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Short Report

Synthesis of Fatty Trichloromethyl-β-diketones and New 1*H*-Pyrazoles as Unusual FAMEs and FAEEs

Alex F. C. Flores,*[,a] Rogerio F. Blanco,[b] Alynne A. Souto,[a] Juliana L. Malavolta[a] and Darlene C. Flores[a]

[a]*Departamento de Química, Universidade Federal de Santa Maria, 97105 900 Santa Maria-RS, Brazil*

[b]*Faculdade de Farmácia, União de Ensino do Sudoeste do Paraná (UNISEP), 85660-000 Dois Vizinhos-PR, Brazil*

A síntese eficiente de novas 1,1,1-tricloro-4-metoxi-3-alquen-2-onas graxas [$Cl_3CC(O)C(R^2)=C(R^1)OMe$, onde R^1 = *n*-hexil, heptil, nonil, undecil, tridecil e R^2 = H] e 1,1,1-tricloro-2,4-alkanediones [$Cl_3CC(O)CHR^2C(O)R^1$, onde R^1 = *n*-pentil e R^2 = Me, R^1 = Et e R^2 = *n*-butil, R^1 = *n*-butil e R^2 = *n*-propil] é apresentada, com bons rendimentos (85-95%) a partir da acilação dos respectivos acetais com cloreto de tricloroacetila. As 1,1,1-tricloro-4-metoxi-3-alquen-2-onas e 1,1,1-tricloro-2,4-alkanediones graxas reagem com cloridrato de hidrazina produzindo os respectivos 1*H*-pirazol-5-carboxilatos, uma classe de novos ésteres metílicos (FAMEs) e etílicos (FAEEs) graxos não comuns. As estruturas moleculares dos compostos sintetizados foram confirmadas por análise elementar e ressonância magnética nuclear (NMR) de ^1H e ^{13}C. As 1,1,1-tricloro-4-metoxi-3-alquen-2-onas graxas e seus derivados 1*H*-pirazol-5-carboxilatos são novos oleoquímicos com propriedades diferenciadas e potencialmente interessantes.

The efficient synthesis of new fatty 1,1,1-trichloro-4-methoxy-3-alken-2-ones [$Cl_3CC(O)C(R^2)=C(R^1)OMe$, where R^1 = *n*-hexyl, heptyl, nonyl, undecyl, tridecyl and R^2 = H] and 1,1,1-trichloro-2,4-alkanediones [$Cl_3CC(O)CHR^2C(O)R^1$, where R^1 = *n*-pentyl and R^2 = Me, R^1 = Et and R^2 = *n*-butyl, R^1 = *n*-butyl and R^2 = *n*-propyl] in good yields (85-95%) from acetal acylation with trichloroacetyl chloride is reported. The fatty 1,1,1-trichloro-4-methoxy-3-alken-2-ones and 1,1,1-trichloro-2,4-alkanediones were reacted with hydrazine hydrochloride, leading to respective 1*H*-pyrazole-5-carboxylates, unusual class of fatty acid methyl (FAMEs) and ethyl (FAEEs) esters. Their structures were confirmed by elemental analysis and ^1H and ^{13}C nuclear magnetic resonance (NMR). The fatty 1,1,1-trichloro-4-methoxy-3-alken-2-ones and 1*H*-pyrazole derivatives are new oleochemicals with potentially interesting and differential properties.

Keywords: fatty ketones, acylation, fatty 1*H*-pyrazoles

Introduction

We have developed a general method for synthesizing a large number of 1,1,1-trihalomethyl-4-alkoxy-3-alken-2-ones, important halogen-containing building blocks, and we have demonstrated their usefulness in bioactive heterocyclic synthesis.[1–3] These 1,3-dielectrophilic precursors have been used as a 3-atom block for the synthesis of 5-, 6- and 7-member heterocycles.[4–6] Conventionally, enol ethers have been prepared from symmetrical ketone or aldehyde acetals. However, the isolation of these enol ethers involves a tedious distillation process and in some cases (e.g., those derived from asymmetrical ketones) a mixture of kinetic and thermodynamic enol ethers is obtained.[7,8] Our method, with *in situ* generating of enol ether, offers a convenient alternative to produce acylated regiospecific derivatives 1,1,1-trihalomethyl-4-alkoxy-3-alken-2-ones. Moreover, the transformation of the trichloromethyl group under mild conditions into carboxylic groups prompted us to devote special attention to these substrates.[9,10]

Among the heterocycles obtained from 1,1,1-trihalomethyl-4-alkoxy-3-alken-2-ones, the pyrazole derivatives have remained the focus of research in particular regarding their biological effects of interest

*e-mail: alex.fcf@ufsm.br

in the agrochemical and pharmaceutical industries.[11–13] Systematic investigations of this class of heterocycle have revealed that pyrazole-containing pharmacoactive agents play an important role in medicinal chemistry, leading to further research on the chemistry of this heterocycle.[14–16]

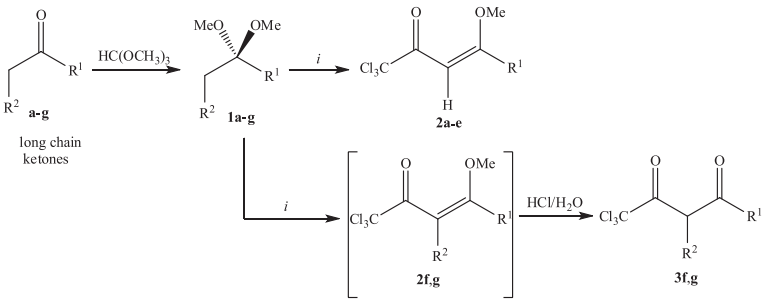
On the other hand, fatty substances are important in the food, pharmaceutical, personal care and paint industries.[17–19] There is a constant commitment to developing new surfactants and detergents with potentially interesting properties.[20,21] As a continuation of our research project on the synthetic potential of acetal acylating method, it is here reported the preparation of a series of new fatty 1,1,1-trichloro-4-alkoxy-3-alken-2-ones derived from fatty ketones and their conversion into 1*H*-pyrazole-carboxylate derivatives substituted with a long fatty chain, which are unusual fatty acid methyl (FAMEs) and ethyl (FAEEs) esters.

Results and Discussion

Dimethoxy ketals **1a**-**g** were synthesized from the acetalization of the respective fatty ketones **a**-**g** with trimethylorthoformate in the presence of *p*-toluenesulfonic acid.[19] The trichloroacylation reactions were carried out in chloroform and pyridine at 30 to 50 °C for 12 h as outlined in Scheme 1. Two equivalents of acylating agent *per* acetal were required to obtain the fatty 1,1,1-trichloro-4-methoxy-3-alken-2-ones **2a**-**g** since one molecule of the acylating reagent promotes the formation of enol ether by trapping a methoxy group from acetal, and the second molecule of acylating reagent promotes the formation of C–C bonds. As previously reported, acetals of alkyl methyl ketones are always acylated at methyl sites.[22] The acylated products **2a**-**e** were obtained as black oil in very good yields of 85-95% (see Supplementary Information (SI) section, Table S1) and high purity (Scheme 1).

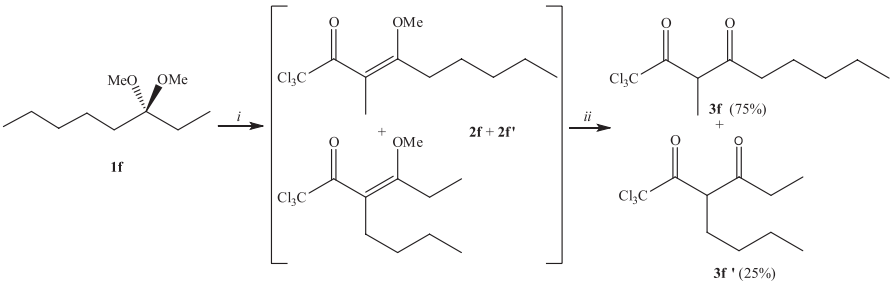
From alkyl methyl ketones (alken-2-ones), acylated products were obtained as 1,1,1-trichloro-4-methoxy-3-alken-2-ones without hydrolysis products from the work-up of acid water solutions. However, acylated products from octan-3-one and nonan-5-one were obtained as the respective trichloromethyl-β-diketones (**3f**,**g**). A mixture of 1,1,1-trichloro-3-methylnonan-2,4-dione (**3f**) and 1,1,1-trichloro-3-butylhexan-2,4-dione (**3f'**) was obtained from octan-3-one, and 1,1,1-trichloro-3-propyloctan-2,4-dione (**3g**) was obtained from nonan-5-one. During the acylation of 3,3-dimethoxyoctane with trichloroacetyl chloride, there was a preference for reactions at ethyl sites, leading to **3f** in larger quantities than the isomer **3f'**, demonstrating that the reaction had some degree of regioselectivity, probably for steric reasons as the reaction selects the lowest substituent between the carbonyl groups. The large sterical volume of the trichloromethyl group is likely one of the factors that prompted hydrolysis of 1,1,1-trichloro-4-methoxy-3-alken-2-ones substituted at position-3 and could help explain the preference of the respective trichloromethyl diketones for nonplanar keto-keto forms (Scheme 2).[23]

The structures of acylated products were characterized based on their nuclear magnetic resonance (NMR) spectra. The ^{1}H NMR signal of the vinylic hydrogen for pattern H-3 of the 1,1,1-trichloro-4-methoxy-3-alken-2-one **3a** appeared during high field analysis, δ 5.9 ppm, and the spectrum showed the characteristic signals of the fatty alkyl chain: a triplet at δ 2.7 ppm (2H, 5-CH_2), a multiplet at δ 1.5 ppm (2H, 6-CH_2), the broad signal from the inner –CH_2– at δ 1.25 ppm, and the triplet from the terminal methyl at δ 0.8 ppm. Further support for fatty acylated products was provided by the ^{13}C NMR spectra. Pattern **3a** showed high field signals from carbonyl C-2 and enol ether C-4 at δ 179.8 and 183.9 ppm, respectively. There was a signal from vinylic C-3 at δ 89.6 ppm, a short signal from CCl_3 at δ 98.05 ppm, an intense signal from the methoxy group at δ 56.1 ppm, signals from methylenes at 22-34 ppm, and a methyl signal at δ 13 ppm from the fatty alkyl chain. For trichloromethyl-β-diketones, the ^{1}H NMR spectrum showed



R^1 = *n*-hexyl(**a**), *n*-heptyl (**b**), *n*-nonyl (**c**), *n*-undecyl (**d**), *n*-tridecyl (**e**);
R^1 = pentyl, R^2 = Me (**f**); R^1 = Et, R^2 = *n*-butyl (**f'**)
R^1 = *n*-butyl, R^2= *n*-propyl (**g**)
(*i*) Trichloroacetyl chloride, pyridine, $CHCl_3$, 12 h, 30-50 °C.

Scheme 1. Synthesis of long chain 1,1,1-trichloro-4-methoxy-3-alken-2-ones and trichloromethyl-β-diketones.



(*i*) Trichloroacetyl chloride, pyridine, $CHCl_3$, 12 h, 30-50 °C.
(*ii*) Acid water solution work up.

Scheme 2. Trichloroacetylation of 3,3-dimethoxyoctane (**1f**).

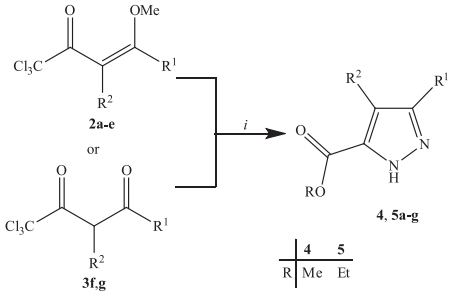
signals from H-3 at 4.5 ppm, for **3b** as a quartet with J_{HH} 6.8 Hz, together with the methyl doublet (J_{HH} 6,8 Hz), demonstrating the presence of the keto form in $CDCl_3$ solution. Signals from the C5 chain were also detected. For **3b'**, the H-3 signal appeared as a doublet of doublets (J_{HH} 8.6 and 5.5 Hz) and the signals from alkyl chains were hidden by those from the predominant product (Scheme 2). The same pattern was observed in the ^{1}H NMR spectrum from **3d**, in winch the signal from H-3 was a doublet of doublets (J_{HH} 8.8 and 5.2 Hz) and the spectrum showed all of the signals from 4-propyl and 3-butyl substituents. The NMR data for the fatty trichlomethylketones obtained are shown in the SI section.

Cyclization of 1,3-dielectrophilic precursors **2a**-**g** and **3f**,**g** with hydrazine hydrochloride proceeded smoothly in alcohol (methanol or ethanol) at reflux for 8 h to produce pyrazole-5-carboxylic esters **4, 5a**-**g** in isolated yields of 93-96% (Table 1). After completion of the reaction, solvent was evaporated and the product was dried in a desiccator with anhydrous $CaCl_2$ (Scheme 3).

Mechanistically, cyclocondensation between precursors 2 and hydrazine hydrochloride proceeds via conjugate

Table 1. Yields of the compounds **4a**-**g** and **5a**-**g**

Compound	R^1	R^2	R	Yield / %
4a	*n*-C_6H_{13}	H	Me	95
4b	*n*-C_7H_{15}	H	Me	93
4c	*n*-C_9H_{19}	H	Me	96
4d	*n*-$C_{11}H_{23}$	H	Me	93
4e	*n*-$C_{13}H_{27}$	H	Me	93
4f	*n*-C_5H_{11}	Me	Me	65
4g	*n*-Bu	*n*-Pr	Me	95
5a	*n*-C_6H_{13}	H	Et	96
5b	*n*-C_7H_{15}	H	Et	95
5c	*n*-C_9H_{19}	H	Et	95
5d	*n*-$C_{11}H_{23}$	H	Et	90
5e	*n*-$C_{13}H_{27}$	H	Et	95
5f	*n*-C_5H_{11}	Me	Et	62
5g	*n*-Bu	*n*-Pr	Et	95

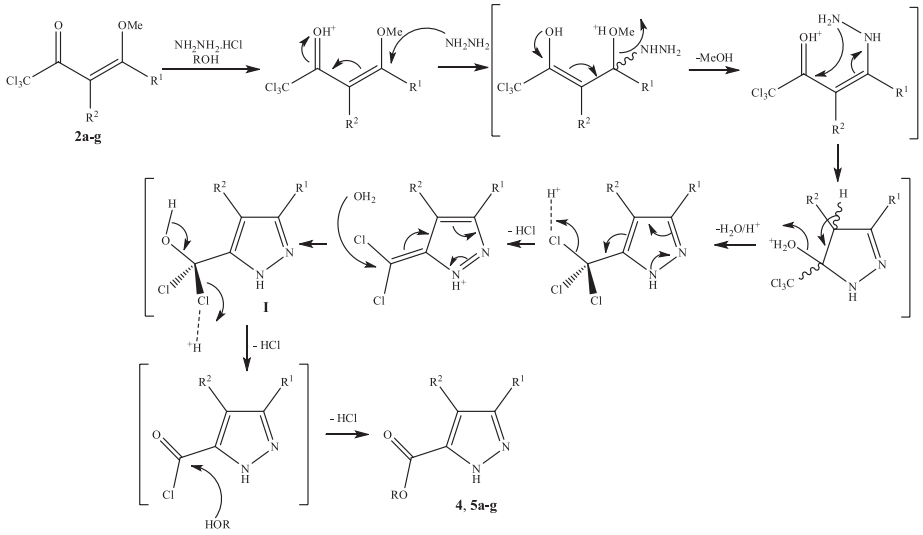


R^1 = *n*-hexyl(**a**), *n*-heptyl (**b**), *n*-nonyl (**c**), *n*-undecyl (**d**), *n*-tridecyl (**e**); R^2 = H
R^1 = *n*-pentyl, R^2 = Me (**f**); R^1 = Et, R^2 = *n*-butyl (**f'**)
R^1 = *n*-butyl; R = *n*-propyl (**g**)
(*i*) $NH_2NH_2.HCl$, ROH (R = Me, Et), reflux, 6 h.

Scheme 3. Synthesis of fatty 1*H*-pyrazole-5-carboxylates from 1,1,1-trichloro-4-methoxy-3-alken-2-ones.

addition of nitrogen into the C-4 of 1,1,1-trichloro-4-methoxy-3-alken-2-ones. Then, one molecule of methanol is eliminated to give the enaminoketone intermediate, which isomerizes to thermodynamically more stable hydrazone. Subsequent cyclization affords the 5-trichloromethyl-5-hydroxy-4,5-dihydro-1*H*-pyrazole intermediates, which are unstable in alcohol medium.[24] Then, one molecule of water is eliminated to give the aromatic 5-trichloromethyl-1*H*-pyrazole intermediate. Further elimination of chloride with the aid of the adjacent nitrogen atom leads to reactive intermediate I, which is attacked by water in the reaction medium, leading to the formation of an acid chloride that reacts with the solvent used in the reaction (MeOH or EtOH) (Scheme 4).

The 1*H*-pyrazole-5-carboxylates were identified based on NMR spectroscopy. The ^{1}H NMR spectrum showed the characteristic signals of the fatty alkyl chain: a triplet at δ 2.7 ppm (2H, 5-CH_2), a multiplet at δ 1.5 ppm (2H, 6-CH_2), the broad signal from the inner –CH_2– at δ 1.25 ppm and the triplet from the terminal methyl at δ 0.8 ppm. The signal from H-4 on the pyrazole ring appeared at δ 6.5-6.6 ppm. The ^{13}C NMR spectra displayed the trichloromethyl carbon as a characteristic small signal at approximately δ 102.7; furthermore, the signals for pyrazole carbons C-3, C-4 and



Scheme 4. Proposed reaction mechanism for cyclocondensation and trichloromethyl alcoholysis.

C-5 appeared at δ 147, 106 and 141 ppm, respectively. For compounds substituted at C-4, the carbon C-4 was deshielded to 122 ppm and C-5 was shielded to 136 ppm. The signal from the carboxyl carbon appeared at 162 ppm.

Conclusion

In conclusion, we have established the versatility of the acetal acylation process for synthesizing fatty 1,1,1-trichloro-4-methoxy-3-alken-2-ones, which are versatile building blocks for heterocyclic compounds. It was found that trichloromethylated precursors react with hydrazine hydrochloride, leading to new methyl or ethyl 1*H*-pyrazole-5-carboxylates, fatty substances with potentially interesting properties.

Experimental

Unless indicated otherwise, all common reagents were used as obtained from commercial suppliers without further purification. All melting points were measured using a Reichert-Thermovar apparatus. Listed yields are of isolated compounds. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker DPX 200 or Bruker DPX 400 spectrometer (^{1}H at 200.13 or 400.13 MHz and ^{13}C at 50.32 or 100.63 MHz) at 300 K, using 5 mm sample tubes, and with a digital resolution of ± 0.01 ppm. $CDCl_3$ was used as a solvent with TMS (tetramethylsilane) as the internal standard.

General procedure for 1,1,1-trichloro-4-methoxy-3-alken-2-ones (**2a**-**g**)

To a stirred solution of dimethoxy acetal derived from fatty ketones **1a**-**g** (30 mmol) and pyridine (60 mmol, 4.8 g) in $CHCl_3$ (30 mL) kept at 0 °C, a solution of trichloroacetyl chloride (60 mmol, 6.8 mL) in $CHCl_3$ (20 mL) was added dropwise at −5 °C. The mixture was stirred for 8-12 h at room temperature (30-50 °C). After, the mixture was quenched with a 2 mol L^{-1} HCl solution (30 mL), the organic layer was separated and dried with Na_2SO_4, the solvent was evaporated, and the residue was distilled to remove methyl trichloroacetate. The products **2a**-**e** were obtained as black oil with high purity, and all are inedited. Yields, NMR data and spectra for 1,1,1-trichloro-4-methoxy-3-alken-2-ones **2a**-**e** are presented in the SI section.

General procedure for 1*H*-pyrazole-5-carboxylate derivatives (**4**, **5**)

A mixture of one precursor **2a**-**e** or **3f**,**g** (10 mmol) and NH_2NH_2.HCl (12 mmol, 0.82 g) in 10 mL alcohol (MeOH or EtOH) was stirred under reflux for 4 to 8 h. Then solvent was evaporated, the residue was dissolved in CH_2Cl_2 (20 mL) and washed with water (15 mL) twice, and the organic layer was dried with Na_2SO_4. After evaporation of the solvent, the residues were obtained as reddish orange oils (R = hexyl, heptyl and nonyl) or brown greases (R = undecyl and tridecyl). Spectroscopic data for derivatives 1*H*-pyrazole carboxylate **4a**-**g** and **5a**-**g** and the full data series can be seen in the SI section.

Methyl 3-hexyl-1*H*-pyrazole-5-carboxylate (**4a**): yield 95%, orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (s, 1H, H4), 3.78 (s, 3H, OMe), 2.60 (t, 2H, H6), 1.53 (qu, 2H, H7), 1.18 (m, 6H, $-(CH_2)_3-$), 0.77 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (CO_2Me), 147.3 (C3), 141.5 (C5), 106.0 (C4), 51.5 (OMe), 31.3, 28.8, 28.6, 25.7, 22.3

(CH_2), 13.8 (Me); MS (70 eV) *m/z* 211 (M^+ + 1, 10), 210 (M^+, 60); anal. calcd. for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; found C, 62.7; H, 8.7.

Methyl 3-heptyl-1*H*-pyrazole-5-carboxylate (**4b**): yield 93%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (s, 1H, H4), 3.77 (s, 3H, OMe), 2.61 (t, 2H, H6), 1.52 (qu, 2H, H7), 1.18 (m, 8H, $-(CH_2)_4-$), 0.77 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (CO_2Me), 147.3 (C3), 141.4 (C5), 106.1 (C4), 51.7 (OMe), 31.6, 28.97, 28.93, 28.8, 25.6, 22.5 (CH_2), 13.9 (Me); MS (70 eV) *m/z* 225 (M^+ + 1, 10), 224 (M^+, 58); anal. calcd. for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99; found C, 64.5; H, 8.9.

Methyl 3-nonyl-1*H*-pyrazole-5-carboxylate (**4c**): yield 96%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (s, 1H, H4), 3.77 (s, 3H, OMe), 2.60 (t, 2H, H6), 1.52 (qu, 2H, H7), 1.18 (m, 12H, $-(CH_2)_6-$), 0.78 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (CO_2Me), 147.2 (C3), 141.6 (C5), 106.0 (C4), 51.5 (OMe), 31.7, 29.3, 29.16, 29.12, 28.99 28.93, 25.6, 22.5 (CH_2), 13.9 (Me); MS (70 eV) *m/z* 253 (M^+ + 1, 12), 252 (M^+, 65); anal. calcd. for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; found C, 66.8; H, 9.5.

Methyl 3-undecyl-1*H*-pyrazole-5-carboxylate (**4d**): yield 93%, brown grease; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.6 (s, 1H, H4), 3.77 (s, 3H, OMe), 2.70 (t, 2H, H6), 1.65 (qu, 2H, H7), 1.28 (m, 16H, $-(CH_2)_8-$), 0.88 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (CO_2Me), 147.2 (C3), 141.6 (C5), 106.0 (C4), 51.5 (OMe), 31.8, 29.57, 29.55, 29.46, 29.27, 29.09, 29.07, 26.1, 22.6 (CH_2), 14.0 (Me); MS (70 eV) *m/z* 281 (M^+ + 1, 9), 280 (M^+, 60); anal. calcd. for $C_{16}H_{28}N_2O_2$: C, 68.53; H, 10.06; found C, 68.3; H, 10.1.

Methyl 3-tridecyl-1*H*-pyrazole-5-carboxylate (**4e**): yield 93%, brown grease; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (s, 1H, H4), 3.77 (s, 3H, OMe), 2.69 (t, 2H, H6), 1.62 (qu, 2H, H7), 1.18 (m, 20H, $-(CH_2)_{10}-$), 0.88 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8 (CO_2Me), 148.1 (C3), 141.2 (C5), 106.2 (C4), 51.7 (OMe), 31.8, 29.61, 29.58, 29.46, 29.28, 29.10, 29.07, 26.1, 22.6 (CH_2), 14.0 (Me); MS (70 eV) *m/z* 309 (M^+ + 1, 15), 308 (M^+, 60); anal. calcd. for $C_{18}H_{32}N_2O_2$: C, 70.09; H, 10.46; found C, 70.0; H, 10.7.

Methyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate (**4f**): yield 65%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H, OMe), 2.60 (s, 2H, H6), 2.22 (t, 3H, 4-CH_3), 1.61 (qu, 2H, H7), 1.18 (m, 4H, $-(CH_2)_2-$), 0.89 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0 (CO_2Me), 148.2 (C3), 135.8 (C5), 117.5 (C4), 51.6 (OMe), 31.4, 28.6, 25.2, 22.3 (CH_2), 13.9 (Me), 8.57 (4-Me); MS (70 eV) *m/z* 211 (M^+ + 1, 6), 210 (M^+, 71); anal. calcd. for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; found C, 62.6; H, 8.5.

Methyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate (**4g**): yield 95%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H, OMe), 2.56 (q, 4H, $-(CH_2)_2-$), 1.55 (m, 2H, $-CH_2-$), 1.48 (m, 2H, $-CH_2-$), 1.30 (m, 2H, $-CH_2-$), 0.85 (t, 3H, Me), 0.83 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 (CO_2Me), 147.1 (C3), 136.1 (C5), 122.2 (C4), 51.4 (OMe), 31.3, 25.2, 24.7, 24.0, 22.3 (CH_2), 13.9, 13.6 (Me); MS (70 eV) *m/z* 225 (M^+ + 1, 8), 224 (M^+, 65); anal. calcd. for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99; found C, 64.3; H, 9.1.

Ethyl 3-hexyl-1*H*-pyrazole-5-carboxylate (**5a**): yield 96%, orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (s, 1H, H4), 4.25 (q, 2H, OCH_2), 2.59 (t, 2H, H6), 1.54 (qu, 2H, H7), 1.25 (t, 3H, Me), 1.19 (m, 6H, $-(CH_2)_3-$), 0.77 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (CO_2Et), 147.7 (C3), 141.4 (C5), 106.1 (C4), 60.8 (OCH_2), 31.4, 28.9, 28.7, 25.8, 22.4 (CH_2), 14.1 (Me), 13.8 (Me); MS (70 eV) *m/z* 225 (M^+ + 1, 12), 224 (M^+, 97); anal. calcd. for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99; found C, 64.4; H, 9.2.

Ethyl 3-heptyl-1*H*-pyrazole-5-carboxylate (**5b**): yield 95%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (s, 1H, H4), 4.26 (q, 2H, OCH_2), 2.60 (t, 2H, H6), 1.54 (qu, 2H, H7), 1.25 (t, 3H, Me), 1.19 (m, 8H, $-(CH_2)_4-$), 0.77 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0 (CO_2Et), 147.5 (C3), 141.6 (C5), 106.0 (C4), 60.7 (OCH_2), 31.6, 29.02, 28.99, 28.87, 25.84, 22.5 (CH_2), 14.2 (Me), 13.9 (Me); MS (70 eV) *m/z* 239 (M^+ + 1, 9), 238 (M^+, 70); anal. calcd. for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.30; found C, 65.2; H, 9.5.

Ethyl 3-nonyl-1*H*-pyrazole-5-carboxylate (**5c**): yield 95%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (s, 1H, H4), 4.28 (q, 2H, OCH_2), 2.60 (t, 2H, H6), 1.56 (qu, 2H, H7), 1.28 (t, 3H, Me), 1.18 (m, 12H, $-(CH_2)_6-$), 0.80 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (CO_2Et), 148.3 (C3), 141.0 (C5), 106.3 (C4), 60.8 (OCH_2), 31.8, 29.4, 29.23, 29.17, 29.05, 29.04, 26.14, 22.5 (CH_2), 14.2 (Me), 13.9 (Me); MS (70 eV) *m/z* 267 (M^+ + 1, 12), 266 (M^+, 70); anal. calcd. for $C_{15}H_{26}N_2O_2$: C, 67.63; H, 9.84; found C, 67.3; H, 10.0.

Ethyl 3-undecyl-1*H*-pyrazole-5-carboxylate (**5d**): yield 90%, brown grease; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.6 (s, 1H, H4), 4.37 (s, 2H, OCH_2), 2.70 (t, 2H, H6), 1.65 (qu, 2H, H7), 1.37 (t, 3H, Me), 1.28 (m, 16H, $-(CH_2)_8-$), 0.89 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8 (CO_2Et), 148.3 (C3), 141.1 (C5), 106.3 (C4), 60.8 (OCH_2), 31.85,

29.57, 29.55, 29.46, 29.27, 29.09, 29.07, 26.1, 22.6 (CH_2), 14.2 (Me), 14.0 (Me); MS (70 eV) *m/z* 295 (M^+ + 1, 17), 294 (M^+, 90); anal. calcd. for $C_{17}H_{30}N_2O_2$: C, 68.53; H, 10.06; found C, 68.3; H, 10.1.

Ethyl 3-tridecyl-1*H*-pyrazole-5-carboxylate (**5e**): yield 95%, brown grease; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (s, 1H, H4), 4.36 (s, 2H, OCH_2), 2.69 (t, 2H, H6), 1.62 (qu, 2H, H7), 1.35 (t, 3H, Me), 1.25 (m, 20H, $-(CH_2)_{10}-$), 0.88 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8 (CO_2Et), 148.1 (C3), 141.2 (C5), 106.2 (C4), 60.8 (OCH_2), 31.8, 29.61, 29.58, 29.46, 29.28, 29.10, 29.07, 26.1, 22.6 (CH_2), 14.2 (Me), 14.0 (Me); MS (70 eV) *m/z* 323 (M^+ + 1, 17), 322 (M^+, 93); anal. calcd. for $C_{19}H_{34}N_2O_2$: C, 70.76; H, 10.63; found C, 70.2; H, 10.9.

Ethyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate (**5f**): yield 62%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.36 (s, 2H, OCH_2), 2.63 (s, 2H, H6), 2.23 (t, 3H, 4-CH_3), 1.63 (qu, 2H, H7), 1.37 (t, 3H, Me), 1.18 (m, 4H, $-(CH_2)_2-$), 0.89 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0 (CO_2Et), 148.2 (C3), 135.8 (C5), 117.5 (C4), 60.3 (OCH_2), 31.4, 28.6, 25.2, 22.3 (CH_2), 14.2 (Me), 13.9 (Me), 8.57 (4-Me); MS (70 eV) *m/z* 239 (M^+ + 1, 8), 238 (M^+, 70); anal. calcd. for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99; found C, 64.0; H, 9.2.

Ethyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate (**5g**): yield 95%, red orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.36 (q, 2H, OCH_2), 2.63 (q, 4H, $-(CH_2)_2-$), 1.62 (m, 2H, $-CH_2-$), 1.53 (m, 2H, $-CH_2-$), 1.38 (m, 2H, $-CH_2-$), 0.85 (t, 3H, Me), 0.83 (t, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5 (CO_2Et), 148.0 (C3), 135.6 (C5), 122.3 (C4), 60.5 (OCH_2), 31.3, 25.3, 24.9, 24.1, 22.4 (CH_2), 14.2 13.9, 13.7 (Me); MS (70 eV) *m/z* 239 (M^+ + 1, 15), 238 (M^+, 85); anal. calcd. for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.30; found C, 65.1; H, 9.8.

Supplementary Information

Supplementary material (spectra data and spectra of synthesized compounds) is available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

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Supplementary Information

Synthesis of Fatty Trichloromethyl-β-diketones and New 1*H*-Pyrazoles as Unusual FAMEs and FAEEs

Alex F. C. Flores,*[,a] Rogerio F. Blanco,[b] Alynne A. Souto,[a] Juliana L. Malavolta[a] and Darlene C. Flores[a]

[a]*Departamento de Química, Universidade Federal de Santa Maria, 97105 900 Santa Maria-RS, Brazil*

[b]*Faculdade de Farmácia, União de Ensino do Sudoeste do Paraná (UNISEP), 85660-000 Dois Vizinhos-PR, Brazil*

^{1}H and ^{13}C NMR data and spectra for 1,1,1-trichloro-4-methoxy-3-alken-2-ones (**2a**-**e**), trichloromethyl-β-diketones (**3f**,**g**) and 1*H*-pyrazole-5-carboxylates (**4a**-**g**, **5a**-**g**) are shown. The ^{1}H and ^{13}C spectra were recorded at 298 K on a Bruker DPX 400 spectrometer (^{1}H at 400.13 MHz, ^{13}C at 100.63 MHz) with digital resolution of ± 0.01 ppm. All the chemical shifts are expressed in ppm, ^{1}H and ^{13}C are reported with respect to internal TMS (tetramethylsilane). 0.1 mol L^{-1} $CDCl_3$ solutions were used except with compounds **2**, 0.1 mol L^{-1} in DMSO-d_6. H-H and C-F coupling constants (*J*) are in Hz. Furthermore, a reaction mechanism for cyclcocondensation between 1,1,1-trichloro-4-methoxy-3-alken-2-ones and hydrazine hydrochloride is proposed.

Table S1. ^{1}H NMR data for 1,1,1-trichloro-4-methoxy-3-alken-2-ones **2** and trichloromethyl-β-diketones **3** in $CDCl_3$, δ in ppm, multiplicity, *J* in Hz

Compound, Yield / %	H-3	H-5	H-6	Others	Me	OMe
2a, 85	5.96	2.78, t, 8.0	1.57, qui, 8.0	1.28-1.39	0.89, t, 6.8	3.79
2b, 92	5.97	2.78, t, 8.0	1.58, qui, 8.0	1.29-1.38	0.89, t, 6.8	3.79
2c, 95	5.97	2.78, t, 8.0	1.57, qui, 8.0	1.27-1.35	0.88, t, 6.8	3.79
2d, 92	5.95	2.77, t, 8.0	1.56, qui, 8.0	1.26-1.34	0.87, t, 6.8	3.78
2e, 90	5.96	2.78, t, 8.0	1.57, qui, 8.0	1.26-1.34	0.88, t, 6.8	3.79
3f, 69	4.47, q, 7.2	2.58, m, 6.8	1.58, m, 7.2	1.32, m	0.9, 0.88t	–
3f', 23	4.42, dd, 8.5, 5.2	–[a]	–[a]	–	–	–
3g, 89	4.43, dd, 8.9, 5.2	2.62, m	1.92, m	1.20-1.40	0.89, 0.96, t, t	–

[a]Overlapping signals.

Table S2. ^{13}C NMR data for for 1,1,1-trichloro-4-methoxy-3-alken-2-ones **2** and trichloromethyl-β- diketones **3** in $CDCl_3$, δ in ppm

Compound	C-1	C-2	C-3	C-4	OMe	Others
2a	98.0	179.9	89.7	184.0	56.2	33.4; 31.4; 28.1; 26.9; 22.5; 13.9
2b	98.0	179.9	89.7	184.0	56.2	33.4; 31.7; 29.4; 28.9; 27.0; 22.5; 14.0
2c	98.0	179.9	89.7	184.0	56.2	33.4; 31.8; 29.4; 29.2; 26.9; 22.6; 14.0
2d	98.0	179.8	89.7	183.9	56.1	33.4; 31.8; 29.4; 29.2; 29.1; 26.9; 22.6; 14.0
2e	98.0	179.9	89.7	184.1	56.2	33.4; 31.9; 29.65; 29.62; 29.59; 29.5; 29.4; 29.3; 27.0; 22.6; 14.0
3f	96.1	186.7	52.5	203.5	–	40.5; 31.1; 23.0; 22.2; 16.3; 13.69
3f'	96.1	185.2	58.6	203.3	–	40.5; 34.3; 31.0; 22.8; 29.6; 7.60
3g	94.4	185.2	58.7	203.5	–	40.7; 33.5; 25.4; 22.0; 21.0; 13.8; 13.7

*e-mail: alex.fcf@ufsm.br

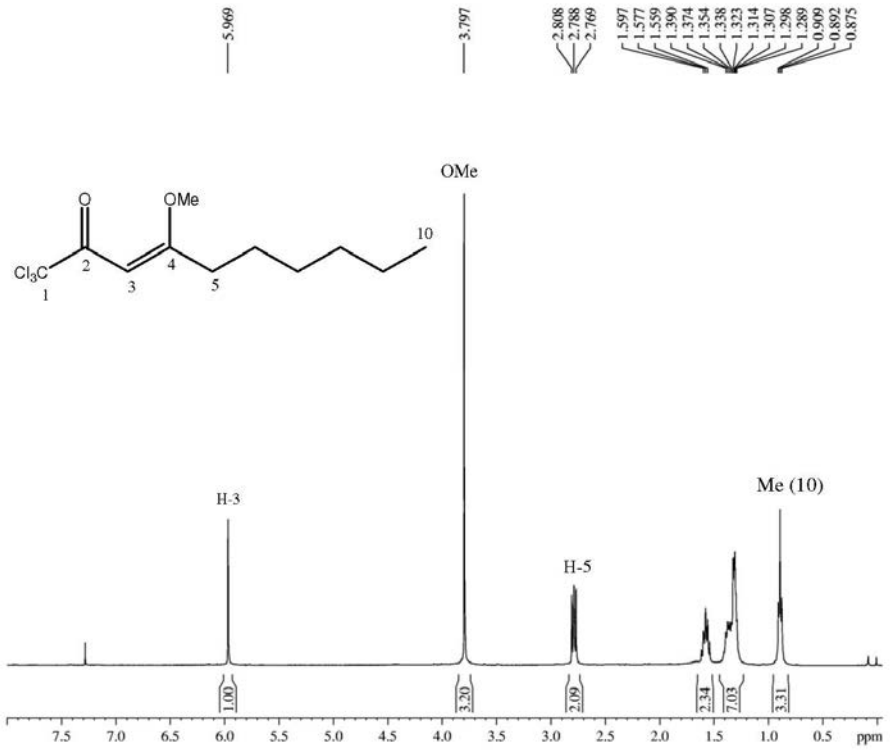

Figure S1.[1]H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-decen-2-one.

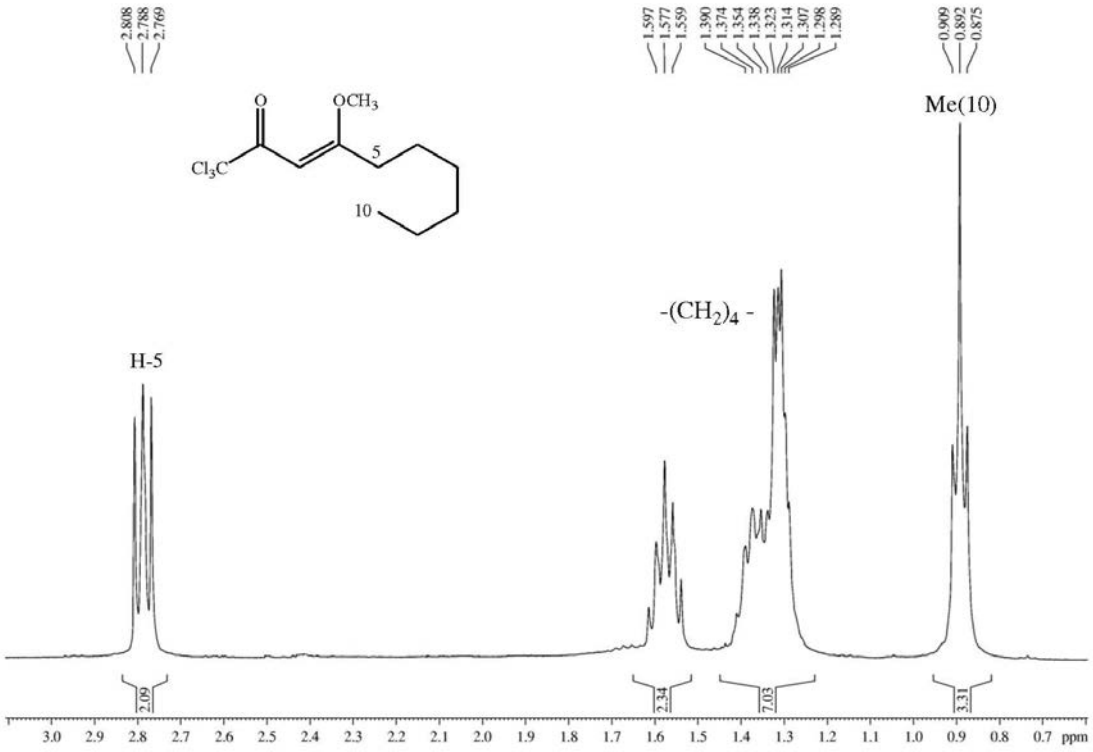

Figure S2. [1]H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-decen-2-one, expanded between 0.6-3.1 ppm.

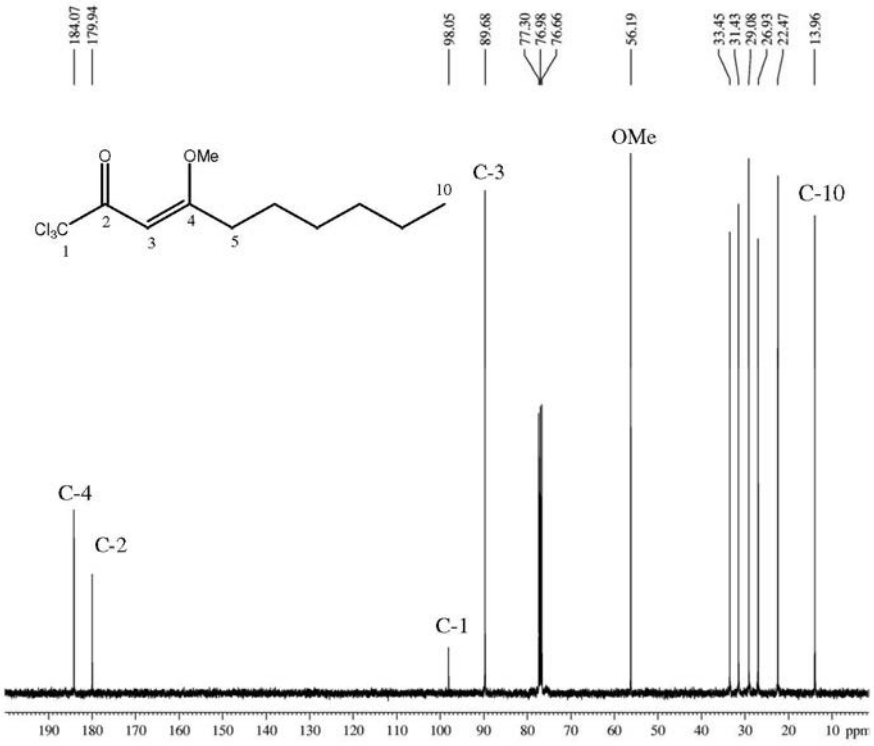

Figure S3. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 1,1,1-trichloro-4-methoxy-4-decen-2-one.

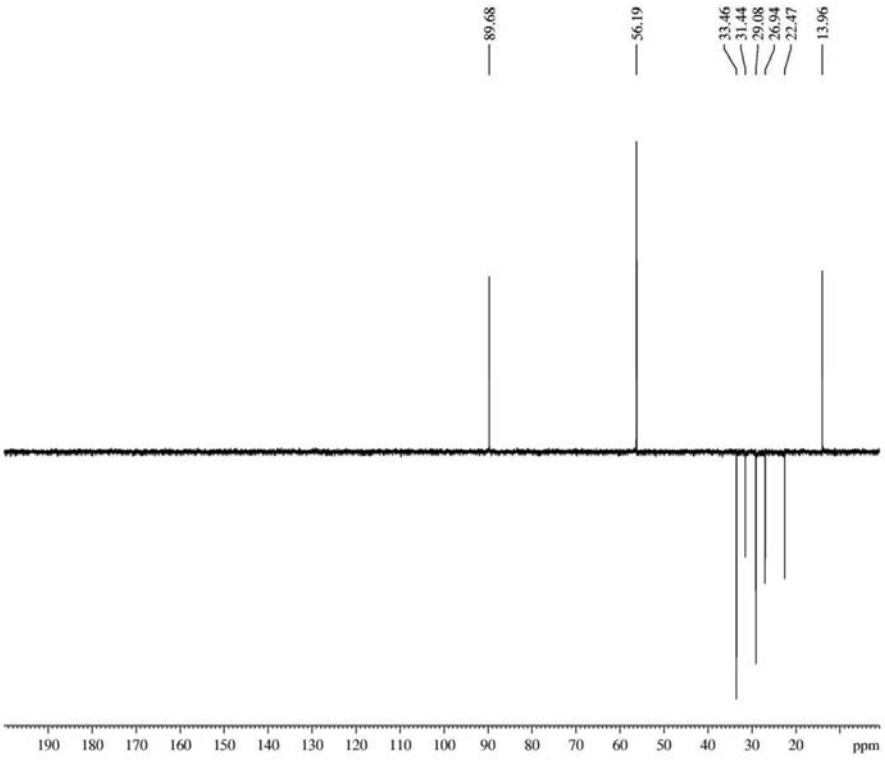

Figure S4. ^{13}C NMR DEPT135 spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-decen-2-one.

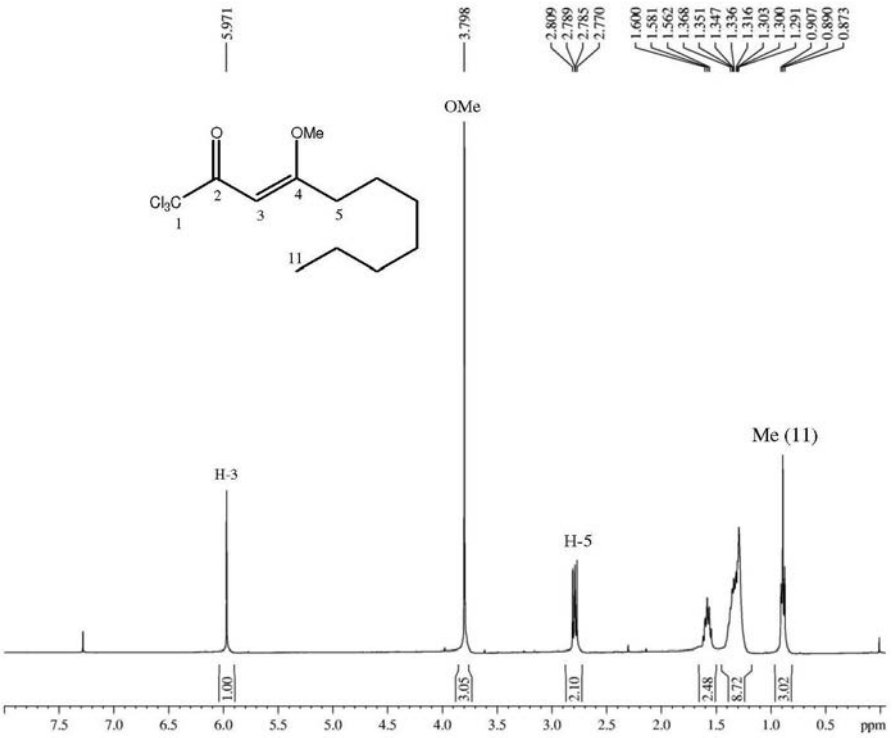

Figure S5. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-undecen-2-one in $CDCl_3$.

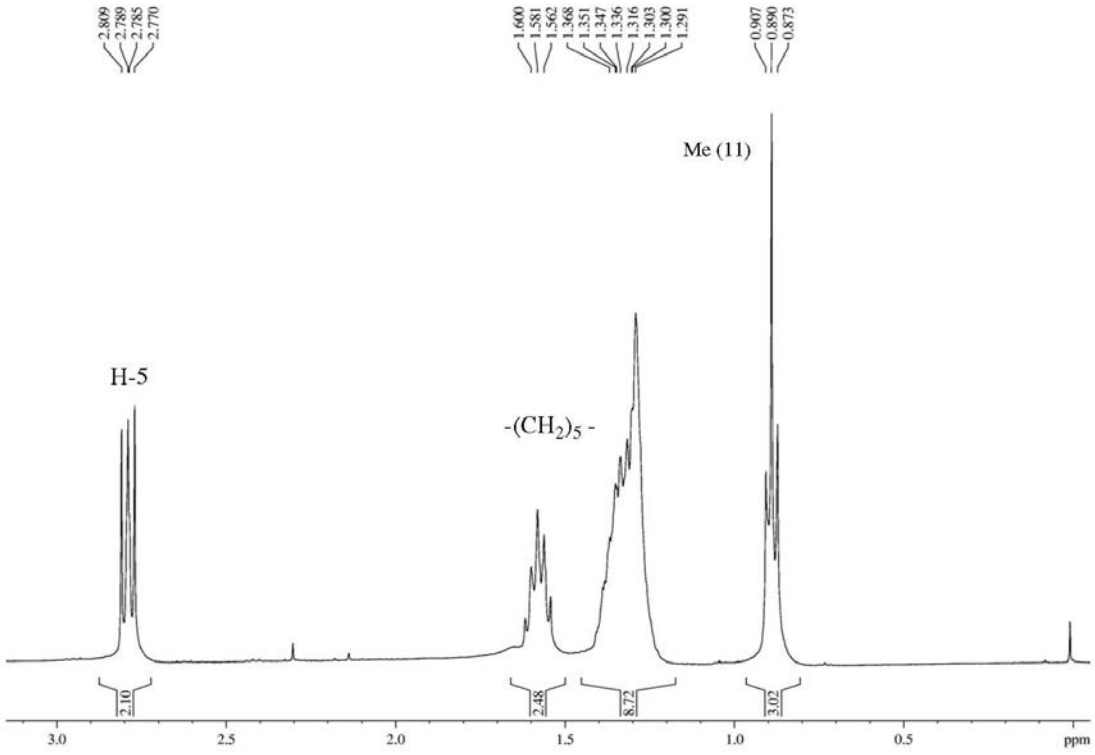

Figure S6. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-undecen-2-one, expanded between 0-3.1 ppm.

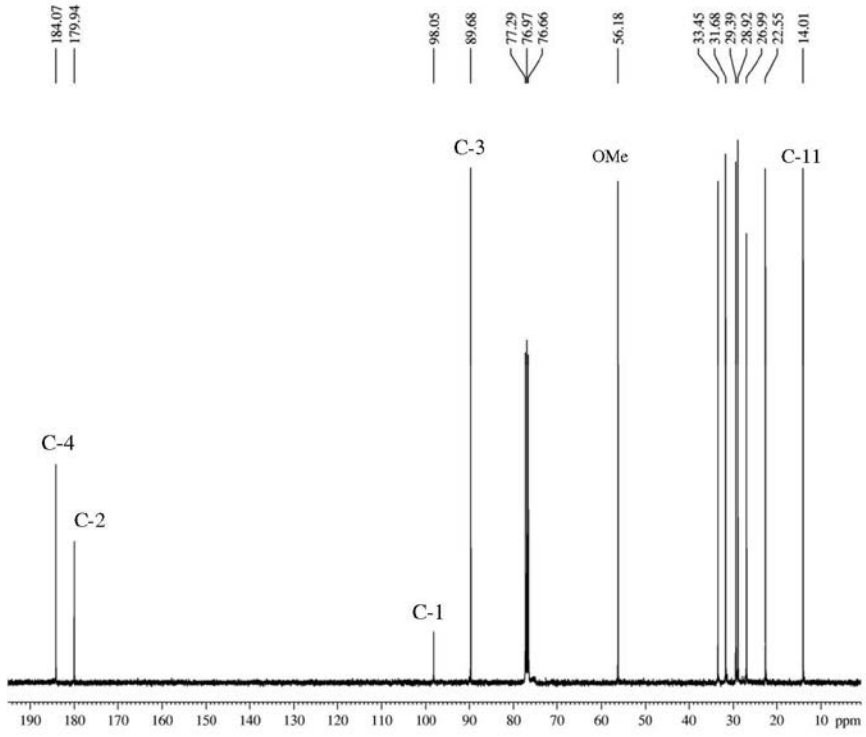

Figure S7. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-undecen-2-one.

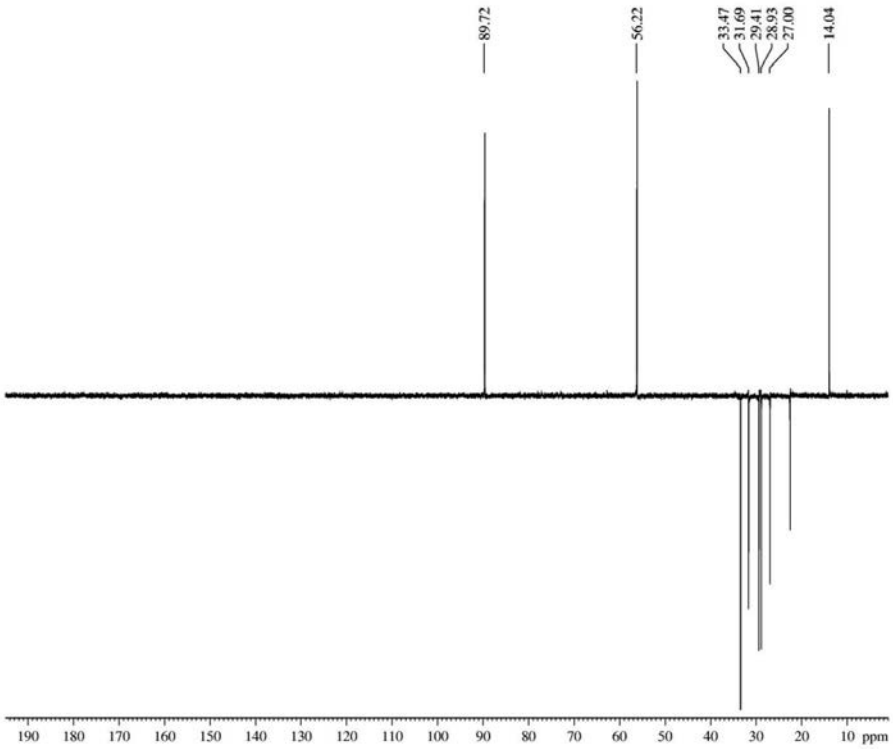

Figure S8. ^{13}C NMR DEPT135 spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-undecen-2-one.

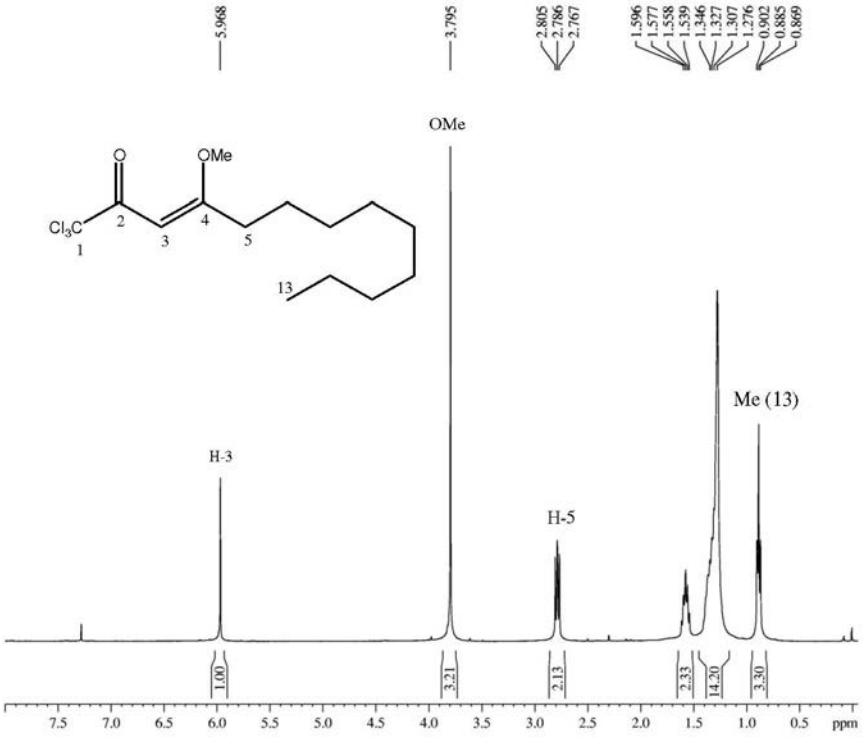

Figure S9. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-tridecen-2-one.

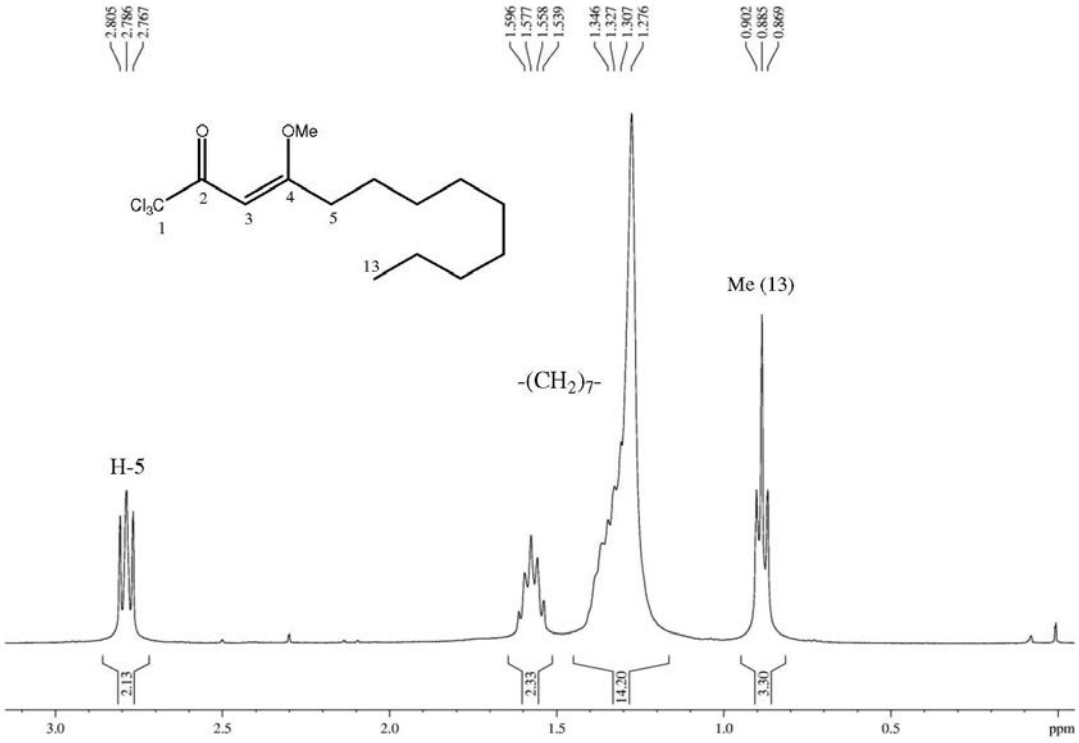

Figure S10. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-tridecen-2-one , expanded between 0 -3,15 ppm.

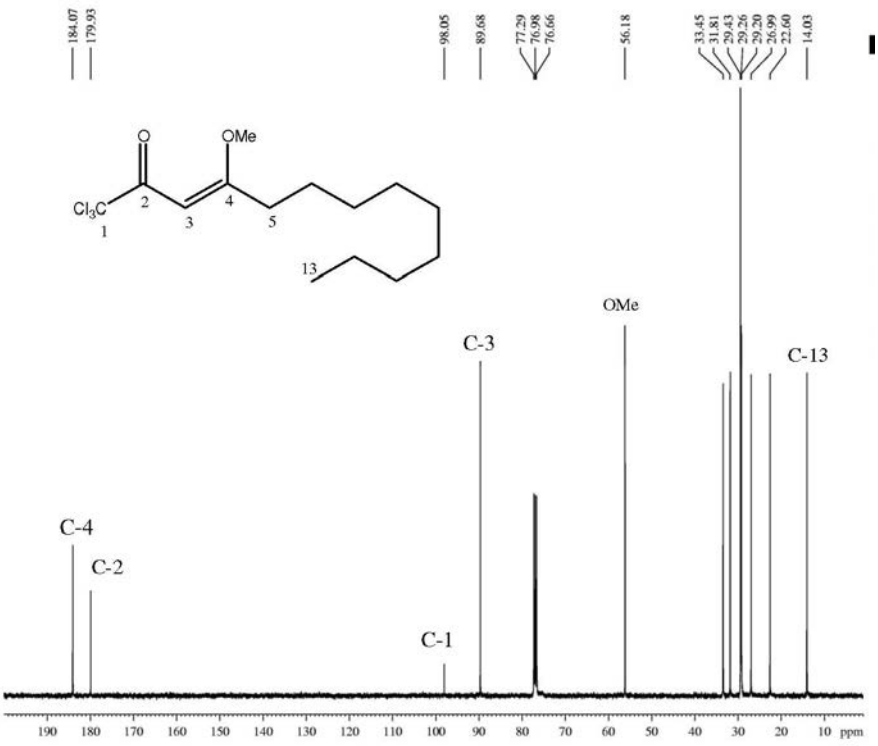

Figure S11. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-4-tridecen-2-one.

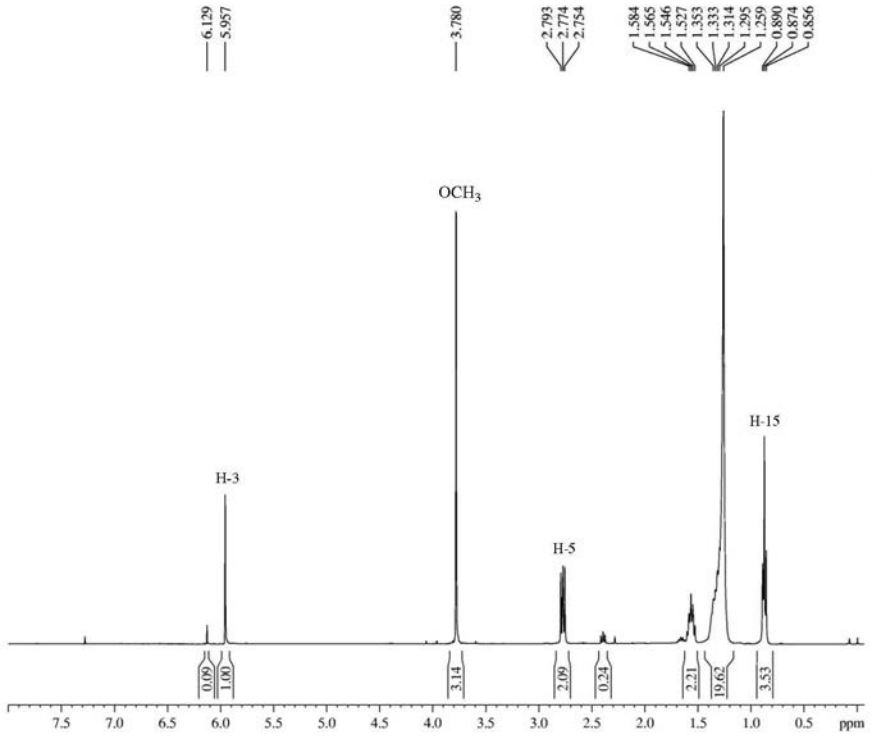

Figure S12. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-pentadecen-2-one.

Figure S13. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-pentadecen-2-one (91%) + 1,1,1-trichloropentadecan-2-one (9%).

Figure S14. ^{13}C NMR DEPT135 spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-pentadecen-2-one (91%) + 1,1,1-trichloropentadecan-2-one (9%).

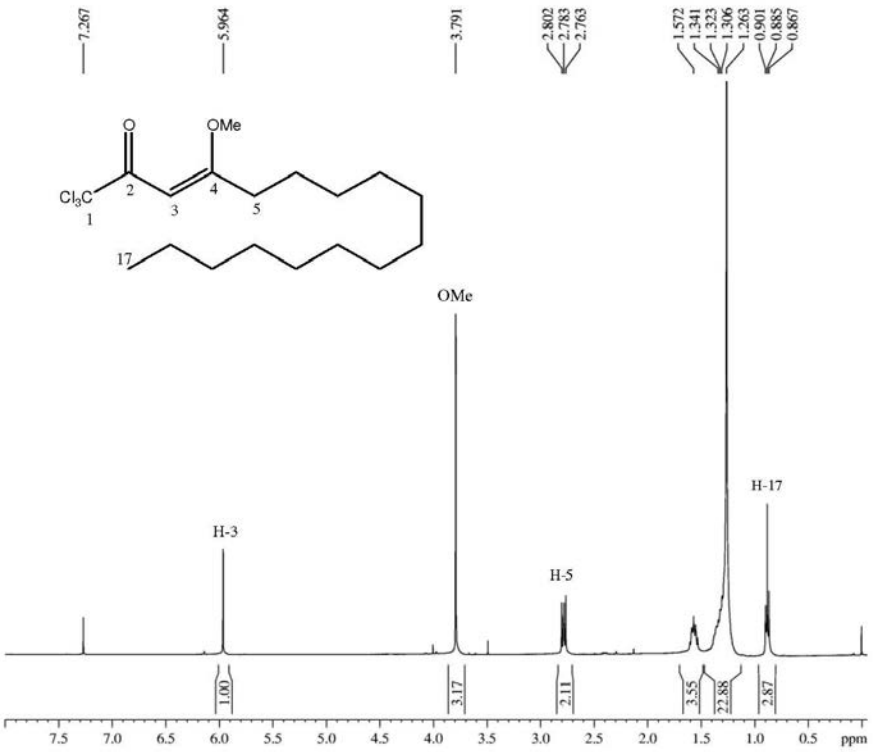

Figure S15. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-heptadecen-2-one.

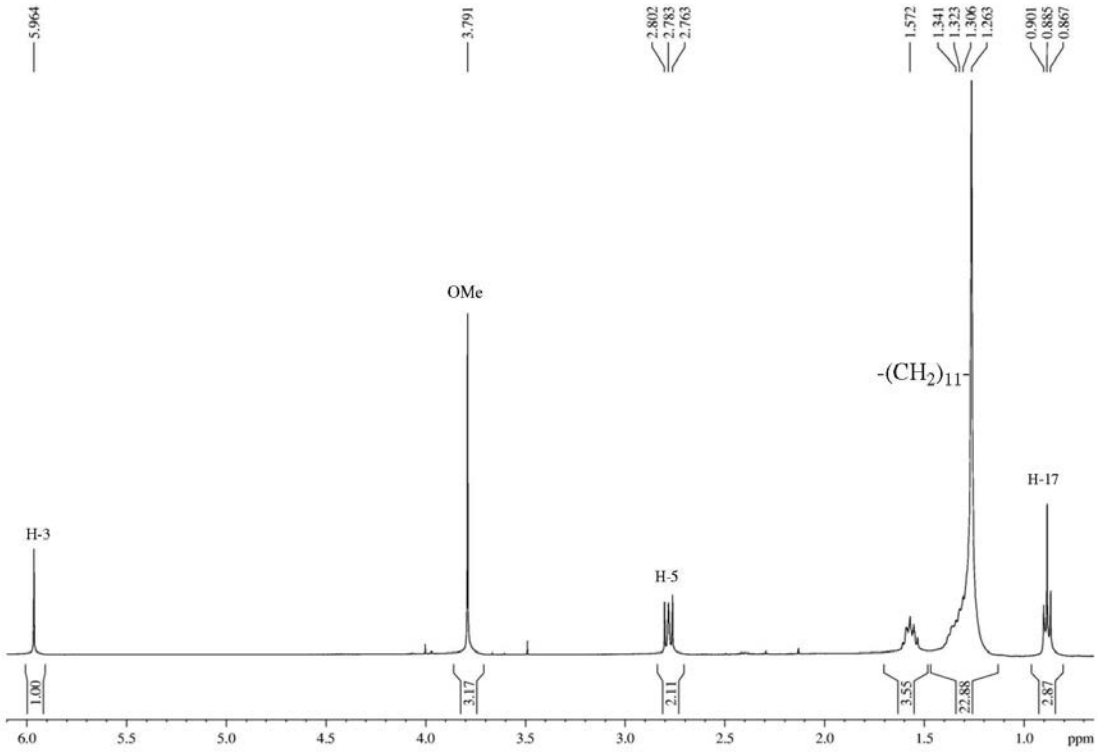

Figure S16. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-heptadecen-2-one , expanded between 0.5-6.1 ppm.

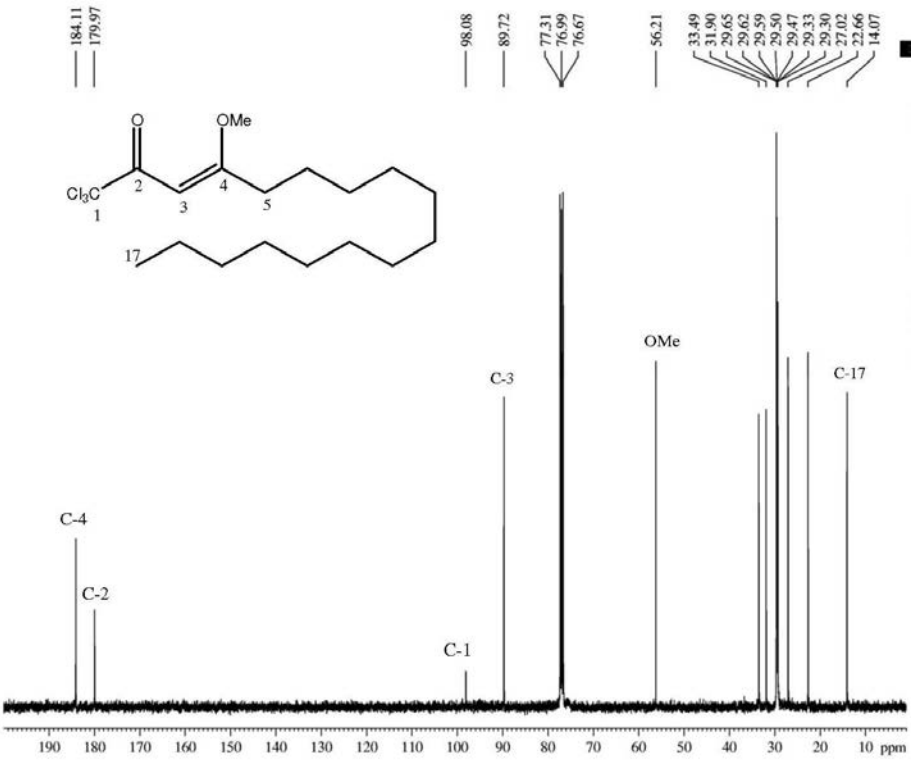

Figure S17. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-heptadecen-2-one.

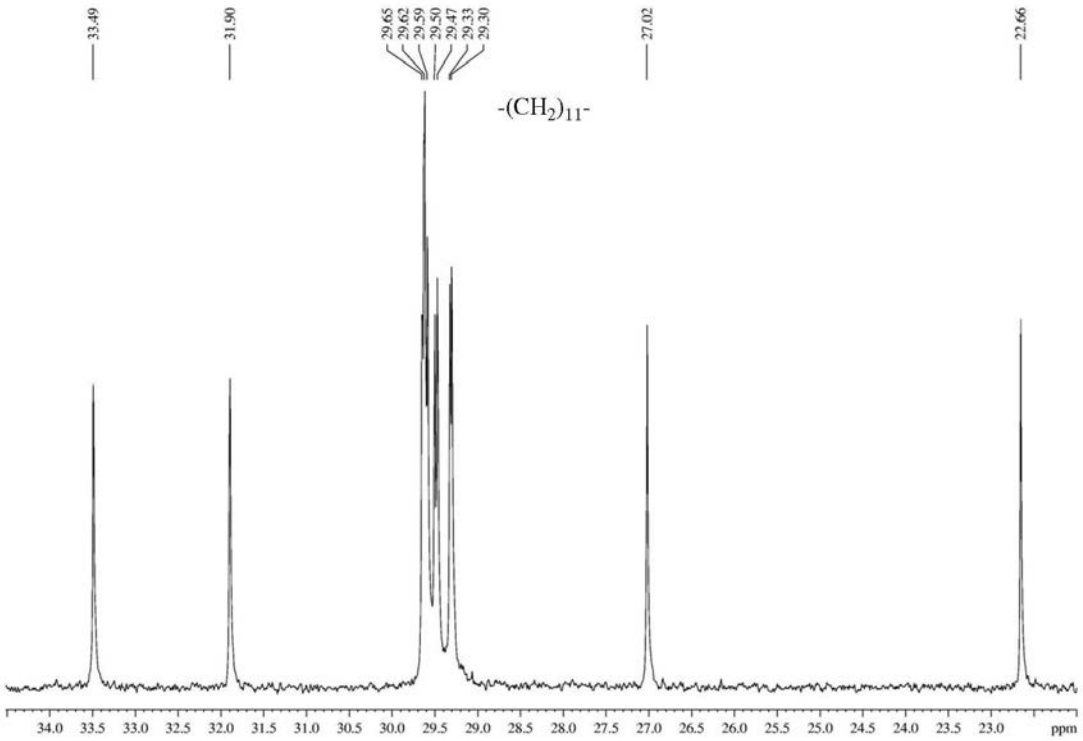

Figure S18. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-4-methoxy-3-heptadecen-2-one, expanded between 22-35 ppm.

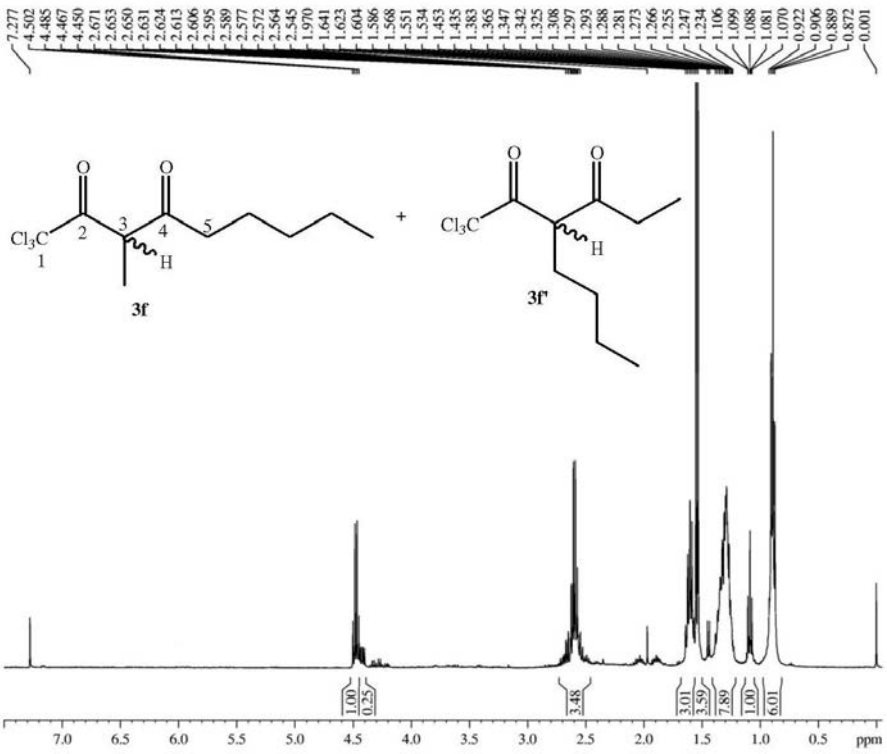

Figure S19. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-3-methylnonan-2,4-dione (ca. 75%) + 1,1,1-trichloro-3-butylhexan-2,4-dione (ca. 25%).

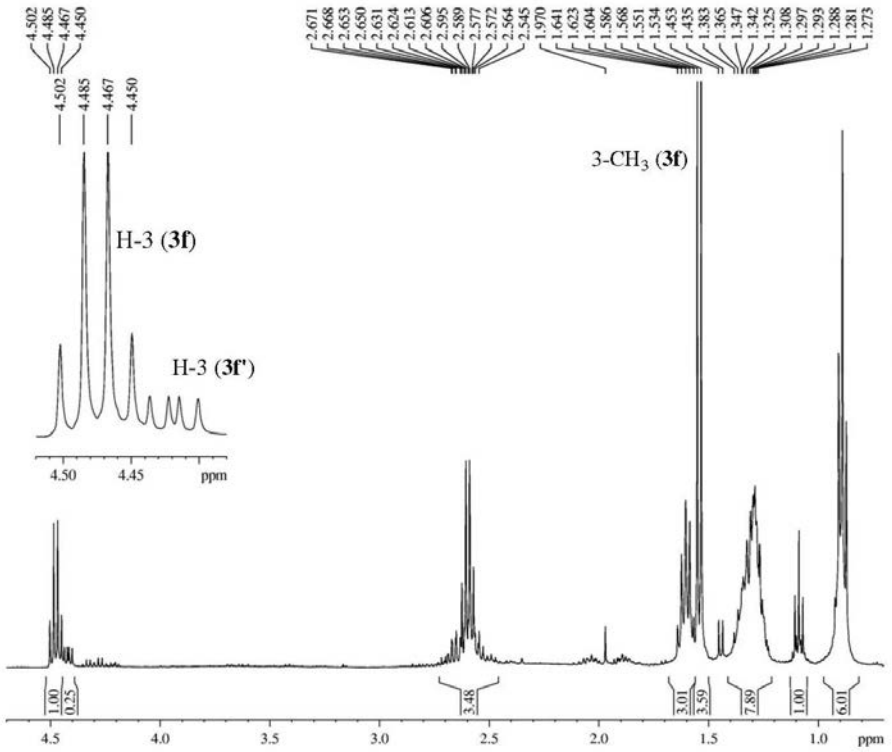

Figure S20. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-3-methylnonan-2,4-dione + 1,1,1-trichloro-3-butylhexan-2,4-dione, expanded between 0,5-4,7 ppm.

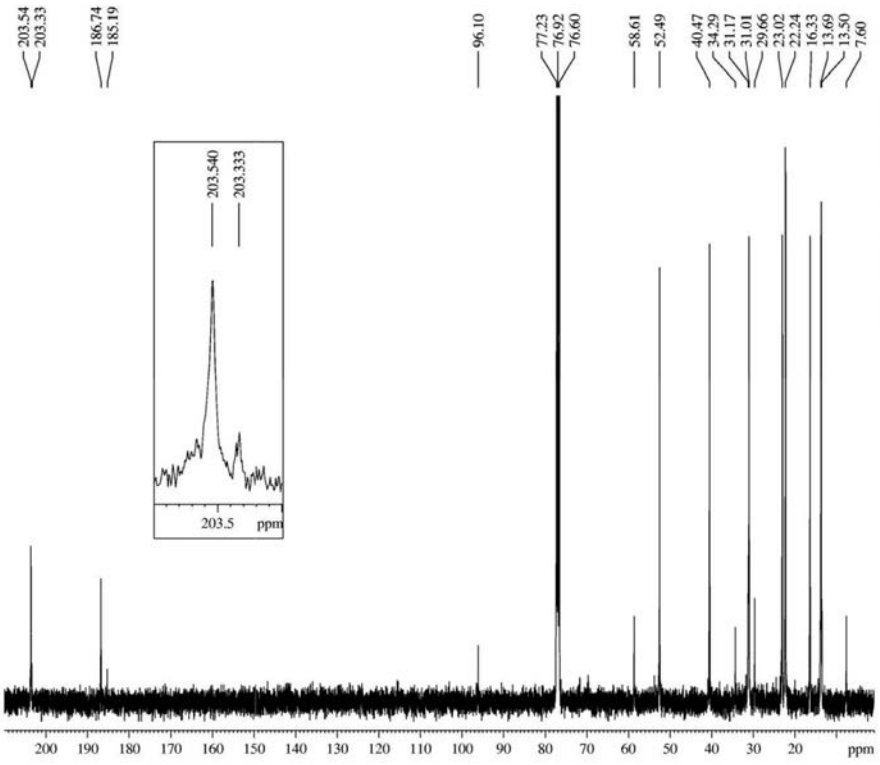

Figure S21. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 1,1,1-trichloro-3-methyl-2,4-nonan-2,4-dione (**3f**) + 1,1,1-trichloro-3-butylhexan-2,4-dione (**3f'**).

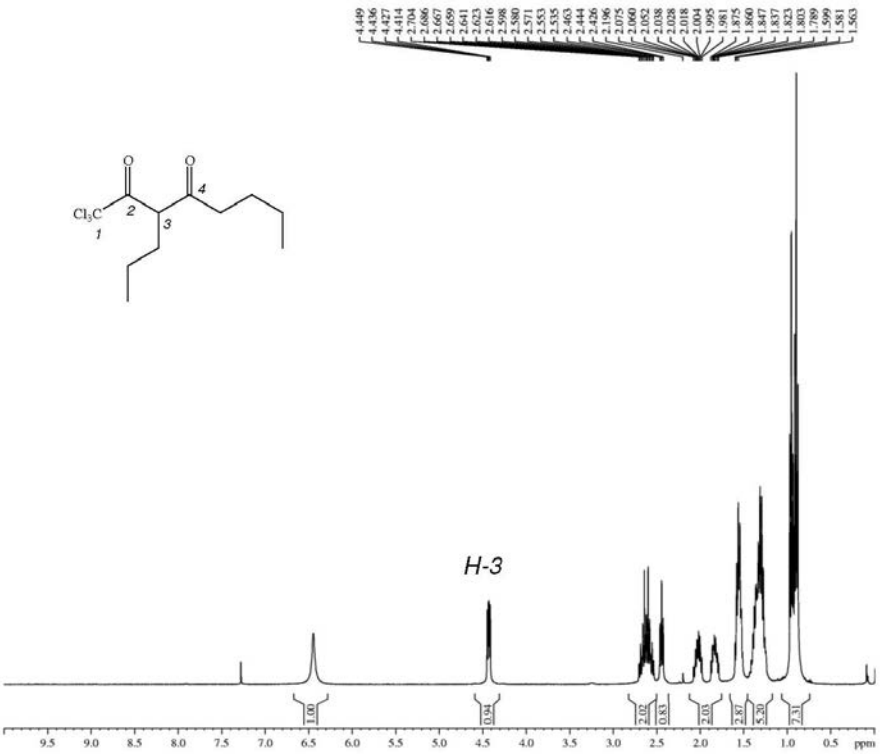

Figure S22. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-3-propyloctan-2,4-dione.

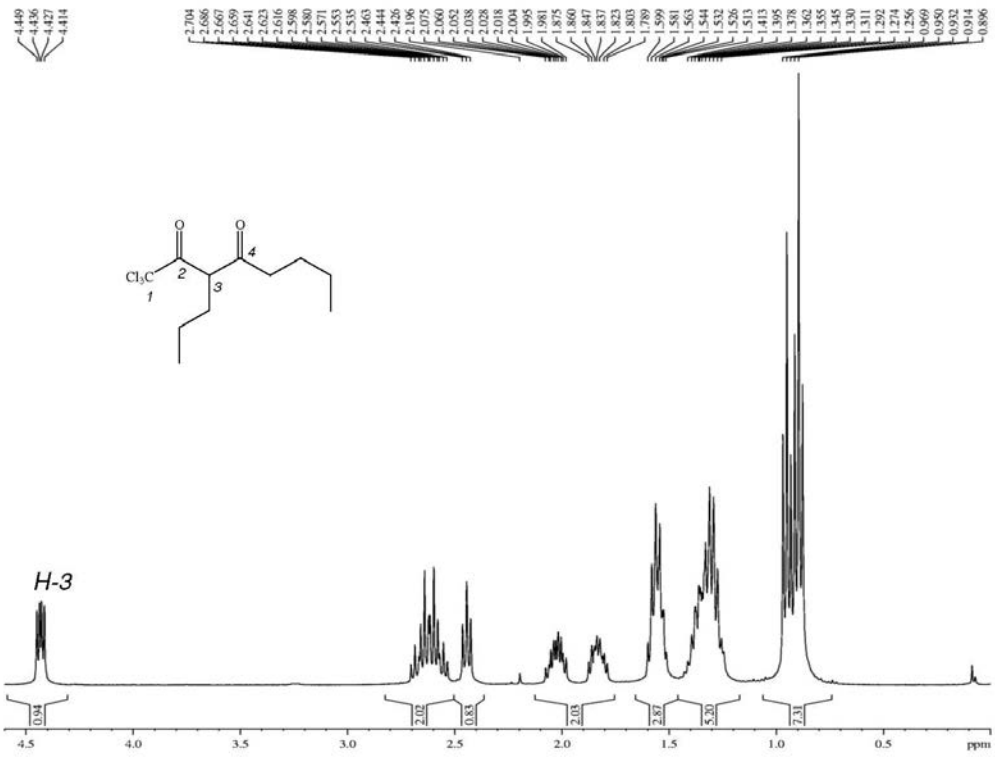

Figure S23. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-3-propyloctan-2,4-dione, expanded between 0-4.6 ppm.

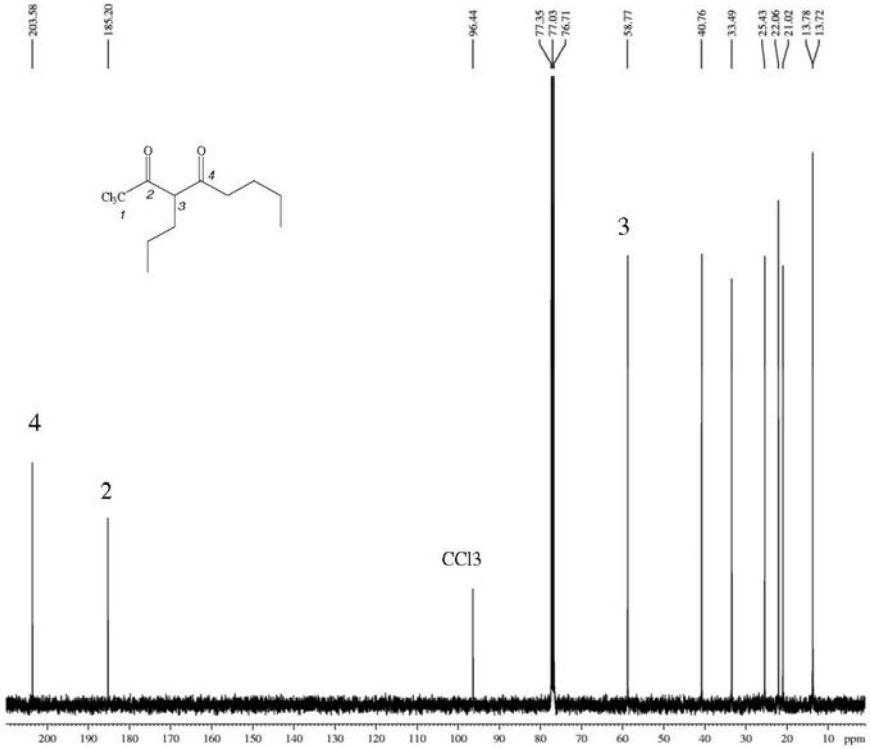

Figure S24. ^{13}C NMR spectrum (400 MHz, $CDCl_3$) of 1,1,1-trichloro-3-propyloctan-2,4-dione.

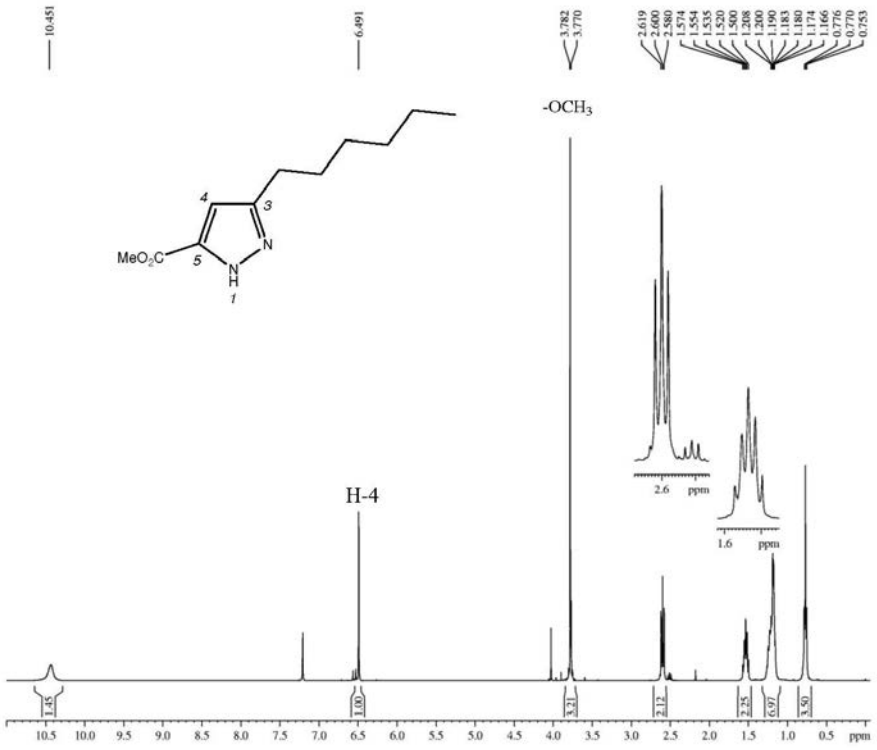

Figure S25. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-hexyl-1*H*-pyrazole-5-carboxylate.

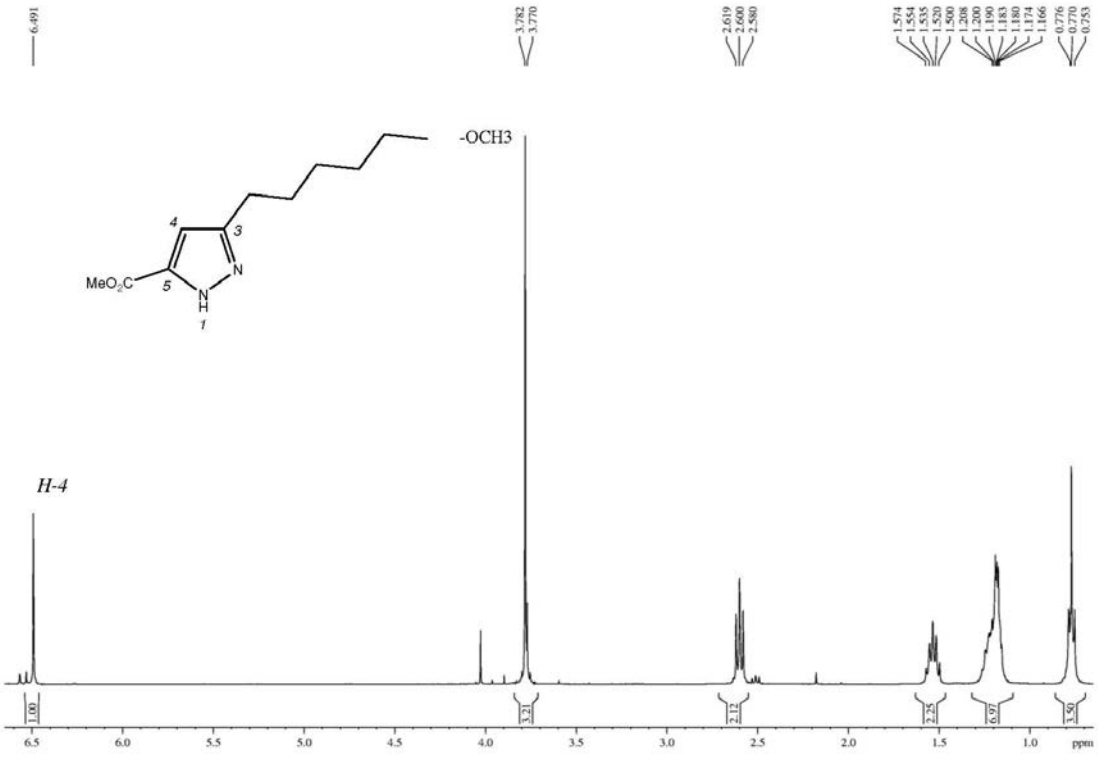

Figure S26. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-hexyl-1*H*-pyrazole-5-carboxylate, expanded between 0.5-6.6 ppm.

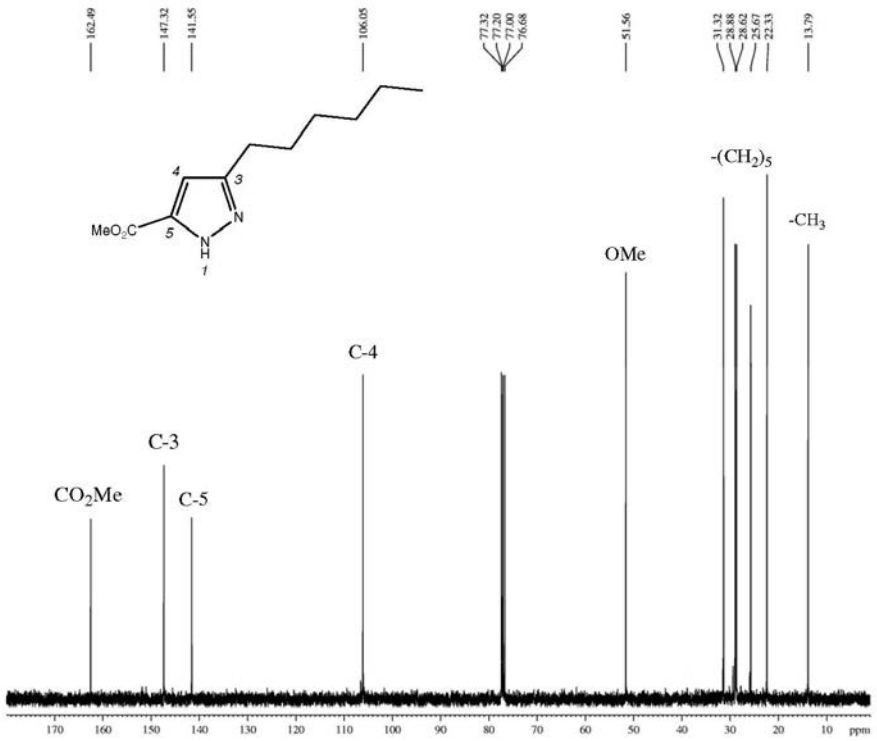

Figure S27. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of methyl 3-hexyl-1*H*-pyrazole-5-carboxylate.

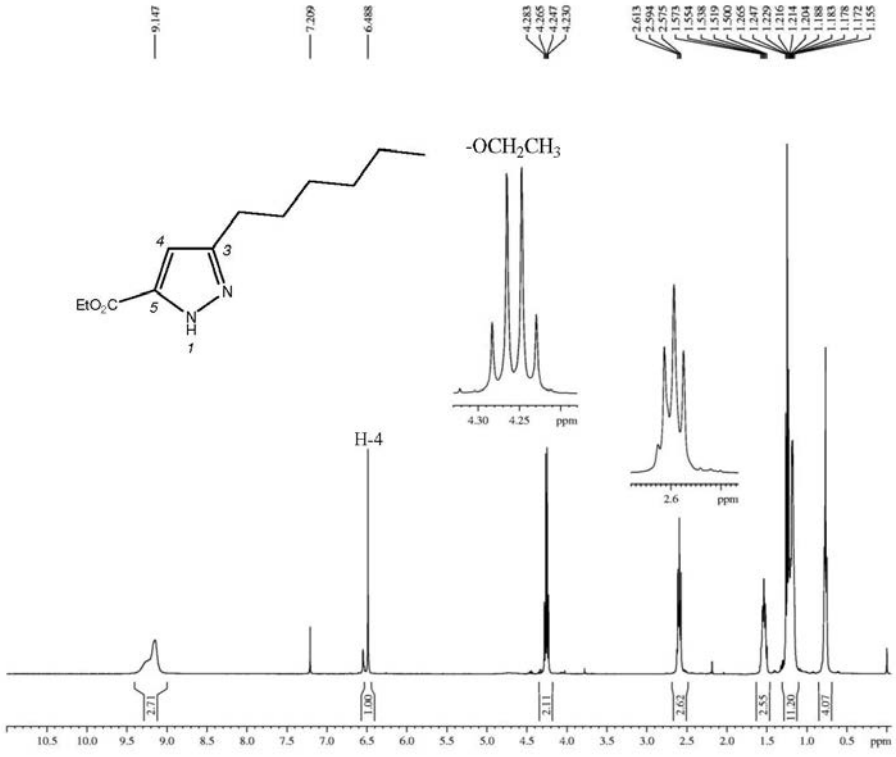

Figure S28. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-hexyl-1*H*-pyrazole-5-carboxylate.

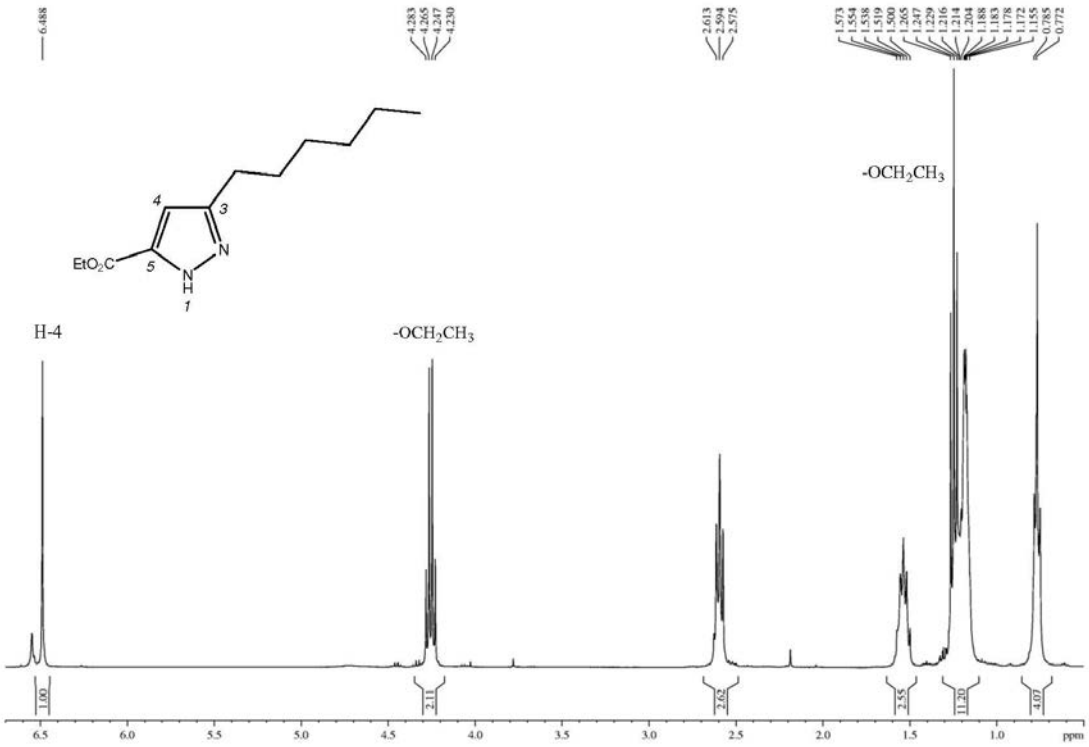

Figure S29. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-hexyl-1*H*-pyrazole-5-carboxylate , expanded between 0.5-6.7 ppm.

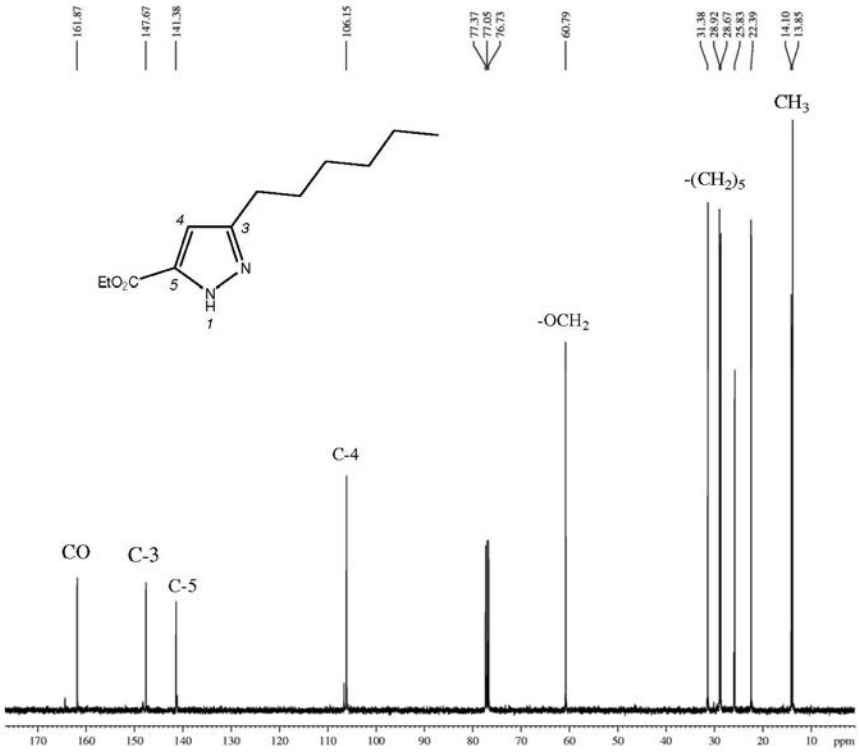

Figure S30. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 3-hexyl-1*H*-pirazole-5-carboxylate.

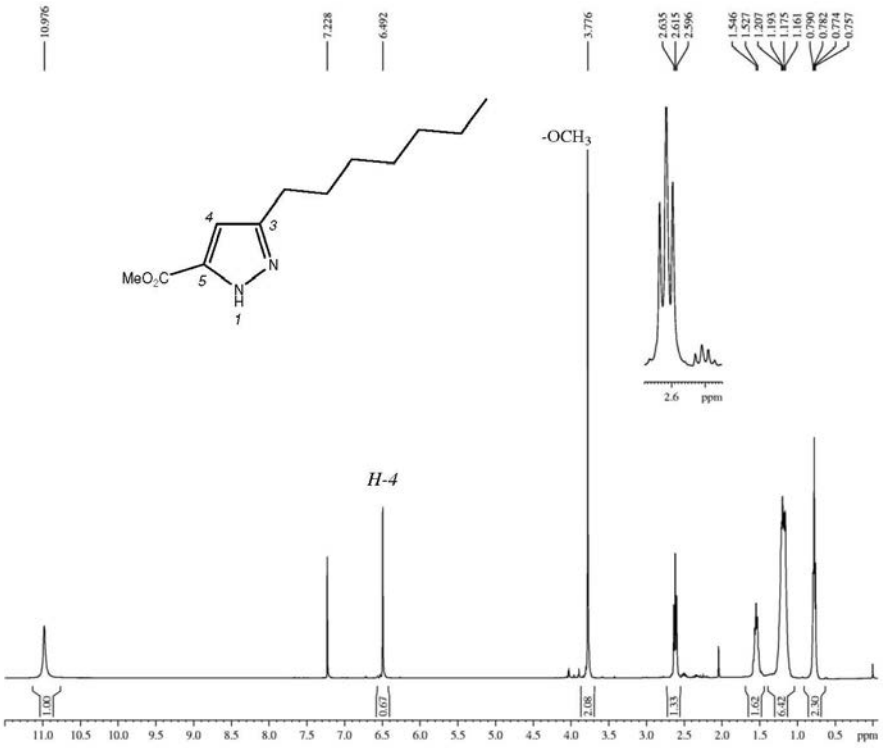

Figure S31. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-heptyl-1*H*-pyrazole-5-carboxylate.

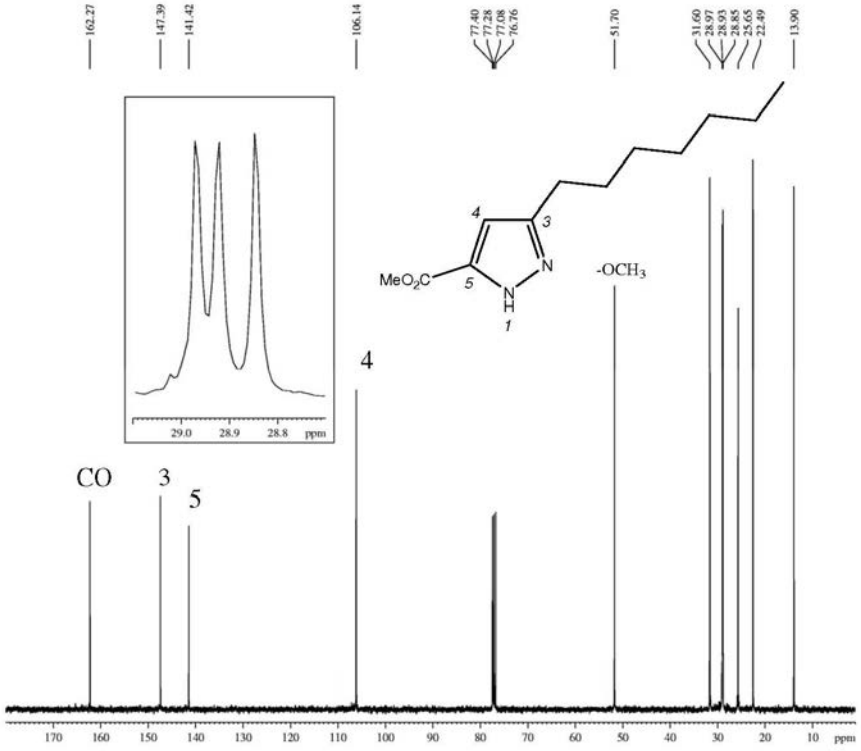

Figure S32. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of methyl 3-heptyl-1*H*-pyrazole-5-carboxylate.

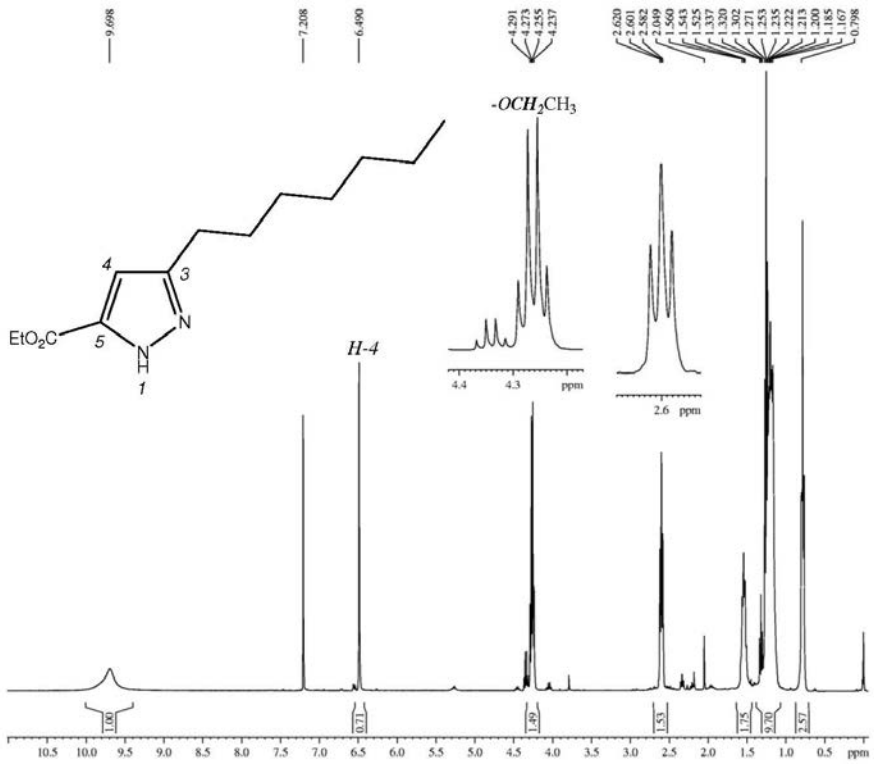

Figure S33. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-heptyl-1*H*-pyrazole-5-carboxylate in $CDCl_3$.

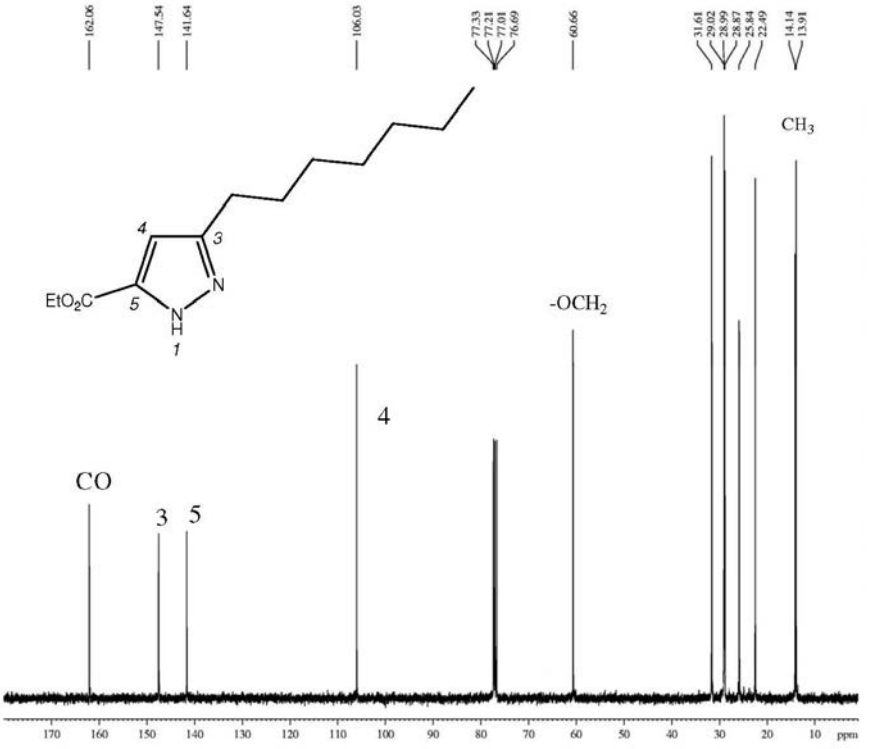

Figure S34. ^{13}C NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-heptyl-1*H*-pyrazole-5-carboxylate.

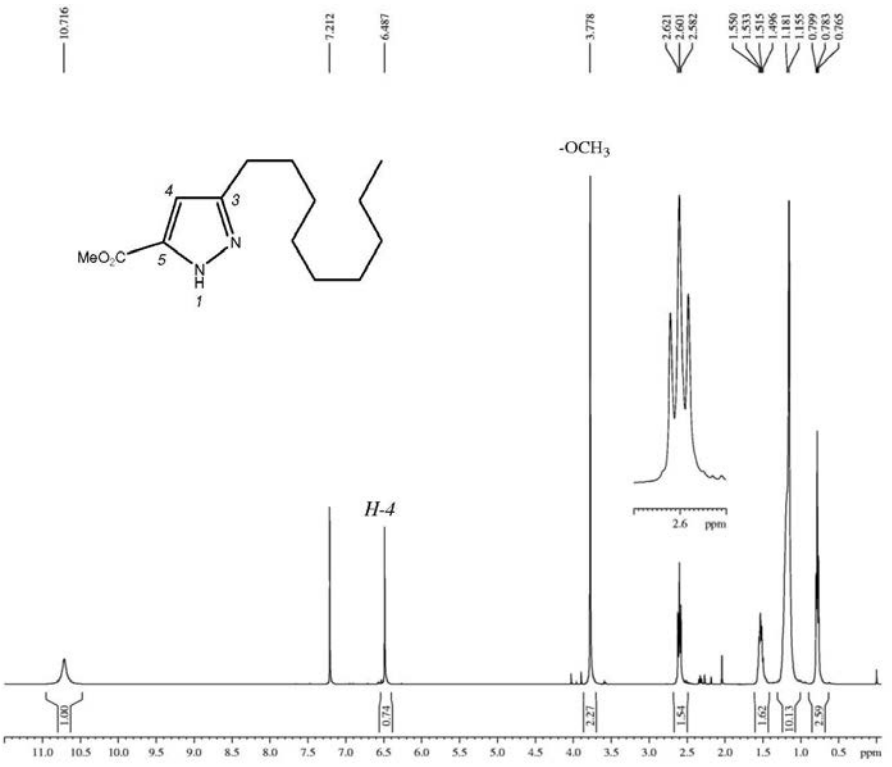

Figure S35. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-nonyl-1*H*-pyrazole-5-carboxylate.

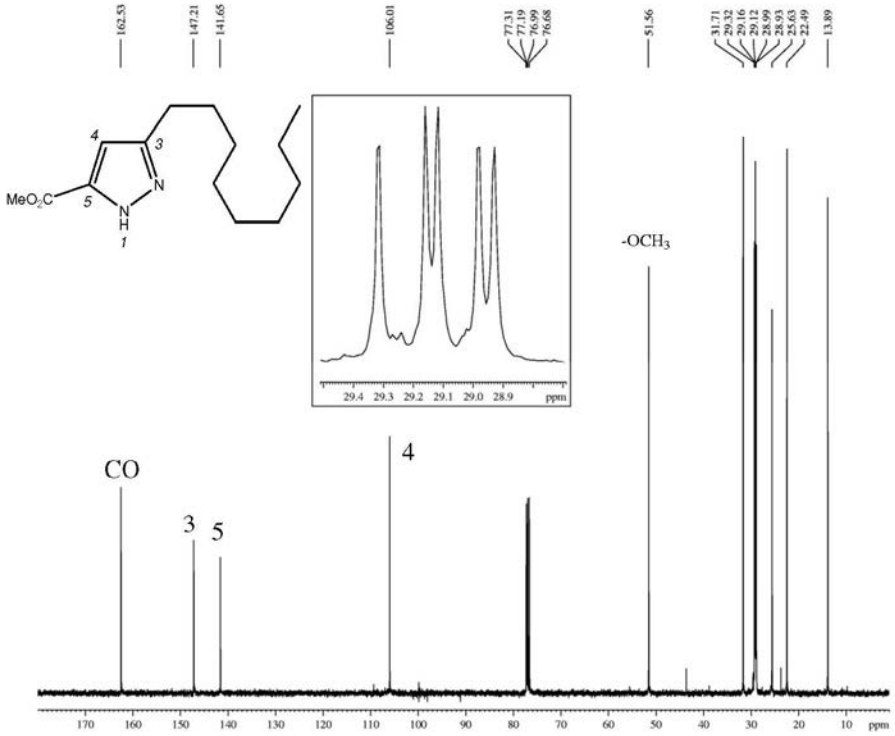

Figure S36. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of methyl 3-nonyl-1*H*-pyrazole-5-carboxylate.

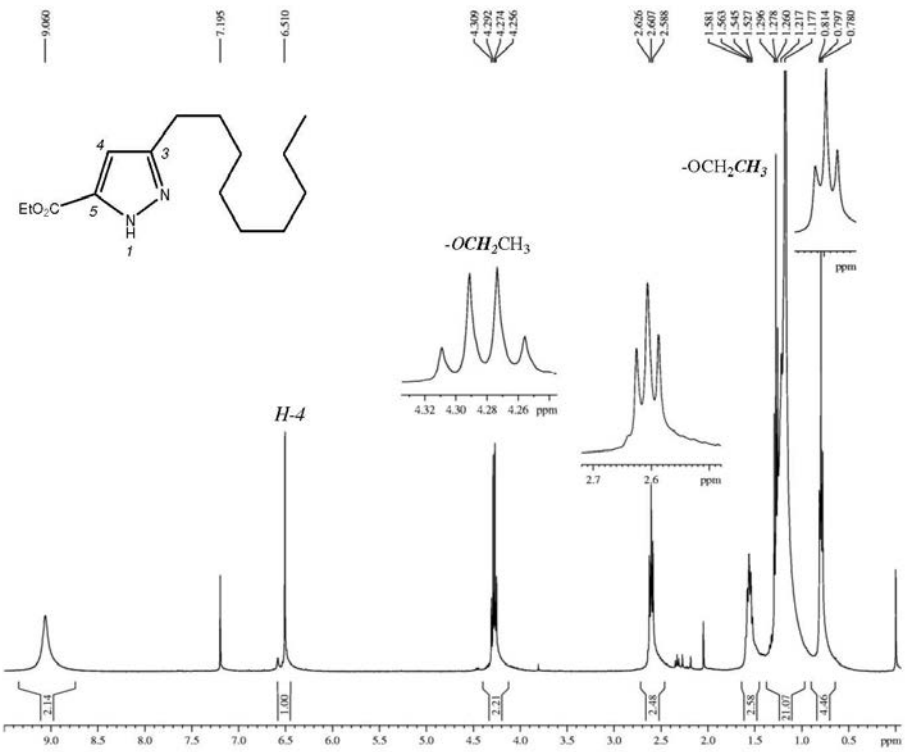

Figure S37. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-nonyl-1*H*-pyrazole-5-carboxylate.

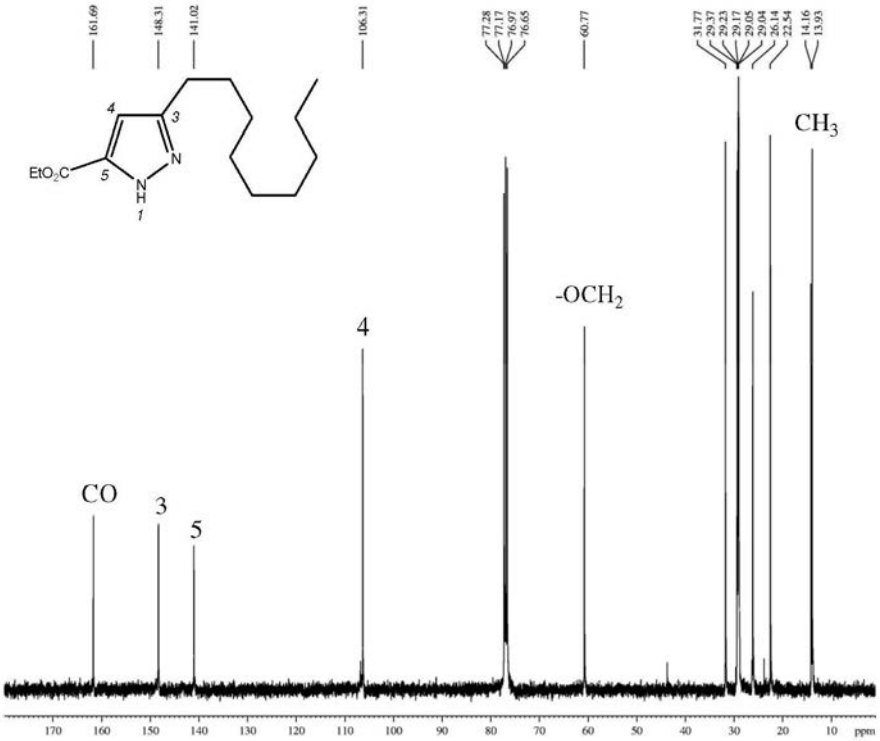

Figure S38. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 3-nonyl-1*H*-pyrazole-5-carboxylate in $CDCl_3$.

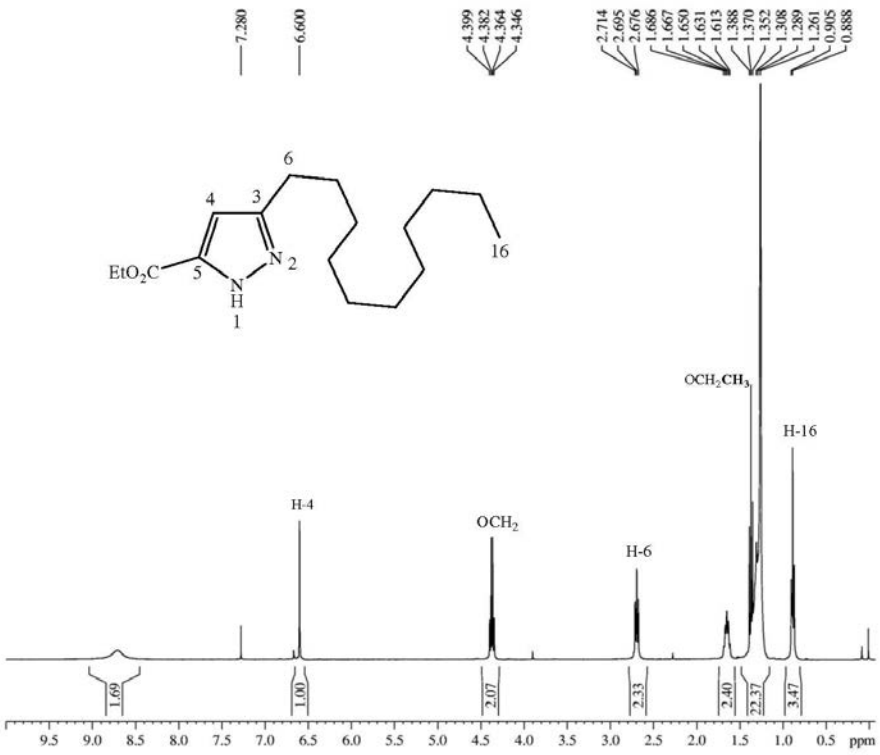

Figure S39. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-undecyl-1*H*-pyrazole-5-carboxylate.

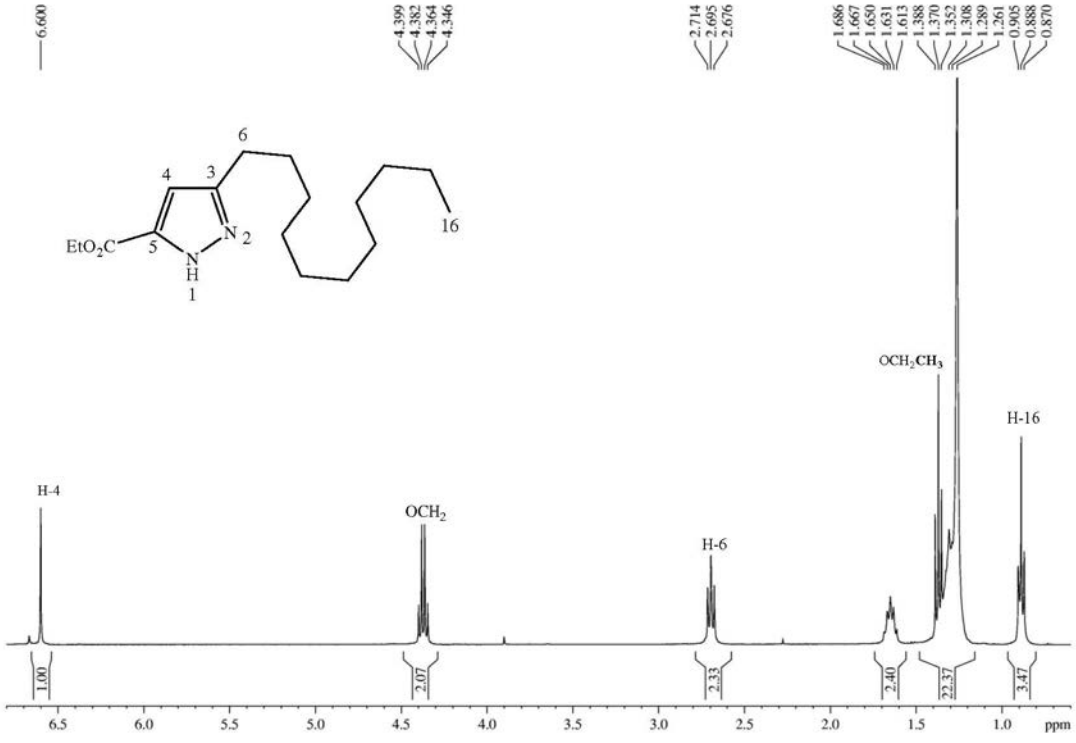

Figure S40. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-undecyl-1*H*-pyrazole-5-carboxylate, expanded between 0.5-6.8 ppm.

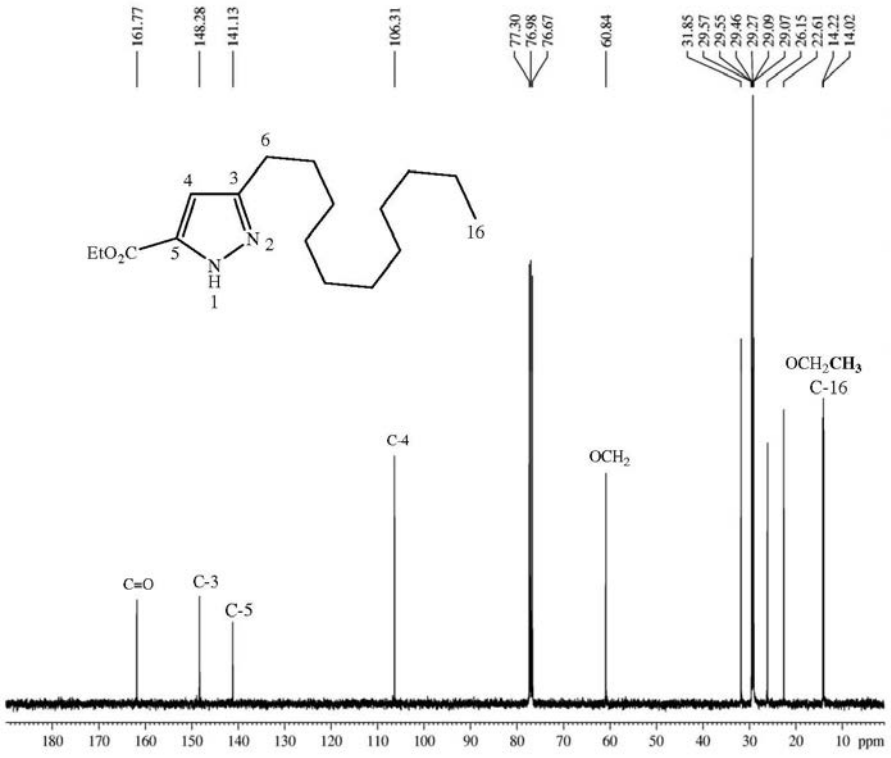

Figure S41. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 3-undecyl-1*H*-pyrazole-5-carboxylate in $CDCl_3$.

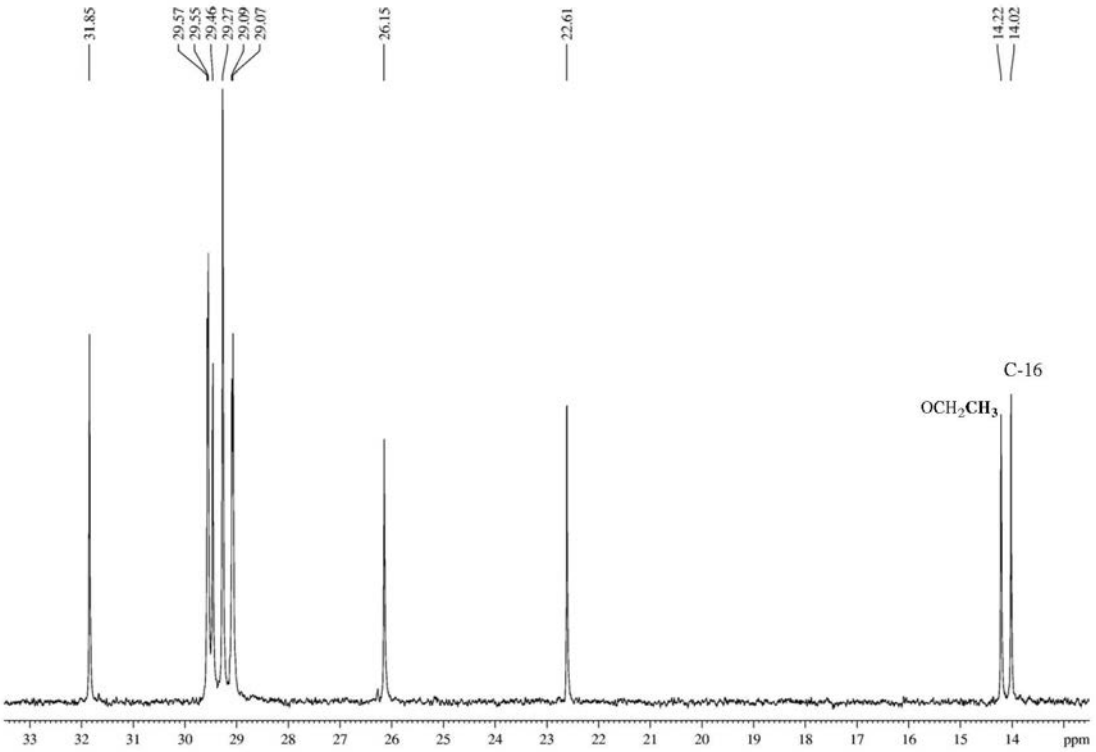

Figure S42. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 3-undecyl-1*H*-pyrazole-5-carboxylate, expanded between 12.5-33.5 ppm.

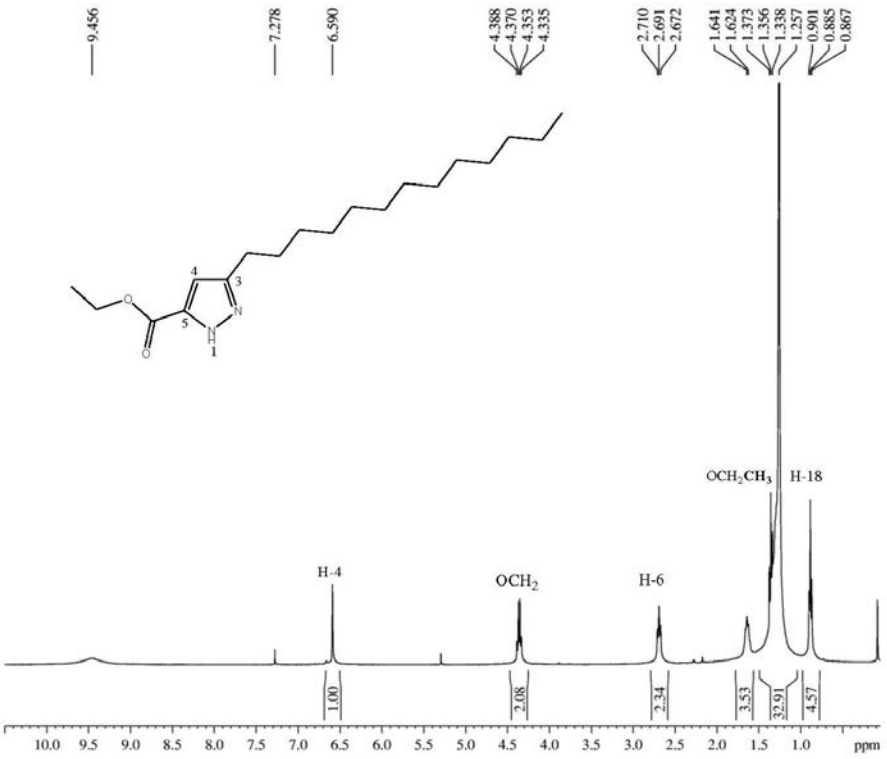

Figure S43. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-tridecyl-1*H*-pyrazole-5- carboxylate.

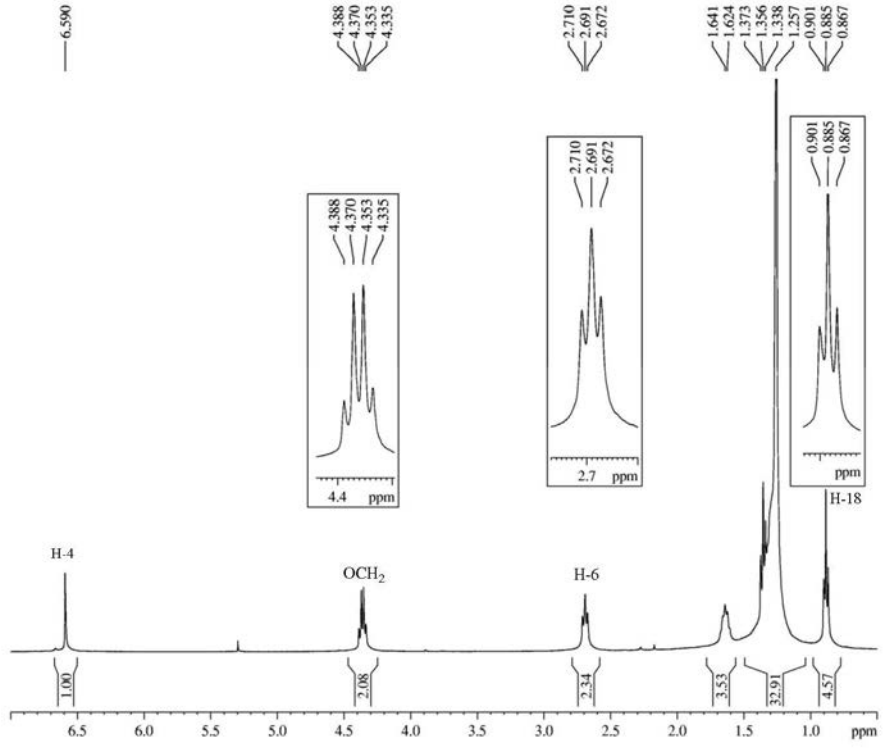

Figure S44. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-tridecyl-1*H*-pyrazole-5- carboxylate, expanded between 0.5-7.0 ppm.

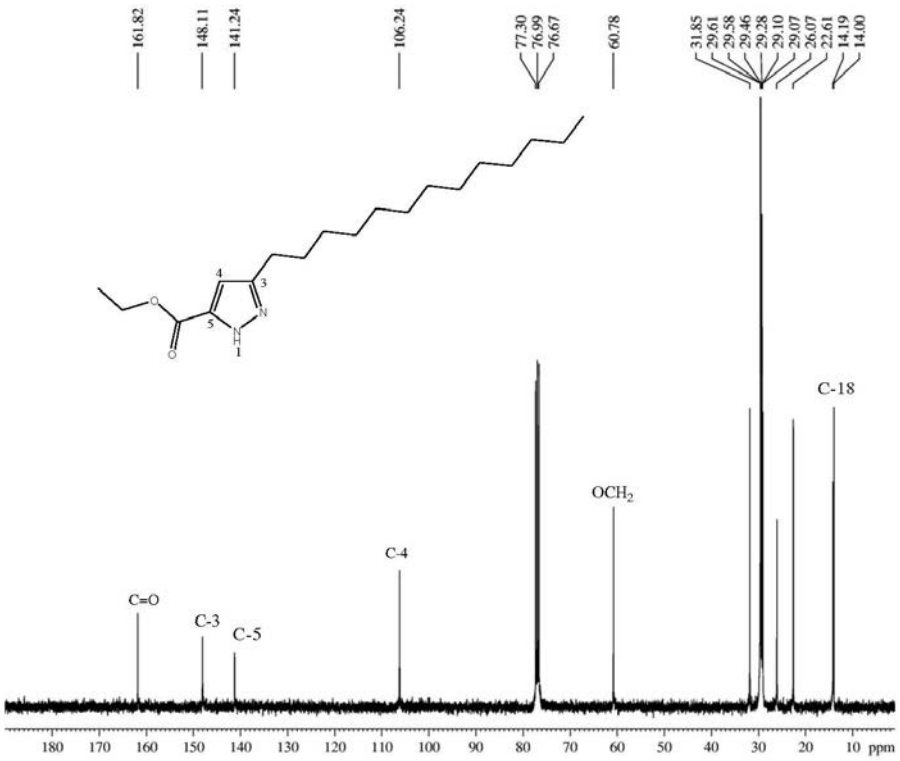

Figure S45. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 3-tridecyl-1*H*-pyrazole-5- carboxylate.

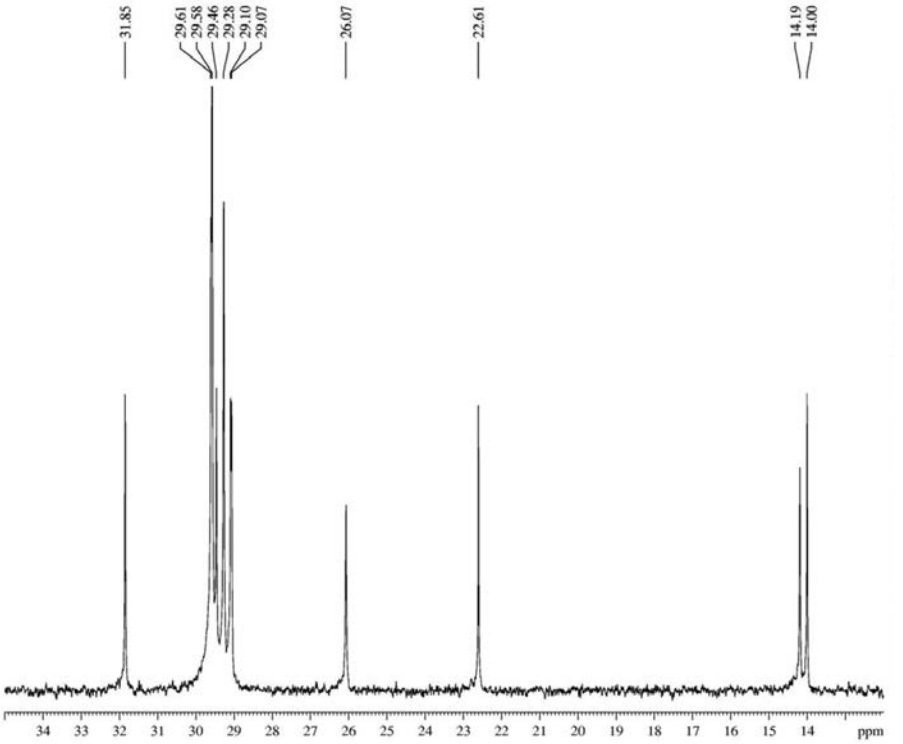

Figure S46. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 3-tridecyl-1*H*-pyrazole-5- carboxylate, expanded between 12-35 ppm.

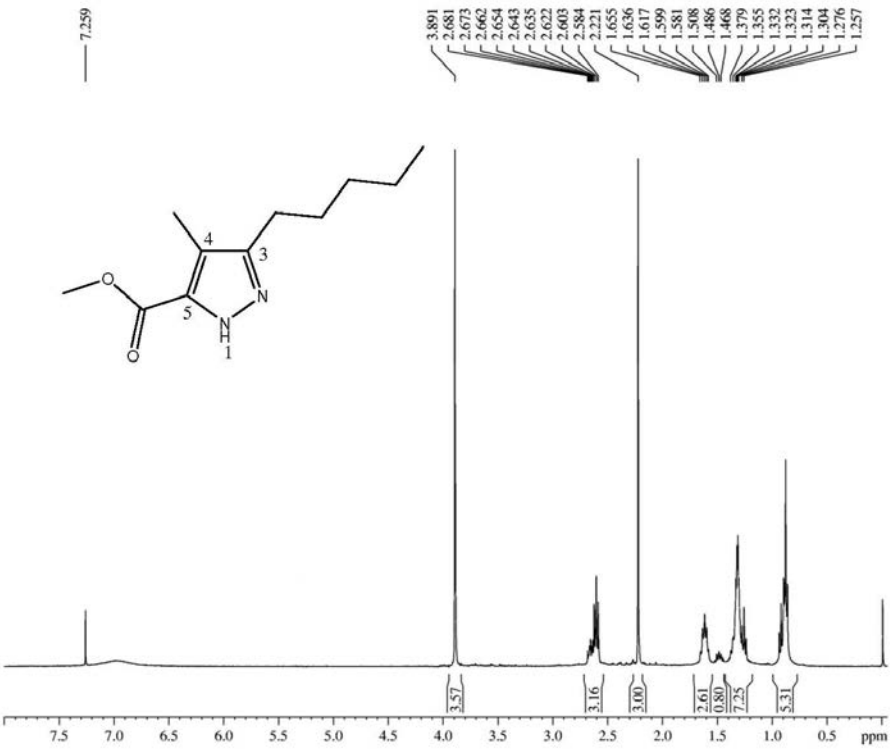

Figure S47. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + methyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate.

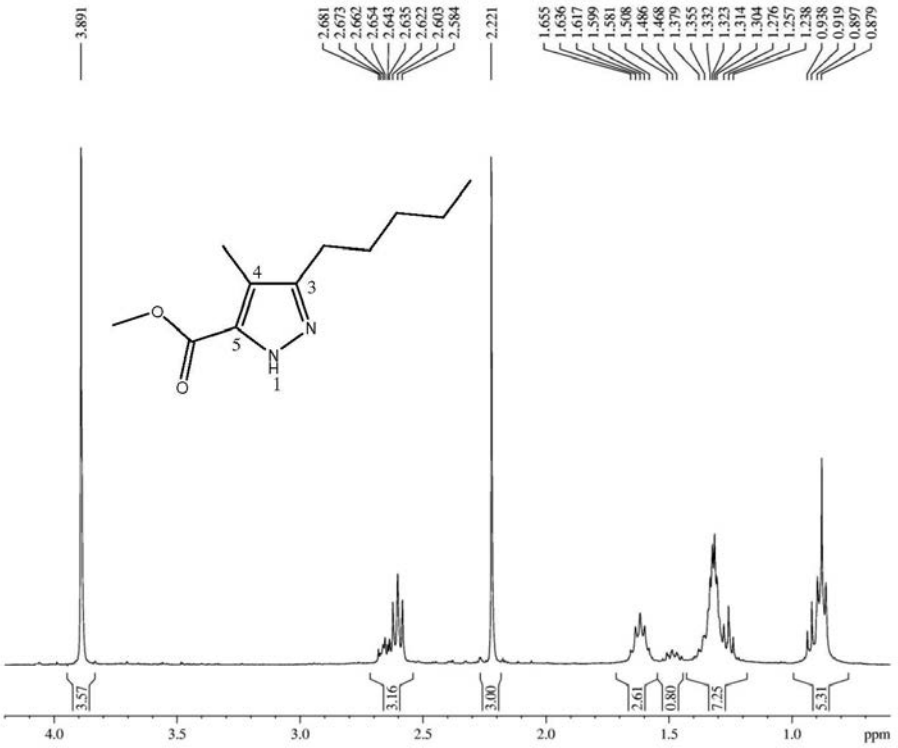

Figure S48. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + methyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate, expanded between 0.6-4.2 ppm.

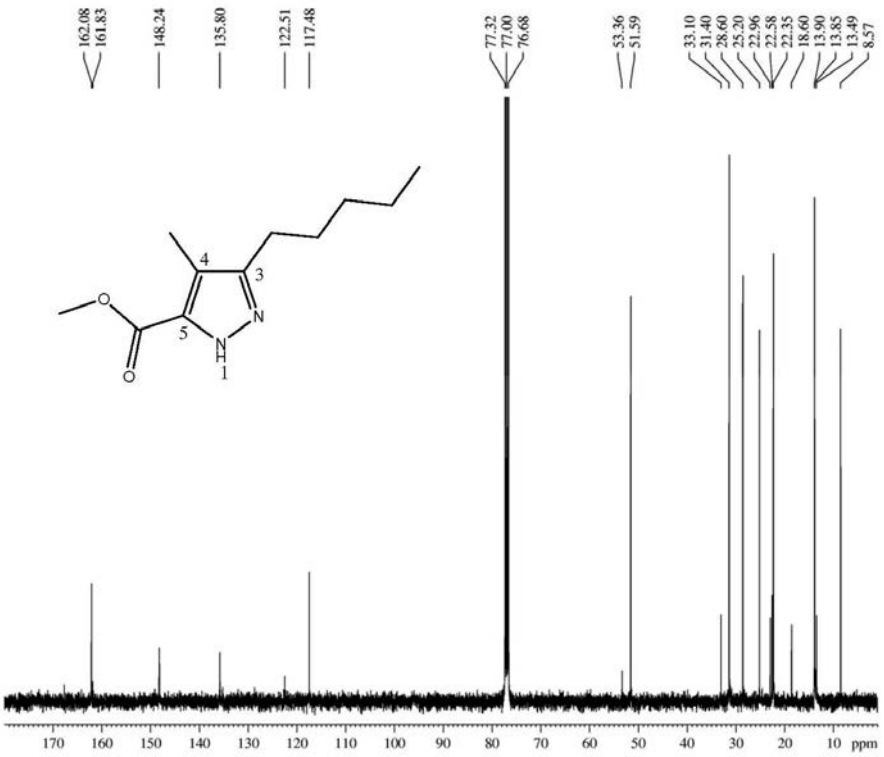

Figure S49. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of methyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + methyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate.

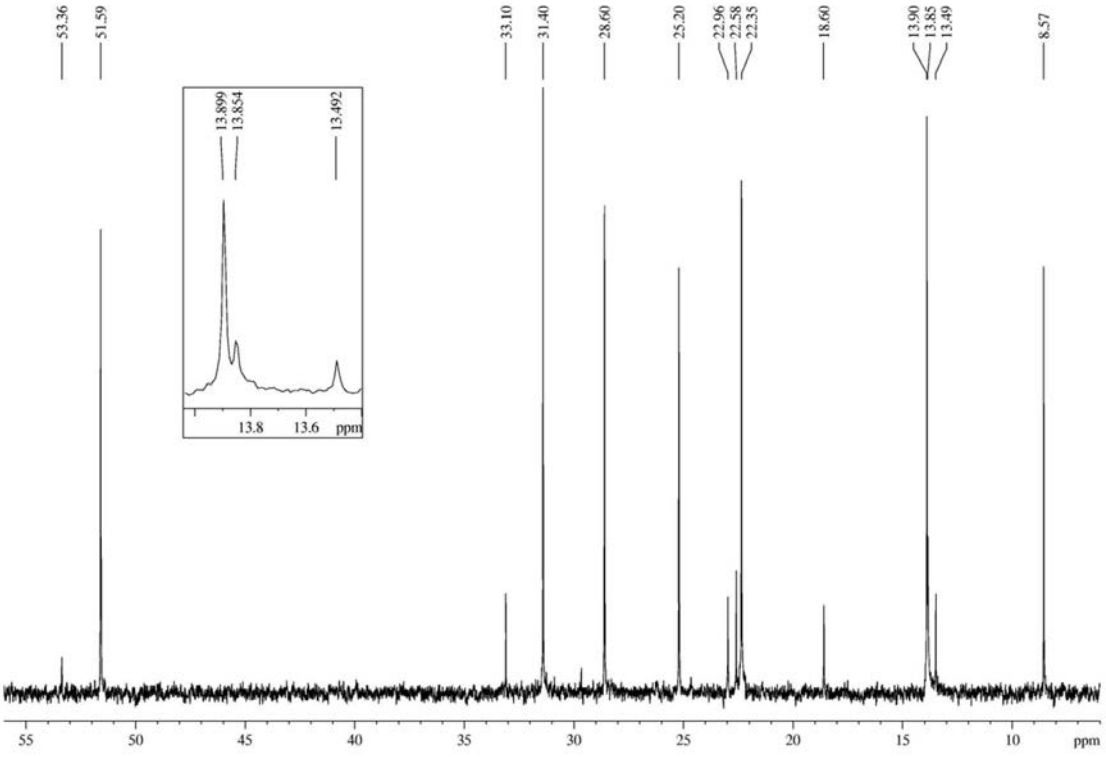

Figure S50. ^{13}C NMR spectrum (400 MHz, $CDCl_3$) of methyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + methyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate, expanded between 6-56 ppm.

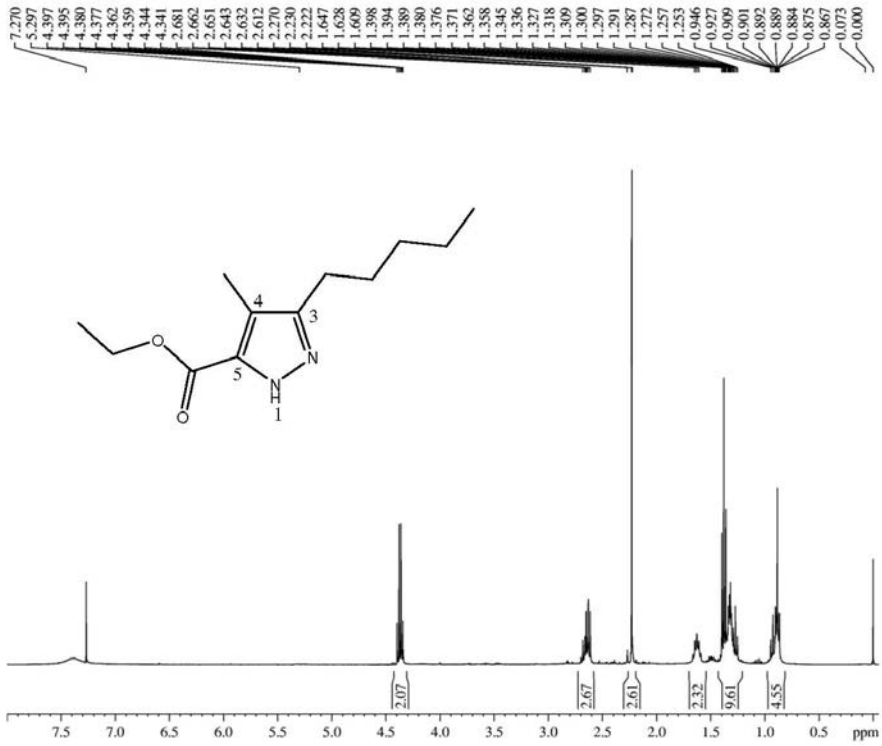

Figure S51. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + ethyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate.

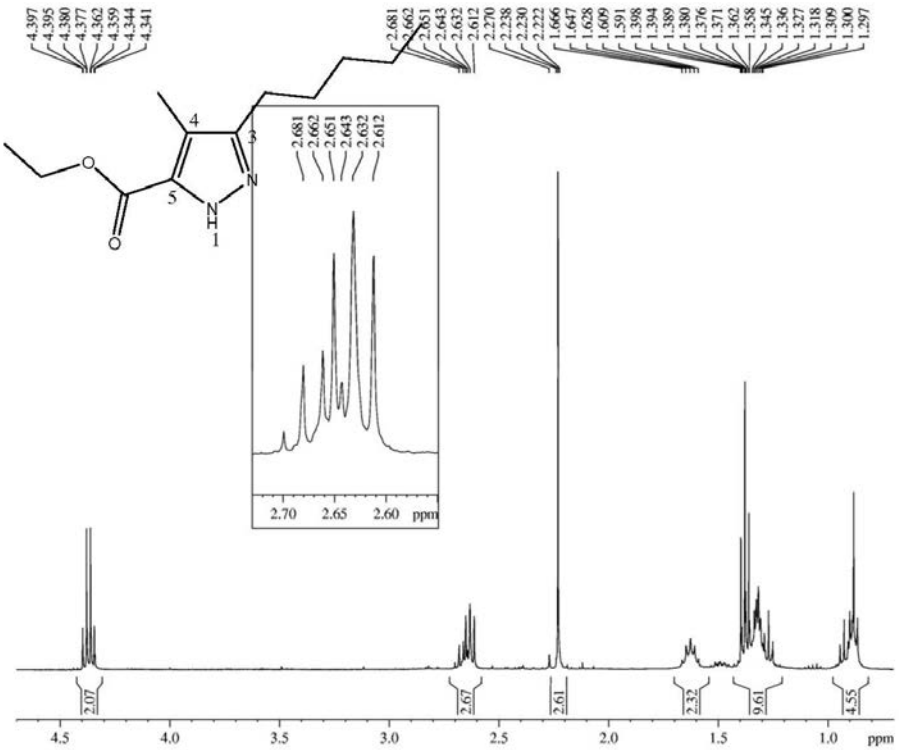

Figure S52. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + ethyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate, expanded between 0.7- 4.7 ppm.

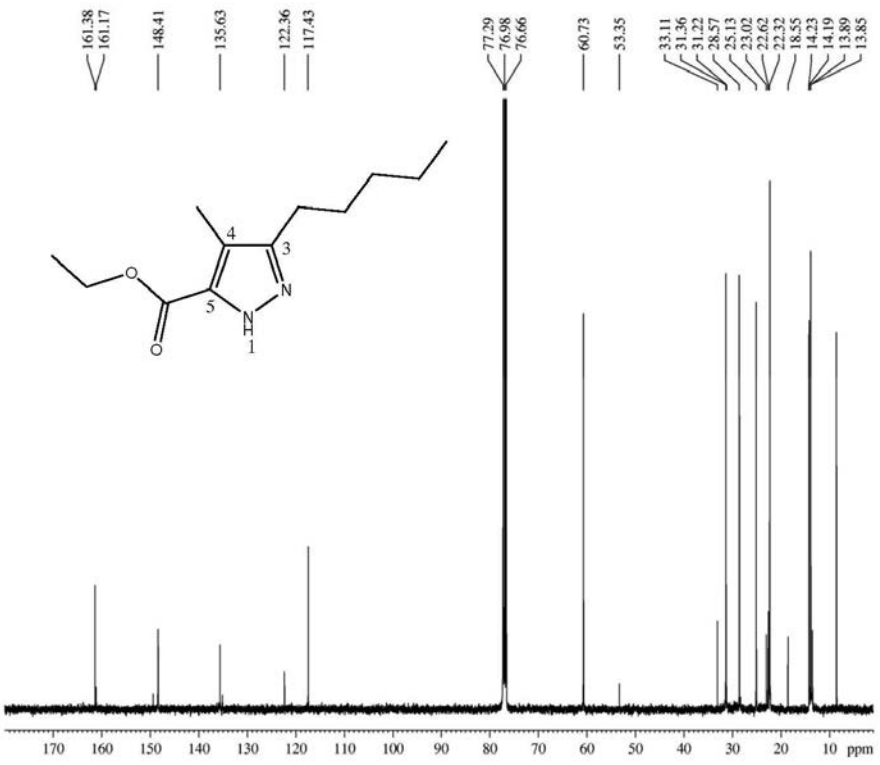

Figure S53. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + ethyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate.

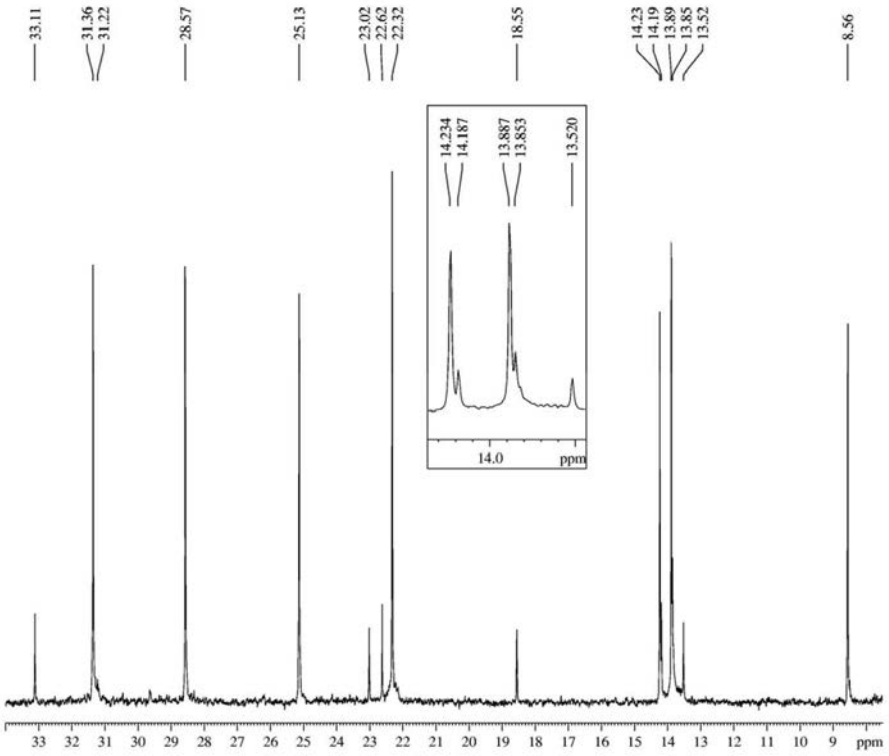

Figure S54. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of ethyl 4-methyl-3-pentyl-1*H*-pyrazole-5-carboxylate + ethyl 4-butyl-3-ethyl-1*H*-pyrazole-5-carboxylate.

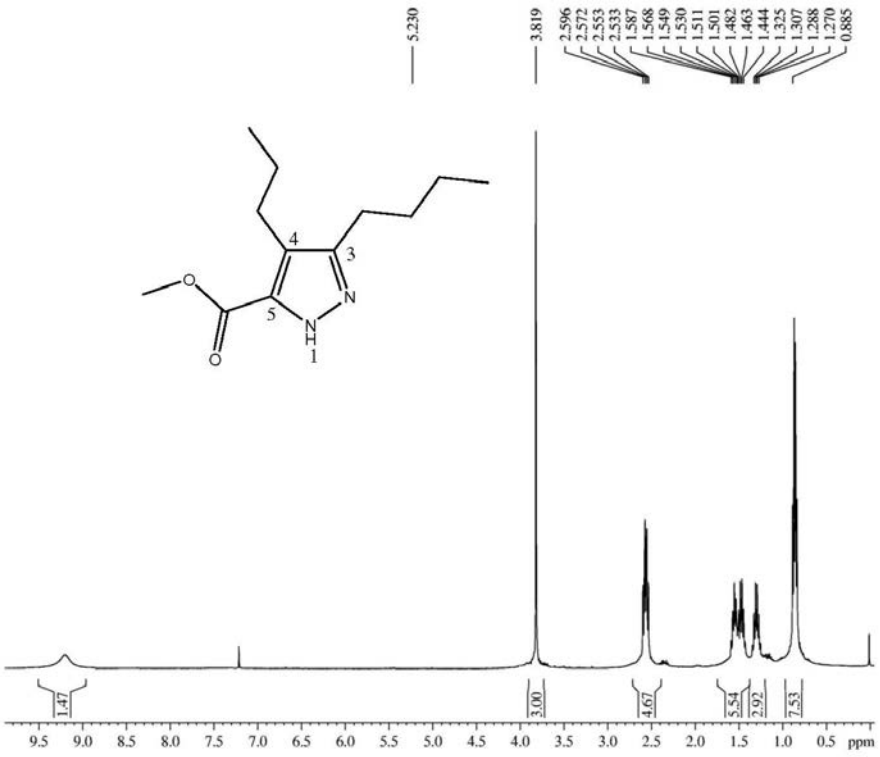

Figure S55. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate.

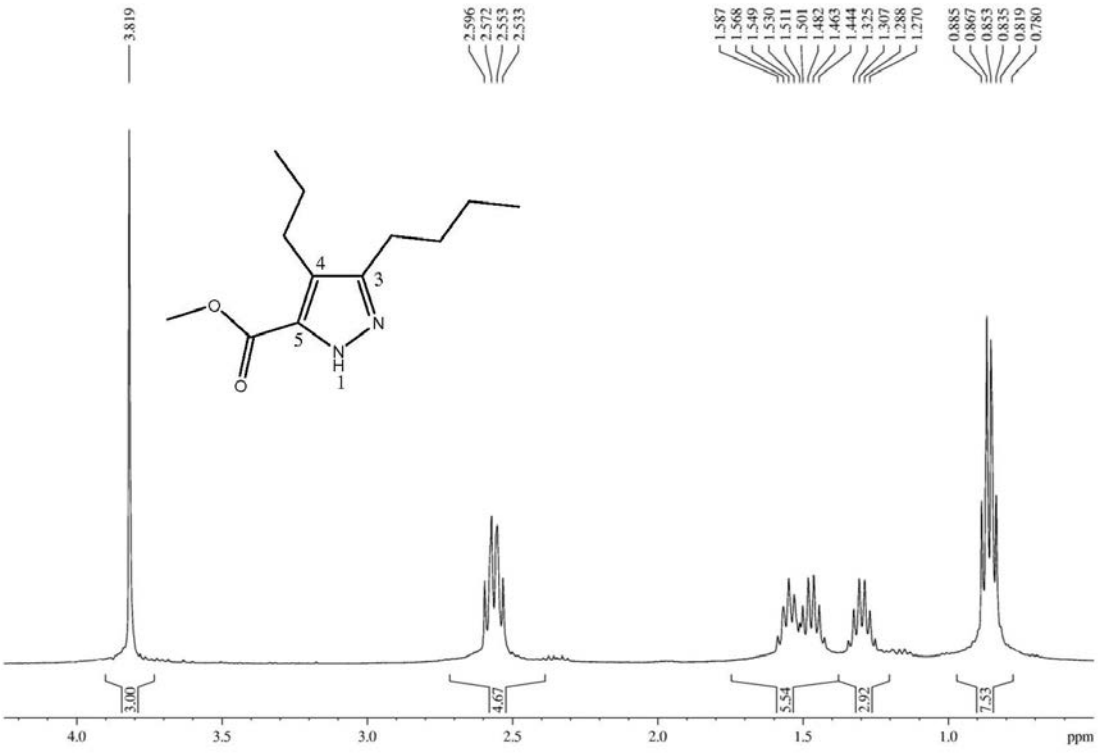

Figure S56. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate , expanded between 0.5-4.2 ppm.

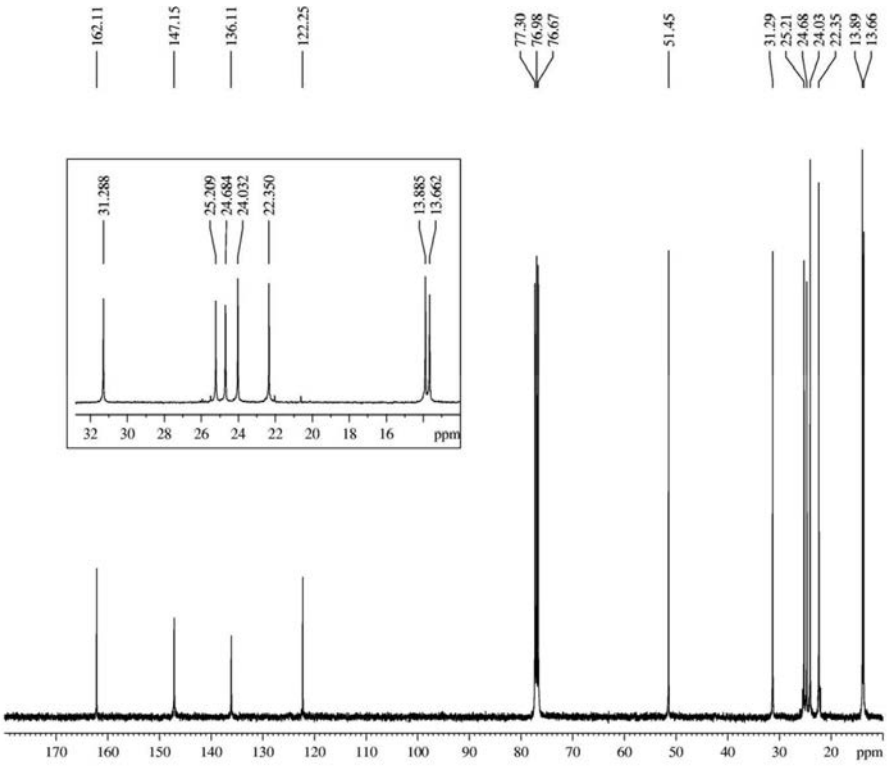

Figure S57. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of methyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate in $CDCl_3$.

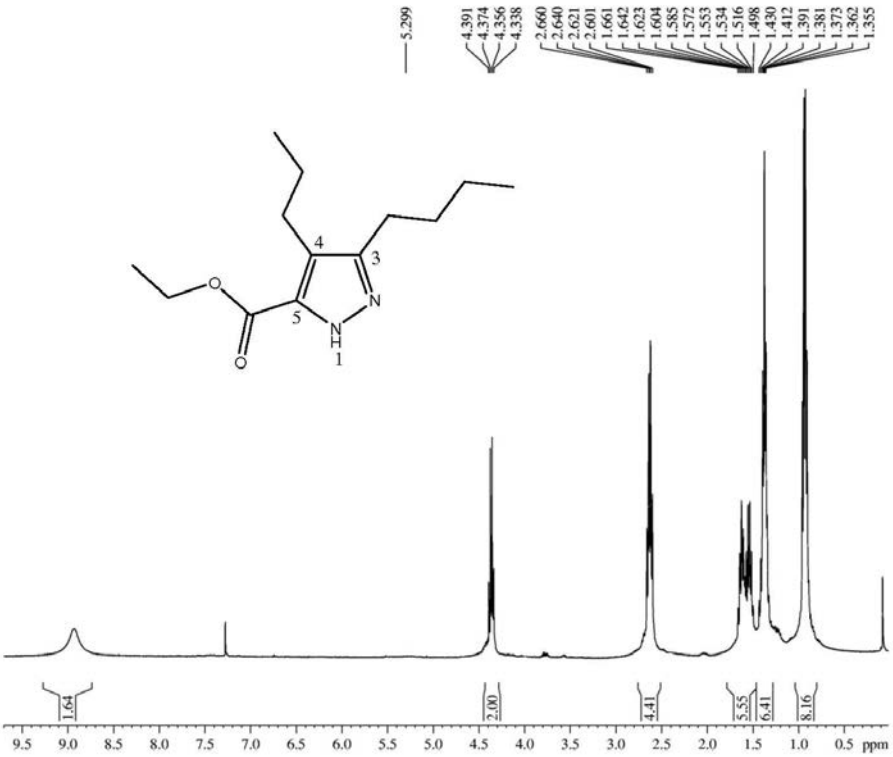

Figure S58. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate in $CDCl_3$.

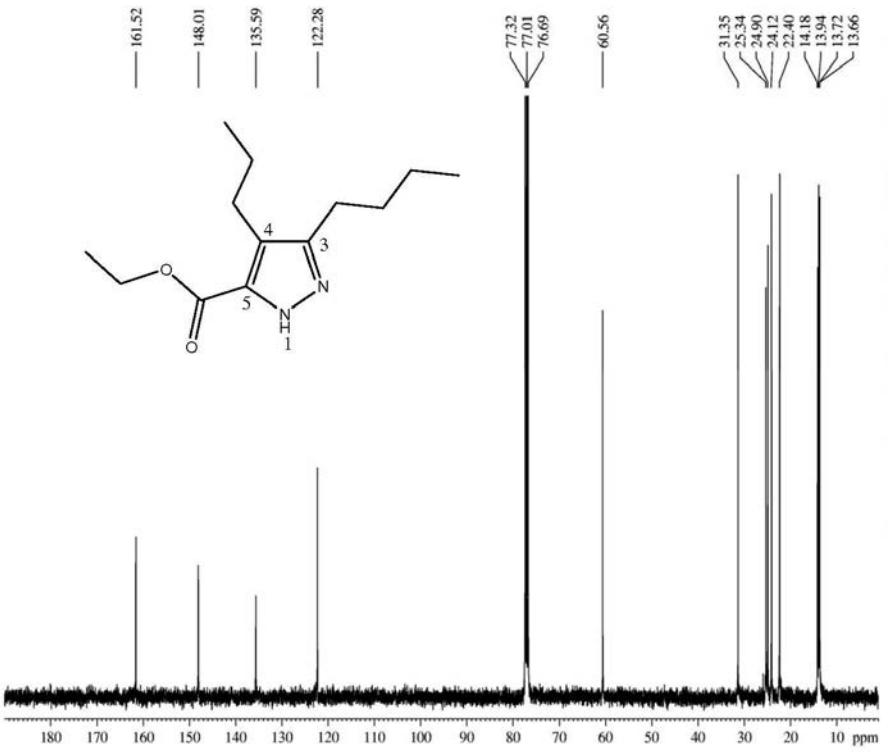

Figure S59. ^{13}C NMR spectrum (400 MHz, $CDCl_3$) of ethyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate.

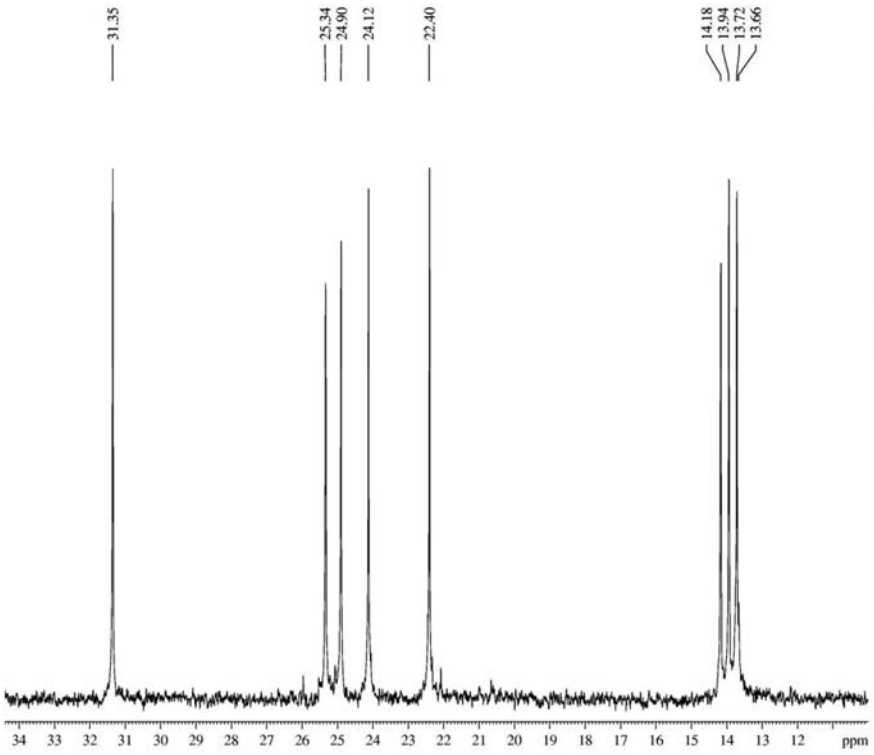

Figure S60. ^{13}C NMR spectrum (400 MHz, $CDCl_3$) of methyl 3-butyl-4-propyl-1*H*-pyrazole-5-carboxylate, expanded between 10-34 ppm.