provisional students who have earned a 4.0 (A) cumulative grade-point average based on at least 12 graded Penn State credits completed during their first semester of admission.

CRC/Outstanding Freshman Award — Spring 2020