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Advances in the cobalt-catalysed Pauson-Khand reaction: development of a sulfide-promoted, microwave-assisted protocol

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Dedicated to the memory of Professor Jonathan M. J. Williams.

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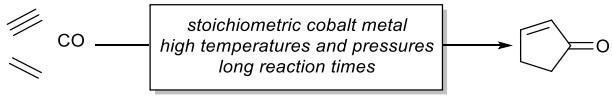
ABSTRACT

The development of a sulfide-promoted, microwave-assisted Pauson-Khand reaction has enabled the formation of fused cyclopentenones using sub-stoichiometric quantities of a cobalt mediator over rapid reaction times and with no requirement for an external source of toxic carbon monoxide gas. This protocol displays applicability to both intra- and intermolecular Pauson-Khand reaction examples.

1. Introduction

At its inception, the Pauson-Khand reaction (PKR) utilised stoichiometric quantities of cobalt metal to promote the formal [2+2+1] cycloaddition of an alkyne, alkene, and a molecule of carbon monoxide to furnish functionalised cyclopentenone products in one step (Scheme 1).[1] The potential of this reaction is clearly evident with this process providing direct access to usefully functionalised five-membered ring species in one synthetic step. However, in the beginning, Pauson-Khand cyclisations often required undesirable, elevated temperatures and prolonged reaction times.[2] Moreover, isolation and purification of the product tended to be problematic, based on the accompanying plethora of organometallic by-products, and the cyclopentenone products were generally afforded in poor yields. Accordingly, it is unsurprising that there has been a considerable drive to develop milder and more dependable PKR conditions. In this regard, dry-state adsorption,[3] ultrasonication,[4] and the use of phosphine oxides[4a] have delivered reaction rate and yield enhancements; however, the applicability of these methods is somewhat limited. Additionally, a range of photochemical methods have been disclosed,[5] including a more recent application utilising a photochemical flow reactor that mediated a range of inter- and intramolecular Pauson-Khand cyclisations.[6] To date, the most significant breakthroughs in terms of increasing the overall efficiency of the stoichiometric PKR has come from the use of amine *N*-oxides,[7] sulfides,[8] or amines[9] as reaction additives. In particular, work by Sugihara showed that the use



Scheme 1. Classical Pauson-Khand Reaction.

of cyclohexylamine or *n*-butyl methyl sulfide as an additive provided annulation products in excellent yields under significantly reduced reaction times.[8a,9a]

Whilst the stoichiometric PKR has displayed prominent synthetic significance, requirements to enhance the wider effectiveness and applicability of this annulation process, alongside a growing environmental awareness, has resulted in the drive towards the development of a catalytic protocol. Utilising sub-stoichiometric quantities of transition metal would, thus, provide a more practically efficient approach to the synthesis of cyclopentenones. As such, over the last number of years there have been marked advancements with regards to the development of an effective catalytic PKR system.[2g,2h,10] In this regard, a number of alternative metals have emerged as powerful catalysts for this transformation, including titanium,[11] ruthenium,[12] rhodium,[13] iridium,[14] and palladium.[15] However, a general limitation regarding the catalytic Pauson-Khand reaction remains in the use of an external source of toxic carbon monoxide gas, which is normally required to achieve efficient annulations.[16] A number of research groups have begun to probe this limitation, and the development of alternative sources of CO

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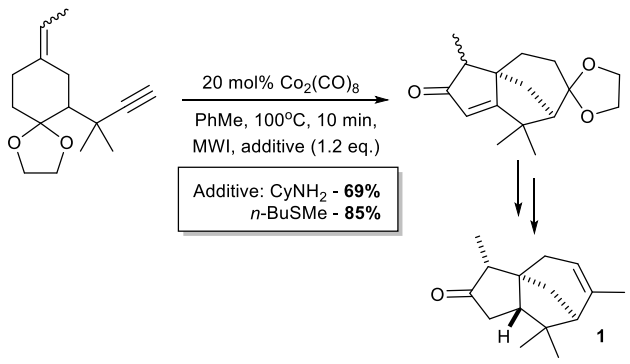
via the use of (sacrificial) aldehydes,[17] and alcohols[18] has gone some way to addressing this issue, generally within the intramolecular reaction scope. Based on this, we sought to develop an alternative process whereby sub-stoichiometric quantities of transition-metal could be used, without the requirement for an external source of carbon monoxide, to deliver functionalised cyclopentenones in a rapid, atom-economical, and efficient manner. In this regard, separate studies by Evans[19] and Groth[20a] have described the use of microwave irradiation conditions in the stoichiometric and catalytic PKR, respectively. With regards the latter, and following pioneering studies by Krafft and Boñaga,[20b] Groth *et al*. employed just 20 mol% of $Co_2(CO)_8$ in conjunction with 1.2 equiv. of cyclohexylamine under microwave irradiation to deliver moderate to good yields of cyclopentenone products.[20a] Despite this notable advance, only reactive (i.e. strained) norbornene was employed, alongside one moderately yielding intramolecular enyne substrate, across the five PKR examples presented in this short communication.

2. Results and Discussion

As part of our ongoing endeavours to elevate the efficiency and applicability of the cobalt-mediated Pauson-Khand annulation process,[4b,7d-f,8b-c,21] we have recently established a direct and efficient pathway for the synthesis of the structurally demanding natural target, 2-*epi*-α-cedren-3-one, **1**, using the PKR as our central transformation (Scheme 2).[21q] As part of this programme we employed a microwave-assisted PKR process, which resulted in the construction of the core carbon skeleton of **1** using sub-stoichiometric quantities of cobalt metal mediator. Interestingly, it was discovered that the employment of *n*-butyl methyl sulfide showed an appreciable enhancement in the reaction yield, as compared to cyclohexylamine[20] as the additive, to deliver the desired PKR product in only 10 minutes. Given this increased level of efficiency with this rather specific substrate, it was envisaged that the developed sulfide-promoted conditions could prove as effective in more simple Pauson-Khand annulations. Furthermore, over the past number of years, we have probed various promoters for the PKR, and, in line with these endeavours to develop more practically accessible and effective reaction conditions, we have demonstrated the use of the long chain, odourless sulfide, *n*-dodecyl methyl sulfide (DodSMe), as an efficient, inexpensive, and non-noxious PKR additive in stoichiometric processes.[8c] Based on all of this, we sought to study the wider applicability of both *n*-BuSMe and DodSMe as additives within microwave-assisted procedures as applied to a number of intra- and intermolecular Pauson-Khand substrates with sub-stoichiometric levels of $Co_2(CO)_8$ mediator and no external source of carbon monoxide.



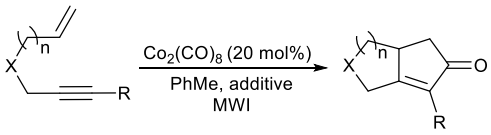
Scheme 2. Towards the synthesis of 2-epi-α-cedren-3-one.[21q]

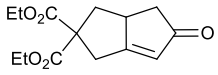
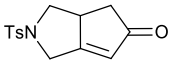
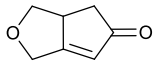
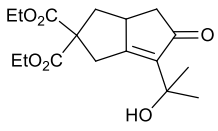
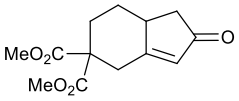
Initial studies looked to the use of the sulfide additives, under microwave irradiation, in the more entropically-favoured intramolecular Pauson-Khand cyclisation. Pleasingly, a rapid conversion to the [5,5]-fused bicyclic cyclopentenone product was observed using just 20 mol% of $Co_2(CO)_8$ over a 10 minute reaction time, and, importantly, without the need for carbon monoxide gas (Table 1, entry 1). With *n*-BuSMe and DodSMe respective 57% and 63% yields of the desired product were achieved; the use of cyclohexylamine resulted in a reduced yield of 33%. It is worth noting here that amendment of the various reaction parameters with DodSMe promoter, including number of additive equivalents, reaction temperature, time, solvent, and concentration, did not lead to further optimised reaction outcomes.

Following the establishment of this procedure, a number of alternative intramolecular Pauson-Khand annulations were performed (Table 1). Pleasingly, in every case, the use of the odourless DodSMe resulted in enhanced chemical yields when compared to both *n*-BuSMe and $CyNH_2$. In the case of *N*-tosyl allylpropargylamino enyne (Entry 2) the use of $CyNH_2$ failed to produce any of the desired cyclopentenone product, with only decomposition being observed. This is in direct agreement with the observations of Sugihara *et al.*, who also noted substrate decomposition when using $CyNH_2$ in a stoichiometric PKR of this particular substrate.[8a]

Having illustrated the applicability of these catalytic conditions in the cyclisation of enynes containing a terminal alkyne, including the additional oxygen tethered derivative within Entry 3, cyclisation of a, generally less reactive,

Table 1. Intramolecular Pauson-Khand reactions.



Entry[a]	Product	Yield[b] CyNH2	n-BuSMe	DodSMe
1		33%	57%	63%[c]
2		0%	45%	50%
3		40%	55%	60%
4[d]		33%	52%	59%
5		47%	58%	61%

[a]Reactions were carried out under microwave irradiation in PhMe (0.125 M) at 100°C for 10 minutes, using 1.2 eq. of additive; [b]Isolated yields following purification; [c]Reaction carried out at 90°C; [d]Reactions were carried out at 120°C for 20 minutes.

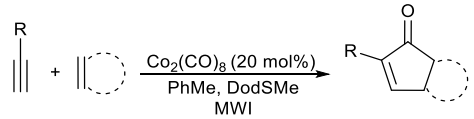
substrate bearing an internal alkyne was probed (Entry 4). Pleasingly, our developed DodSMe protocol delivered the desired cyclopentenone product in a good 59% yield, with an increase of only 20°C and 10 minutes reaction time being required. With application to [5,5]-fused cyclopentenone synthesis demonstrated, an attempt to form the generally more demanding [6,5] system was assessed. In this case, good yields were obtained, with DodSMe, once again, proving the most proficient promoter, delivering a 61% yield of the [6,5]-fused cyclopentenone product (Entry 5).

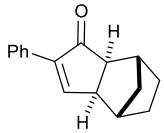
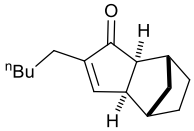
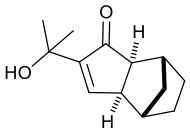
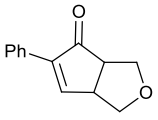
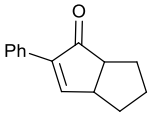
Encouraged by the successful application of our developed conditions in an intramolecular sense, we proceeded to probe a range of, generally more demanding, intermolecular examples (Table 2).[2] Initial studies looked to the annulation of various alkyne substrates with the known reactive alkene partner, norbornene (Entries 1-3). Pleasingly, our developed conditions with DodSMe provided good yields of the desired cyclopentenone products in extremely short reaction times. Considering the published results on such substrates, this set of preparatively accessible reaction conditions with only 20 mol% of the precious metal mediator compare favourably with alternative known methods, and especially those which use stoichiometric cobalt sources over more prolonged reaction times.

Having displayed efficient reactivity with an alkene known to perform well within a PKR manifold, we turned our attention to the simple, unstrained, and, indeed, notoriously troublesome olefin partner, 2,5-dihydrofuran (Entry 4).[2] Gratifyingly, the use of the developed conditions with DodSMe under microwave promotion delivered the cyclopentenone product in a 44% yield. Whilst this yield could be considered relatively modest, the same transformation carried out under an equivalent thermal protocol with stoichiometric cobalt source produces a 55% yield after a prolonged reaction time of 5 days.[8c] To further widen the scope of our system, another more demanding alkene substrate, cyclopentene, was investigated (Entry 5). As with 2,5-dihydrofuran, the use of cyclopentene as an olefin partner has required prolonged (multiple day) reaction times to achieve acceptable chemical yields of the enone product.[8c] Upon applying our catalytic conditions, a modest yield of 22% was achieved after only 10 minute reaction time.

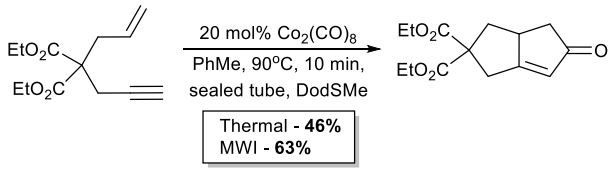
As a final investigation as part of this study, a reaction was carried out, in a sealed tube, under thermal promotion, enabling a direct analysis of the effect of microwave energy. As shown in Scheme 3, a substantial increase in chemical yield is observed upon applying microwave irradiation as opposed to the thermally promoted system.

Table 2. Intermolecular Pauson-Khand Reactions



Entry[a]	Product	Yield[b]
1		60%
2[c]		67%
3[c]		73%
4[d]		44%
5		22%

[a]All reactions were carried out under microwave irradiation in PhMe (0.125 M) at 100°C for 10 min, using 1.2 eq. of DodSMe; [b]Isolated yields following purification; [c]Reaction carried out at 90°C; [d]Reaction carried out in PhMe (1 M).



Scheme 3. Direct comparison of microwave and thermal promotion.

3. Conclusions

Practically efficient and operationally simple reaction conditions for a microwave-promoted, catalytic Pauson-Khand reaction have been realised, which produce good yields of cyclopentenone products over a panel of substrates. Notable features of these conditions are the short reaction times, alongside the elimination of the requirement for an external source of toxic carbon monoxide gas. Successful Pauson-Khand transformations can be executed using both *n*-BuSMe and the odourless sulfide, DodSMe, with the latter prevailing in terms of overall efficiency, especially in comparison with cyclohexylamine as a PKR promotor. The developed system, as described herein, is tolerant of intramolecular examples containing heteroatoms, both terminal and internal alkynes, and is capable of generating both [5,5] and [6,5] bicyclic enones. Finally, this system can also be applied in an intermolecular reaction mode, importantly, utilising both reactive and less reactive alkene partners.

4. Experimental section

4.1. General

Chromatographic separations were performed either on Prolabo silica gel (230-400 mesh) or on prepacked Bond Elute® silica columns. Thin layer chromatography was carried out using Merck silica plates coated with fluorescent indicator F254, and analysed using a Mineralight UVGL-25 lamp or developed using potassium permanganate or vanillin dips.

FTIR spectra were obtained on a Nicolet Impact 400D machine. ^{1}H and ^{13}C NMR were recorded on a Bruker DMX 400 or a Bruker WM 400 spectrometer at 400 MHz and 100 MHz, respectively.

Chemical shifts are reported in parts per million (ppm) and are referenced to the appropriate solvent peak. Coupling constants refer to $^{3}J_{H\text{-}H}$ interactions, unless otherwise stated, and are reported in Hz. High resolution mass spectra were recorded on a Micromass Autospec (FAB) or Finnigan MAT 900XLT (EI/CI) instrument at the EPSRC Mass Spectrometry facility at the University of Wales, Swansea. Elemental analyses were carried out using a Carlo Erba 1106 CHN analyser.

Reactions were performed in the microwave using a CEM Discovery apparatus.

4.2. Reagents

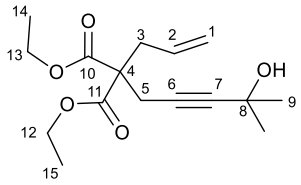
All reagents were obtained from commercial suppliers and were used without additional purification. Petrol refers to the fraction of b.p. 30-40 °C.

4.3. Intermediates and products

All compounds prepared are known, with the exception of those detailed below. Full experimental details, including references to known cyclopentenone products and their corresponding starting materials, are provided in the supplementary material.

Table 1, entry 4:

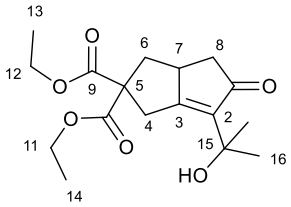
Preparation of starting enyne (diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate)



A 100 mL round-bottomed flask was oven-dried (overnight, 140ºC) and cooled under N_2. Diethyl 6-hepten-1-yne-4,4-dicarboxylate[22] (2.96 g, 12.4 mmol), was added and the flask was purged with N_2. Dry THF (40 mL) was added *via* syringe. The solution was cooled to -78°C in a dry ice-acetone bath and *n*-butyllithium (5 mL, 2.5 M in hexanes, 12.5 mmol) was added *via* syringe over 5 min. On completion of the addition, dry acetone (10 mL, 136.4 mmol) was added *via* syringe. The reaction solution was then stirred at -78°C for a further 30 min, warmed to room temperature, and quenched by the addition of saturated ammonium chloride solution (20 mL). The THF was removed *in vacuo* and diethyl ether (30 mL) and water (20 mL) were added. The organic layer was separated and the aqueous layer extracted with further quantities of diethyl ether (2 x 20 mL). The combined organics were washed with water (20 mL) and dried over Na_2SO_4. Solvents were removed *in vacuo* and the residue purified by flash column chromatography (eluent: 50% diethyl ether in petrol) to give the desired product as a viscous clear oil (2.97 g, 81% yield).

FTIR (liq. film): 3480, 3080, 2981, 2935, 2909, 2874, 2239, 1734, 1642 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.66 (ddt, J = 17.0 Hz, J = 10.0 Hz, J = 7.5 Hz, 1H, H^{2}), 5.20 (dt, J = 17.0 Hz, ^{4}J = 1.3 Hz, 1H, H^{1}), 5.15 (dt, J = 10.0 Hz, ^{4}J = 1.3 Hz, 1H, H^{1}), 4.23 (q, J = 7.1 Hz, 2H, H$^{12/13}$), 4.22 (q, J = 7.1 Hz, 2H, H$^{12/13}$), 2.81 (s, 2H, H^{5}), 2.80 (dt, J = 7.5 Hz, ^{4}J = 1.3 Hz, 2H, H^{3}), 1.95 (br s, 1H, OH), 1.50 (s, 6H, H^{9}), 1.28 ppm (t, J = 7.0 Hz, 6H, H^{14,15}); ^{13}C NMR ($CDCl_3$): δ 169.3, 131.4, 119.1, 87.9, 76.5, 64.6, 61.0, 56.4, 36.0, 31.0, 22.2, 13.6 ppm; HRMS (FAB): $C_{16}H_{25}O_5$ [M+H]$^{+}$ required 297.1702; found 297.1716; Microanalysis: $C_{16}H_{24}O_5$ required C, 64.61; H, 7.99; found C, 64.84; H, 8.16%.

Diethyl 6-(1-hydroxy-1-methylethyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate.



A 10 mL CEM microwave vessel was equipped with a stirrer bar and diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate (0.148 g, 0.5 mmol), toluene (4 mL), and DodSMe (0.159 mL, 0.6 mmol) were added. To the tube was added octacarbonyl dicobalt (0.034 g, 0.1 mmol) and the vessel was sealed immediately. The reaction vial was then placed in the microwave and heated 120°C for 20 minutes. The crude reaction mixture was then purified directly *via* column chromatography (eluent: diethyl ether) to yield the titled compound (0.096 g, 59% yield).

FTIR (CH_2Cl_2): 3475, 1728, 1689, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.31-4.22 (m, 4H, H^{11,12}), 4.11 (s, 1H, OH), 3.40 (s, 2H, H^{4}), 3.05-2.97 (m, 1H, H^{7}), 2.83 (dd, ^{2}J = 12.5 Hz, J = 7.4 Hz, 1H, H^{8}), 2.68 (dd, ^{2}J = 18.0 Hz, J = 6.3 Hz, 1H, H^{6}), 2.17 (dd, ^{2}J = 18.0 Hz, J = 3.4 Hz, 1H, H^{6}), 1.70 (t, ^{2}J = 12.5 Hz, ^{3}J = 12.5 Hz, 1H, H^{8}), 1.48 (s, 6H, H^{16}), 1.32 (t, J = 7.1 Hz, 3H, H$^{13/14}$), 1.30 ppm (t, J = 7.1 Hz, 3H, H$^{13/14}$); ^{13}C NMR ($CDCl_3$): δ 209.6, 175.9, 170.9, 170.3, 140.8, 70.0, 61.7, 61.5, 60.7, 42.9, 41.5, 37.9, 35.3, 28.6, 28.4, 13.5 ppm; HRMS (EI): $C_{17}H_{24}O_6$ [M]$^{+}$ required 324.1572; found 324.1541; Microanalysis: $C_{17}H_{24}O_6$ required C, 62.91; H, 7.30; found C, 62.95; H, 7.46%.

Acknowledgments

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Supplementary Material

Supplementary material for this article can be found online at https://doi.org/XXX. Full experimental details are provided, including references to known compounds. Scanned ^{1}H and ^{13}C NMR spectra for novel compounds are also included.

Advances in the cobalt-catalysed Pauson-Khand reaction: development of a sulfide-promoted, microwave-assisted Protocol

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SUPPLEMENTARY MATERIAL

General

All reagents were obtained from commercial suppliers and were used without additional purification. With regards to the intramolecular Pauson-Khand reactions, individual references for the known enyne substrates are provided within. All starting substrates for the intermolecular reactions are commercially available.

Petrol refers to the fraction of b.p. 30-40°C.

Chromatographic separations were performed either on Prolabo silica gel (230-400 mesh) or on prepacked Bond Elute® silica columns. Thin layer chromatography was carried out using Merck silica plates coated with fluorescent indicator F_{254}, and analysed using a Mineralight UVGL-25 lamp or developed using potassium permanganate or vanillin dips.

FTIR spectra were obtained on a Nicolet Impact 400D machine. ^{1}H and ^{13}C NMR were recorded on a Bruker DMX 400 or a Bruker WM 400 spectrometer at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in parts per million (ppm) and are referenced to the appropriate solvent peak. Coupling constants refer to $^{3}J_{H\text{-}H}$ interactions, unless otherwise stated, and are reported in Hz. High resolution mass spectra were recorded on a Micromass Autospec (FAB) or Finnigan MAT 900XLT (EI/CI) instrument at the EPSRC Mass Spectrometry facility at the University of Wales, Swansea. Elemental analyses were carried out using a Carlo Erba 1106 CHN analyser.

Reactions were performed in the microwave using a CEM Discovery apparatus.

Intramolecular Pauson-Khand Reactions (Table 1)

General Procedure

To a 10 mL CEM microwave vessel, equipped with a stirrer bar, were added the enyne substrate, toluene, and the additive. To the tube was added octacarbonyl dicobalt and the vessel was sealed immediately. The reaction vial was then placed in the microwave and heated at the appropriate temperature for the allotted time. The crude reaction mixture was then purified directly *via* column chromatography to yield the desired product.

The following experiments were carried out according to the above ***General Procedure***. The data are presented as (a) quantity of enyne, (b) volume of toluene, (c) quantity of additive, (d) quantity of $Co_2(CO)_8$, (e) temperature, (f) reaction time, (g) column eluent, and (h) product quantity and yield.

Preparation of diethyl 5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate.[1]

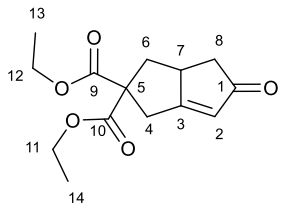


Table 1, entry 1, use of $CyNH_2$:

(a) Diethyl 6-hepten-1-yne-4,4-dicarboxylate,[2] 0.119 g, 0.5 mmol, (b) 4 mL, (c) $CyNH_2$, 0.067 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) 1:1 petrol/diethyl ether, and (h) 0.044 g, 33% yield.

Table 1, entry 1, use of n-BuSMe:

(a) Diethyl 6-hepten-1-yne-4,4-dicarboxylate,[2] 0.119 g, 0.5 mmol, (b) 4 mL, (c) *n*-BuSMe, 0.074 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) 1:1 petrol/diethyl ether, and (h) 0.074 g, 57% yield.

Table 1, entry 1, use of DodSMe:

(a) Diethyl 6-hepten-1-yne-4,4-dicarboxylate,[2] 0.119 g, 0.5 mmol, (b) 4 mL, (c) DodSMe, 0.159 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 90°C, (f) 10 minutes, (g) 1:1 petrol/diethyl ether, and (h) 0.084 g, 63% yield.

FTIR (CH_2Cl_2): 3085, 2939, 1730, 1705, 1636 cm^{-1}.

^1H NMR ($CDCl_3$): δ 5.89 (s, 1H, H^2), 4.24-4.13 (m, 4H, $H^{11,12}$), 3.32 (d, ^2J = 19.0 Hz, 1H, H^4), 3.22 (d, ^2J = 19.0 Hz, 1H, H^4), 3.08 (m, 1H, H^7), 2.76 (dd, ^2J = 12.8 Hz, J = 7.7 Hz, 1H, H^8), 2.59 (dd, ^2J = 17.9 Hz, J = 6.4 Hz, 1H, H^6), 2.10 (dd, ^2J = 18.0 Hz, J = 3.1 Hz, 1H, H^6), 1.71 (m, 1H, H^8), 1.25 (t, J = 7.1 Hz, 3H, $H^{13/14}$), 1.23 ppm (t, J = 7.1 Hz, 3H, $H^{13/14}$).

Preparation of 2,3,3a,4-tetrahydro-2-(p-toluenesulfonyl)cyclopenta[c]pyrrol-5(1H)-one.[1]

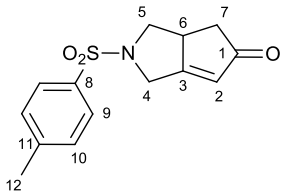


Table 1, entry 2, use of $CyNH_2$:

(a) *N*-(2-Propenyl)-*N*-2-propynyl)-*p*-toluenesulfonamide,[3] 0.125 g, 0.5 mmol, (b) 4 mL, (c) $CyNH_2$, 0.067 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.00 g, 0% yield.

Table 1, entry 2, use of n-BuSMe:

(a) *N*-(2-Propenyl)-*N*-2-propynyl)-*p*-toluenesulfonamide,[3] 0.125 g, 0.5 mmol, (b) 4 mL, (c) *n*-BuSMe, 0.074 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.062 g, 45% yield.

Table 1, entry 2, use of DodSMe:

(a) *N*-(2-Propenyl)-*N*-2-propynyl)-*p*-toluenesulfonamide,[3] 0.125 g, 0.5 mmol, (b) 4 mL, (c) DodSMe, 0.159 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.069 g, 50% yield.

FTIR (CH_2Cl_2): 1720, 1650 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H, H^9), 7.35 (d, *J* = 8.1 Hz, 2H, H^{10}), 6.00 (s, 1H, H^2), 4.32 (d, ^2J = 16.5 Hz, 1H, H^4), 4.04 (d, ^2J = 16.4 Hz, 1H, H^4), 4.05-4.01 (m, 1H, H^5), 3.19-3.12 (m, 1H, H^6), 2.66-2.58 (m, 1H, H^5), 2.59 (d, ^2J = 17.8 Hz, 1H, H^7), 2.45 (s, 3H, H^{12}), 2.07 ppm (m, 1H, H^7).

Preparation of 3,3a,4,5-tetrahydrocylopenta[c]furan-5(1H)-one.[4]

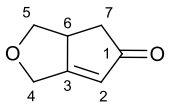


Table 1, entry 3, use of $CyNH_2$:

(a) Allylpropargyl ether,[5] 0.048 g, 0.5 mmol, (b) 4 mL, (c) $CyNH_2$, 0.067 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.025 g, 40% yield.

Table 1, entry 3, use of n-BuSMe:

(a) Allylpropargyl ether,[5] 0.048 g, 0.5 mmol, (b) 4 mL, (c) *n*-BuSMe, 0.074 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.034 g, 55% yield.

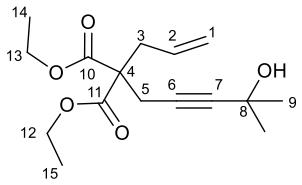
Table 1, entry 3, use of DodSMe:

(a) Allylpropargyl ether,[5] 0.048 g, 0.5 mmol, (b) 4 mL, (c) DodSMe, 0.159 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.037 g, 60% yield.

FTIR (CH_2Cl_2): 1715, 1648 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ 6.08 (s, 1H, H^2), 4.67 (d, ^2J = 16.0 Hz, 1H, H^4), 4.52 (d, ^2J = 16.0 Hz, 1H, H^4), 4.33 (m, 1H, H^7), 3.37-3.24 (m, 2H, $H^{6,7}$), 2.66 (dd, ^2J = 17.8 Hz, *J* = 2.4 Hz, 1H, H^5), 2.15 ppm (dd, ^2J = 17.6 Hz, *J* = 2.4 Hz, 1H, H^5).

Preparation of diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate.



A 100 mL round-bottomed flask was oven-dried (overnight, 140ºC) and cooled under N_2. Diethyl 6-hepten-1-yne-4,4-dicarboxylate[2] (2.96 g, 12.4 mmol), was added and the flask was purged with N_2. Dry THF (40 mL) was added *via* syringe. The solution was cooled to -78ºC in a dry ice-acetone bath and *n*-butyllithium (5 mL, 2.5 M in hexanes, 12.5 mmol) was added *via* syringe over 5 min. On completion of the addition, dry acetone (10 mL, 136.4 mmol) was added *via* syringe. The reaction solution was then stirred at -78ºC for a further 30 min, warmed to room temperature, and quenched by the addition of saturated ammonium chloride solution (20 mL). The THF was removed *in vacuo* and diethyl ether (30 mL) and water (20 mL) were added. The organic layer was separated and the aqueous layer extracted with further quantities of diethyl ether (2 x 20 mL). The combined organics were washed with water (20 mL) and dried over Na_2SO_4. Solvents were removed *in vacuo* and the residue purified by flash column chromatography (eluent: 50% diethyl ether in petrol) to give the desired product as a viscous clear oil (2.97 g, 81% yield).

FTIR (liq. film): 3480, 3080, 2981, 2935, 2909, 2874, 2239, 1734, 1642 cm^{-1}.

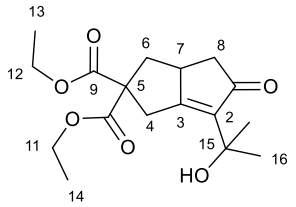
^1H NMR ($CDCl_3$): δ 5.66 (ddt, J = 17.0 Hz, J = 10.0 Hz, J = 7.5 Hz, 1H, H^2), 5.20 (dt, J = 17.0 Hz, ^4J = 1.3 Hz, 1H, H^1), 5.15 (dt, J = 10.0 Hz, ^4J = 1.3 Hz, 1H, H^1), 4.23 (q, J = 7.1 Hz, 2H, $H^{12/13}$), 4.22 (q, J = 7.1 Hz, 2H, $H^{12/13}$), 2.81 (s, 2H, H^5), 2.80 (dt, J = 7.5 Hz, ^4J = 1.3 Hz, 2H, H^3), 1.95 (br s, 1H, OH), 1.50 (s, 6H, H^9), 1.28 ppm (t, J = 7.0 Hz, 6H, $H^{14,15}$).

^{13}C NMR ($CDCl_3$): δ 169.3, 131.4, 119.1, 87.9, 76.5, 64.6, 61.0, 56.4, 36.0, 31.0, 22.2, 13.6 ppm.

HRMS (FAB): $C_{16}H_{25}O_5$ $[M+H]^+$ required 297.1702; found 297.1716.

Microanalysis: $C_{16}H_{24}O_5$ required C, 64.61; H, 7.99; found C, 64.84; H, 8.16%.

Preparation of diethyl 6-(1-hydroxy-1-methylethyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate.



The following experiments were carried out according to the ***General Procedure*** described on page 2. The data are presented as (a) quantity of enyne, (b) volume of toluene, (c) quantity of additive, (d) quantity of $Co_2(CO)_8$, (e) temperature, (f) reaction time, (g) column eluent, and (h) product quantity and yield.

Table 1, entry 4, use of $CyNH_2$:

(a) Diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate, 0.148 g, 0.5 mmol, (b) 4 mL, (c) $CyNH_2$, 0.067 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 120°C, (f) 20 minutes, (g) 2:1 diethyl ether/petrol, and (h) 0.054 g, 33% yield.

Table 1, entry 4, use of n-BuSMe:

(a) Diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate, 0.148 g, 0.5 mmol, (b) 4 mL, (c) *n*-BuSMe, 0.074 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 120°C, (f) 20 minutes, (g) diethyl ether, and (h) 0.084 g, 52% yield.

Table 1, entry 4, use of DodSMe:

(a) Diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate, 0.148 g, 0.5 mmol, (b) 4 mL, (c) DodSMe, 0.159 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 120°C, (f) 20 minutes, (g) diethyl ether, and (h) 0.096 g, 59% yield.

FTIR (CH_2Cl_2): 3475, 1728, 1689, 1650 cm^{-1}.

^1H NMR ($CDCl_3$): δ 4.31-4.22 (m, 4H, $H^{11,12}$), 4.11 (s, 1H, OH), 3.40 (s, 2H, H^4), 3.05-2.97 (m, 1H, H^7), 2.83 (dd, ^2J = 12.5 Hz, J = 7.4 Hz, 1H, H^8), 2.68 (dd, ^2J = 18.0 Hz, J = 6.3 Hz, 1H, H^6), 2.17 (dd, ^2J = 18.0 Hz, J = 3.4 Hz, 1H, H^6), 1.70 (t, ^2J = 12.5 Hz, ^3J = 12.5 Hz, 1H, H^8), 1.48 (s, 6H, H^{16}), 1.32 (t, J = 7.1 Hz, 3H, $H^{13/14}$), 1.30 ppm (t, J = 7.1 Hz, 3H, $H^{13/14}$).

^{13}C NMR ($CDCl_3$): δ 209.6, 175.9, 170.9, 170.3, 140.8, 70.0, 61.7, 61.5, 60.7, 42.9, 41.5, 37.9, 35.3, 28.6, 28.4, 13.5 ppm.

HRMS (EI): $C_{17}H_{24}O_6$ $[M]^+$ required 324.1572; found 324.1541.

Microanalysis: $C_{17}H_{24}O_6$ required C, 62.91; H, 7.30; found C, 62.95; H, 7.46%.

Preparation of 1,2,4,6,7,7a-hexahydro-2-oxo-5H-indene-5,5-dicarboxylate.[6]

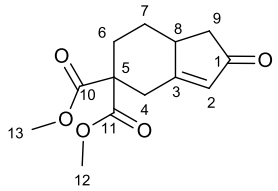


Table 1, entry 5, use of $CyNH_2$:

(a) Dimethyl oct-7-en-1-yn-4,4-dicarboxylate,[7] 0.112 g, 0.5 mmol, (b) 4 mL, (c) $CyNH_2$, 0.067 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.059 g, 47% yield.

Table 1, entry 5, use of n-BuSMe:

(a) Dimethyl oct-7-en-1-yn-4,4-dicarboxylate,[7] 0.112 g, 0.5 mmol, (b) 4 mL, (c) *n*-BuSMe, 0.074 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.072 g, 58% yield.

Table 1, entry 5, use of DodSMe:

(a) Dimethyl oct-7-en-1-yn-4,4-dicarboxylate,[7] 0.112 g, 0.5 mmol, (b) 4 mL, (c) DodSMe, 0.159 mL, 0.6 mmol, (d) 0.034 g, 0.1 mmol, (e) 100°C, (f) 10 minutes, (g) diethyl ether, and (h) 0.077 g, 61% yield.

FTIR (CH_2Cl_2): 1730, 1700, 1628 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ 5.96 (s, 1H, H^2), 3.75 (s, 3H, $H^{12/13}$), 3.71 (s, 3H, $H^{12/13}$), 3.48 (dd, ^2J = 14.0 Hz, ^4J = 2.1 Hz, 1H, H^4), 2.68-2.48 (m, 4H, $H^{4,6,7,9}$), 2.13-2.08 (m, 1H, H^7), 1.99-1.85 (m, 2H, $H^{8,9}$), 1.29 ppm (app. qd, J = 13.5 Hz, J = 3.4 Hz, 1H, H^6).

Intermolecular Pauson-Khand Reactions (Table 2)

General Procedure

To a 10 mL CEM microwave vessel, equipped with a stirrer bar, were added alkyne substrate, toluene, olefin, and additive. To the tube was added octacarbonyl dicobalt and the vessel was sealed immediately. The reaction vial was then placed in the microwave and heated at the appropriate temperature for the allotted time. The crude reaction mixture was then purified directly *via* column chromatography to yield the desired product.

The following experiments were carried out according to the above ***General Procedure***. The data are presented as (a) quantity of alkyne, (b) volume of toluene, (c) quantity of olefin, (d) quantity of additive, (e) quantity of $Co_2(CO)_8$, (f) temperature, (g) reaction time, (h) column eluent, and (i) product quantity and yield.

Preparation of 3a,4,5,6,7,7a-hexahydro-2-phenyl-4,7-methano-1H-inden-1-one.[6]

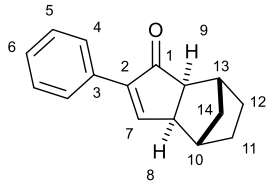


Table 2, entry 1:

(a) Phenyl acetylene, 0.055 mL, 0.5 mmol, (b) 4 mL, (c) norbornene, 0.471 g, 5.00 mmol, (d) DodSMe, 0.159 mL, 0.6 mmol, (e) 0.034 g, 0.1 mmol, (f) 100°C, (g) 10 minutes, (h) diethyl ether, and (i) 0.067 g, 60% yield.

FTIR (CH_2Cl_2): 1782, 1697, 1617 cm^{-1}.

^1H NMR ($CDCl_3$): δ 7.72-7.70 (m, 2H, $H^{4/5}$), 7.65 (d, J = 2.9 Hz, 1H, H^7), 7.41-7.30 (m, 3H, $H^{4/5,6}$), 2.71-2.69 (m, 1H), 2.50 (d, J = 4.4 Hz, 1H), 2.37 (d, J = 5.0 Hz, 1H), 2.28-2.27 (m, 1H), 1.75-1.55 (m, 2H), 1.40-1.30 (m, 2H), 1.15-1.11 (m, 1H), 1.02-0.98 (m, 1H).

Preparation of 2-pentyl-3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-1-one.[6]

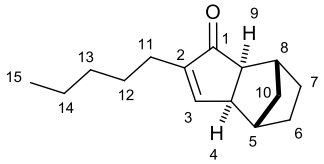


Table 2, entry 2:

(a) Hept-1-yne, 0.049 g, 0.5 mmol, (b) 4 mL, (c) norbornene, 0.471 g, 5.00 mmol, (d) DodSMe, 0.159 mL, 0.6 mmol, (e) 0.034 g, 0.1 mmol, (f) 90°C, (g) 10 minutes, (h) 5% ether/petrol, and (i) 0.073 g, 67% yield.

FTIR (CH_2Cl_2): 3357, 2950, 1780, 1722, 1670, 1626 cm^{-1}.

^1H NMR ($CDCl_3$): δ 7.08 (s, 1H, H^3), 2.58-2.54 (m, 1H, H^4), 2.39-2.37 (m, 1H, H^9), 2.17-2.13 (m, 4H, $H^{5,8,11}$), 1.67-1.44 (m, 4H, $H^{6,7}$), 1.33-1.25 (m, 6H, $H^{14,13,12}$), 0.95-0.86 ppm (m, 5H, $H^{10,15}$).

Preparation of 3a,4,5,6,7,7a-hexahydro-2-(1-hydroxy-1-nethylethyl)-4,7-methano-1H-inden-1-one.[8]

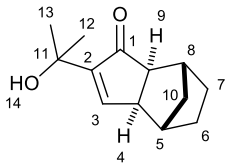


Table 2, entry 3:

(a) 2-Methyl-3-butyn-2-ol, 0.042 g, 0.5 mmol, (b) 4 mL, (c) norbornene, 0.471 g, 5.00 mmol, (d) DodSMe, 0.159 mL, 0.6 mmol, (e) 0.034 g, 0.1 mmol, (f) 90°C, (g) 10 minutes, (h) 33% diethyl ether/petrol, and (i) 0.075 g, 73% yield.

FTIR (CH_2Cl_2): 3533, 2966, 2889, 1700, 1622 cm^{-1}.

^1H NMR ($CDCl_3$): δ 7.18 (d, J = 2.5 Hz, 1H, H^3), 3.85 (s, 1H, H^{14}), 2.57-2.55 (m, 1H, H^4), 2.39-2.38 (m, 1H, H^8), 2.20 (d, J = 5.0 Hz, 1H, H^9), 2.17 (d, J = 4.0 Hz, 1H, H^5), 1.69-1.63 (m, 2H, $H^{6/7}$), 1.36-1.22 (m, 2H, $H^{6/7}$), 1.40 (s, 6H, $H^{12,13}$), 1.00-0.98 ppm (m, 2H, H^{10}).

Preparation of 3,3a-dihydro-5-phenyl-1H-cyclopenta[c]furan-4(6aH)-one.[9]

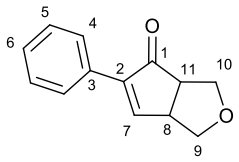


Table 2, entry 4:

(a) Phenyl acetylene, 0.055 ml, 0.5 mmol, (b) 0.5 mL, (c) 2,5-dihydrofuran, 0.350 g, 5.00 mmol, (d) DodSMe, 0.159 mL, 0.6 mmol, (e) 0.034 g, 0.1 mmol, (f) 100°C, (g) 10 minutes, (h) diethyl ether, and (i) 0.044 g, 44% yield.

FTIR (CH_2Cl_2): 1782, 1697, 1617 cm^{-1}.

^1H NMR ($CDCl_3$): δ 7.70-7.68 (m, 3H, $H^{4/5,6}$), 7.40-7.34 (m, 3H, $H^{4/5,7}$), 4.22 (d, *J* = 8.6 Hz, 1H, $H^{8/11}$), 3.94 (d, *J* = 9.2 Hz, 1H, $H^{8/11}$), 3.80-3.70 (m, 2H, $H^{9/10}$), 3.55-3.47 (m, 1H, $H^{9/10}$), 3.14-3.10 ppm (m, 1H, $H^{9/10}$).

Preparation of 2-phenyl-4,5,6,6a-tetrahydro-3aH-pentalen-1-one.[10]

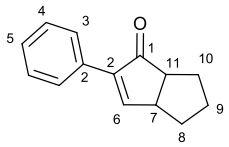


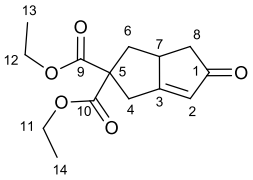
Table 2, entry 5:

(a) Phenyl acetylene, 0.055 ml, 0.5 mmol, (b) 4 mL, (c) cyclopentene, 0.442 mL, 5.00 mmol, (d) DodSMe, 0.159 mL, 0.6 mmol, (e) 0.034 g, 0.1 mmol, (f) 100°C, (g) 10 minutes, (h) 10% diethyl ether/petrol, and (i) 0.022 g, 22% yield.

FTIR (CH_2Cl_2): 3156, 2940, 1739, 1599, 1468 cm^{-1}.

^1H NMR ($CDCl_3$): δ 7.71 (d, *J* = 7.2 Hz, 2H, $H^{3/4}$), 7.66 (d, *J* = 3.2 Hz, 1H, H^6), 7.40-7.32 (m, 3H, $H^{3/4,5}$), 3.38-3.33 (m, 1H, $H^{7/11}$), 2.95-2.92 (m, 1H, $H^{7/11}$), 2.01-2.00 (m, 1H, $H^{8/9/10}$), 1.83-1.74 (m, $3H^{8/9/10}$), 1.67-1.61 (m, 1H, $H^{8/9/10}$), 1.35-1.21 ppm (m, 1H, $H^{8/9/10}$).

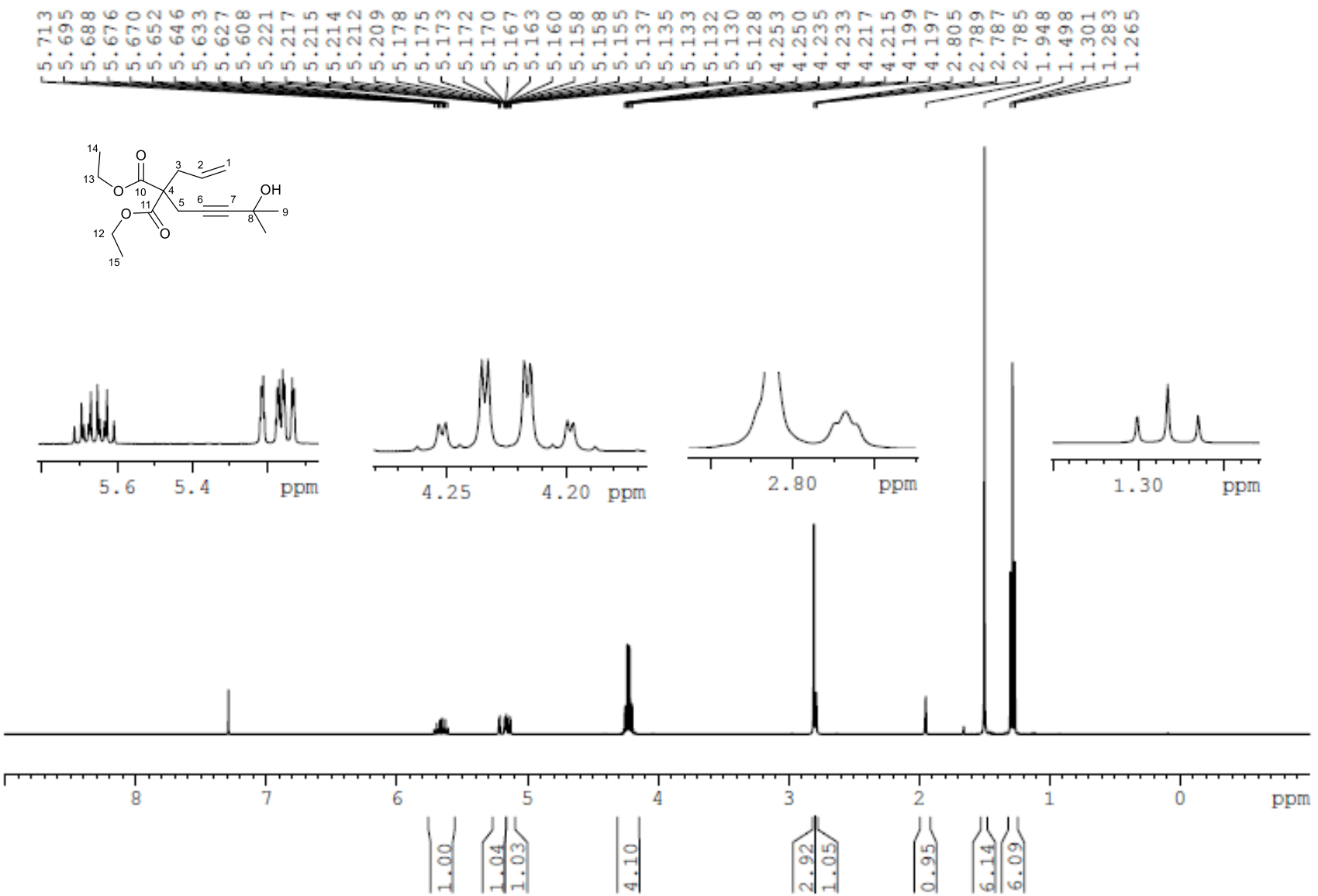
Thermally-promoted PKR (Scheme 3)



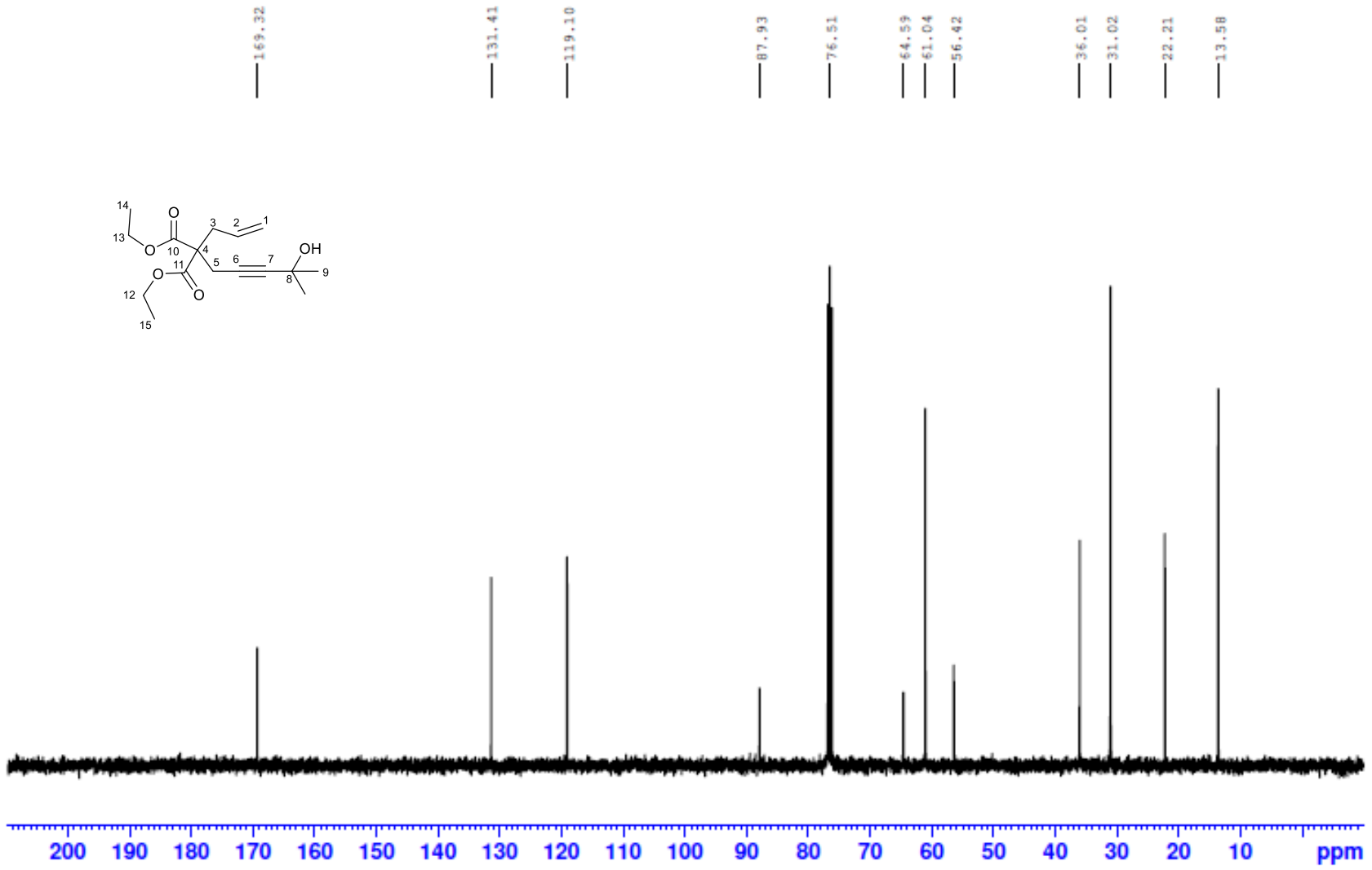
To a 10 mL CEM microwave vial, equipped with a stirrer bar, were added diethyl 6-hepten-1-yne-4,4-dicarboxylate (0.119 g, 0.5 mmol), dodecyl methyl sulfide (0.130 g, 0.6 mmol), and toluene (4 mL). Octacarbonyl dicobalt (0.034 g, 0.1 mmol) was added and the tube was sealed immediately. The tube was then placed in a pre-heated oil bath at 90°C for 10 minutes. The crude product was purified directly *via* column chromatography (eluent: 10-50% diethyl ether in petrol) yielding the desired cyclopentenone product (0.061 g, 46% yield).

The analytical data for this compound is detailed on page 3.

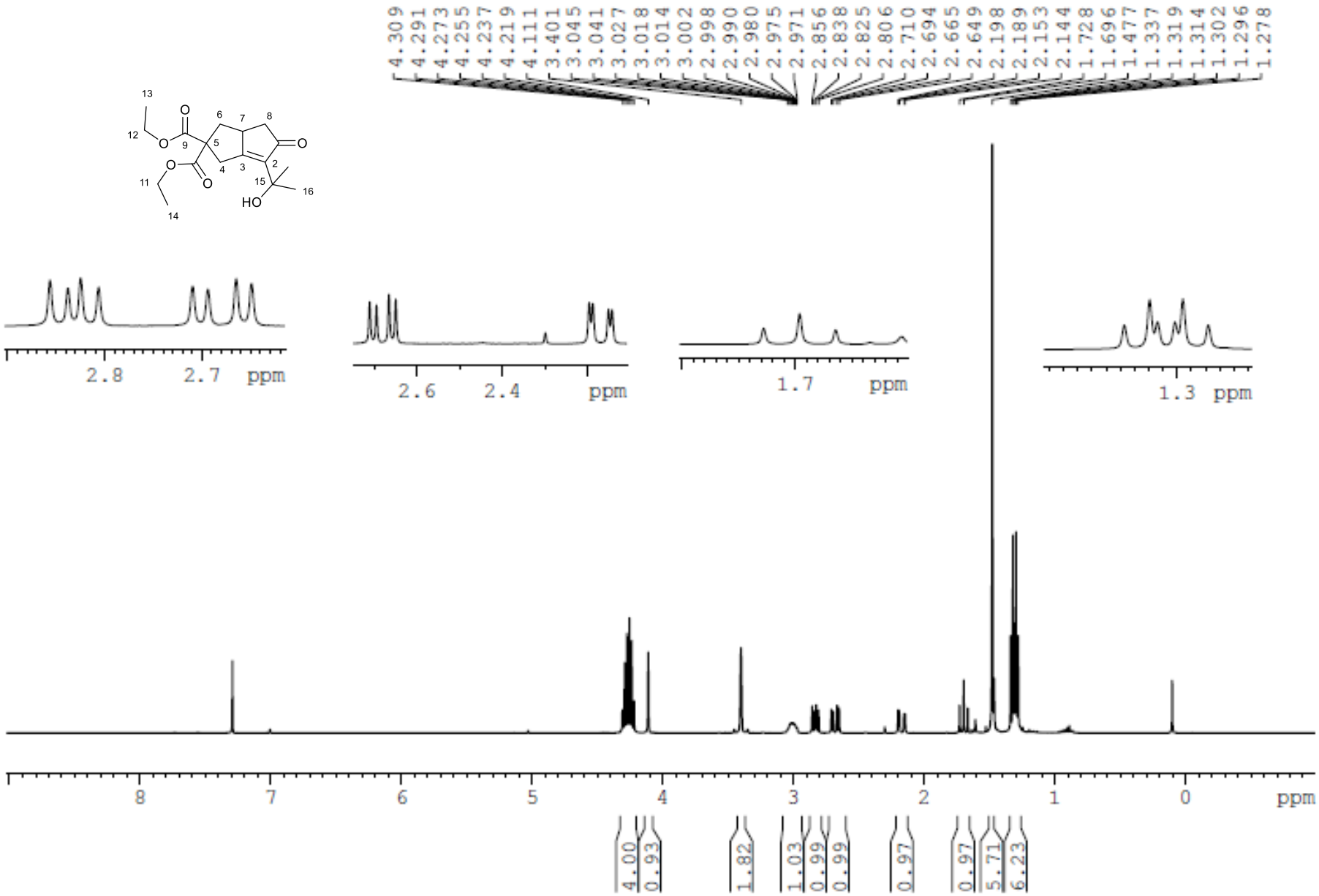
[1]H NMR Spectrum for Diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate.



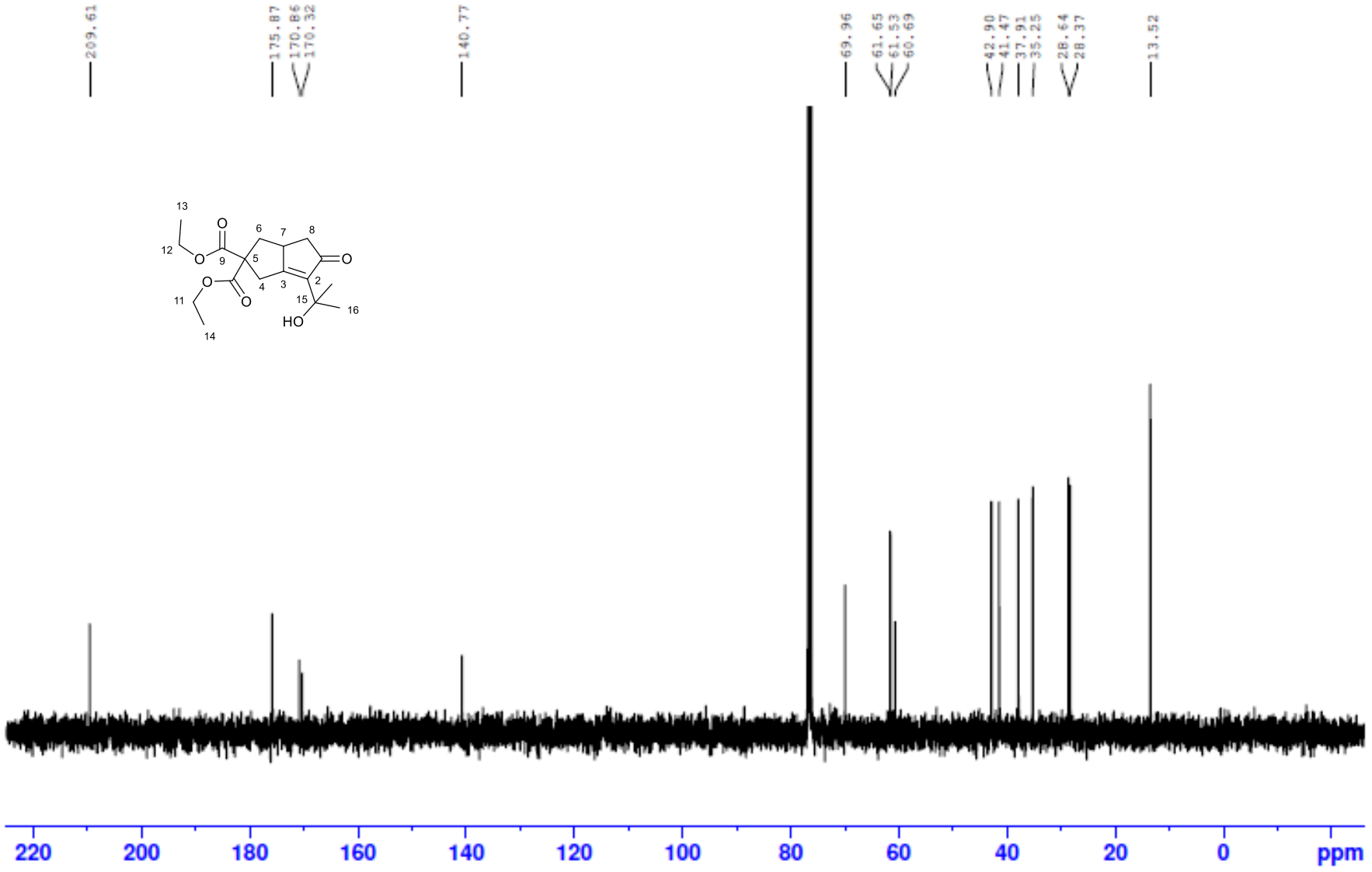
^{13}C NMR Spectrum for Diethyl 8-hydroxy-8-methylnon-1-en-6-yne-4,4-dicarboxylate.



[1]H NMR Spectrum for Diethyl 6-(1-hydroxy-1-methylethyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate



^{13}C NMR Spectrum for Diethyl 6-(1-hydroxy-1-methylethyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate



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