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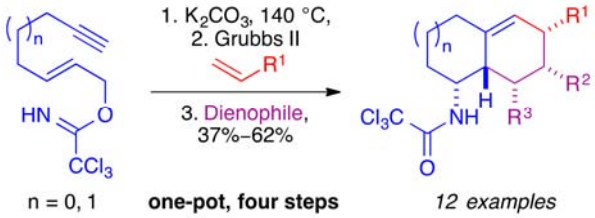

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Diastereoselective synthesis of highly substituted polycyclic scaffolds via a one-pot four-step tandem catalytic process

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ABSTRACT

A rapid and diastereoselective synthesis of highly substituted aminobicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes from alkyne derived allylic alcohols has been developed using a one-pot multi-bond forming tandem catalytic process. Overman rearrangement of the allylic trichloroacetimidates was followed by a ring closing enyne metathesis/cross metathesis sequence of reactions in which both steps were catalysed by Grubbs 2nd generation catalyst. The resulting *exo*-diene was then subjected to a hydrogen bonding directed Diels-Alder reaction forming an *endo*-adduct as a single diastereomer. Variation of the cross metathesis partner and dienophile allowed examination of the scope of this one-pot process and the preparation of a diverse series of highly substituted polycyclic scaffolds.

1. Introduction

Amino substituted polycyclic compounds are found widely throughout the natural world and as key components in many medicinally important compounds.[1] In particular, saturated and partially saturated forms of amino substituted bicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes are present in a diverse structural range of natural products such as the guanidine alkaloid netamine A (**1**),[2] the neurotrophic agent (+)-nankakurine A (**2**)[3] and the potent analgesic (–)-morphine (**3**) (Fig. 1).[4] These motifs are also found in many synthetically generated medicines that are used to treat a range of diseases associated with the central nervous system[5] and inhibit processes such as the proliferation of malignant cells.[6] As a result of the natural abundance and significant pharmacological activity of amino substituted bicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes, many synthetic approaches have been developed for their preparation.[3b,7–13] In general, these bicyclic compounds have typically been prepared from functionalised monocyclic species where the second ring system is formed through pericyclic reactions such as Diels-Alder[3b,10] and 1,3-dipolar cycloadditions.[8] For example, Brummond and co-workers utilised a Rh(I)-catalysed cycloisomerisation of an allene-ynone and the resulting 2-alkylidene-3-vinylcyclopentenone could be trapped in a Diels-Alder reaction to give the corresponding aminobicyclo[4.3.0]nonane in good overall yield.[10b] Other strategies have involved the stereoselective hydroboration of hexahydroindenes and octahydronaphthalenes which, following *syn*-migration gave secondary organoboranes.[11] Subsequent amination allowed access to both amino substituted bicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes.

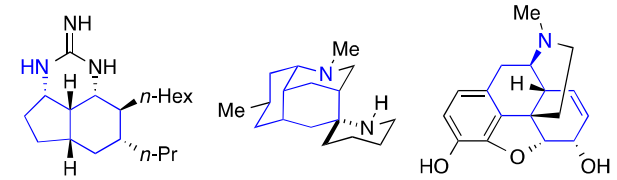
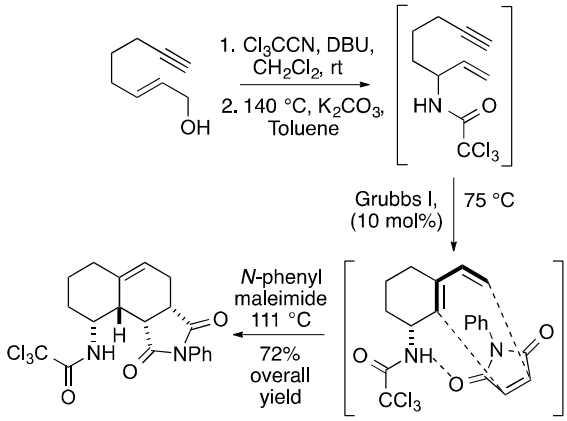


Fig. 1. Amino substituted bicyclo[4.3.0]nonane and bicyclo[4.4.0]decane containing natural products.

In an alternative approach to these compounds, we recently reported the rapid and efficient diastereoselective synthesis of amino substituted bicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes using a one-pot multi-reaction process that utilised an Overman rearrangement of alkyne derived allylic alcohols, a ring closing enyne metathesis (RCEYM) reaction and a hydrogen bonding directed Diels-Alder reaction (e.g. Scheme 1).[12] This strategy allowed the consecutive formation of both rings, the late-stage incorporation of functional groups through the Diels-Alder reaction and gave a variety of structural types with up to four stereogenic centres. Although adapting this process for the synthesis of C1-amino substituted indanes and tetralins,[13] we were interested in extending this series of reactions to access compounds of greater complexity through a higher level of substitution. We now report the development and scope of a novel one-pot four-step multi-reaction process that incorporates a cross metathesis (CM) reaction and is conducted using the same Ru(II)-complex that catalyses a RCEYM step. Overall, this tandem catalytic process allows the preparation of highly

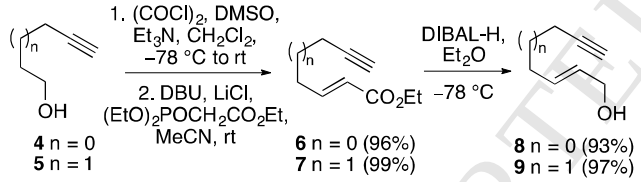
substituted aminobicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes with up to five stereogenic centres. We also describe preliminary studies in the use of a disubstituted alkyne as a substrate for a one-pot three-step multi-reaction process resulting in the preparation of a 5-aryl amino substituted bicyclo[4.3.0]nonane in good overall yield.



Scheme 1. One-pot synthesis of aminobicyclo[4.4.0]decanes.

2. Results and discussion

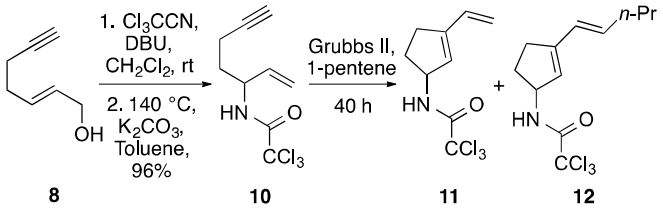
In this study, (2*E*)-hept-2-en-6-yn-1-ol (**8**) and (2*E*)-oct-2-en-7-yn-1-ol (**9**) were used as substrates for the one-pot multi-reaction processes. As previously reported, these were prepared from 4-pentyn-1-ol (**4**) and 5-hexyn-1-ol (**5**), respectively, using a highly efficient approach involving a one-pot Swern oxidation and Horner-Wadsworth-Emmons reaction to give the corresponding (*E*)-α,β-unsaturated esters (Scheme 2).[12,13] Reduction with DIBAL-H gave allylic alcohols **8** and **9** in excellent overall yield.



Scheme 2. Synthesis of alkyne derived allylic alcohols **8** and **9**.

Before attempting a one-pot four-step multi-reaction process, optimisation studies were performed on the tandem catalytic RCEYM/CM sequence of reactions.[14,15] Initially, (2*E*)-hept-2-en-6-yn-1-ol (**8**) was converted to the corresponding allylic trichloroacetamide **10** in 96% overall yield by formation of the imidate, followed by an Overman rearrangement under thermal conditions (Table 1).[16] Using 1-pentene as the CM partner and batch addition of Grubbs 2nd generation catalyst (5 and then 2.5 mol%), the one-pot RCEYM/CM of enyne **10** was investigated. Based on our previous experience of RCEYM reactions of compounds such as **10**, the first attempt was conducted at 75 °C (entry 1). This gave the RCEYM/CM product **12** in 41% yield with intermediate compound **11** also isolated in 16% yield. It was proposed that despite the process being conducted in a sealed tube, the elevated temperature could be restricting the CM reaction with the relatively volatile 1-pentene. Therefore, the second attempt was conducted at room temperature and gave an improved 74% yield of **12** (entry 2). Other variables such as decreasing or increasing the reaction concentration (entries 3 and 4) or increasing the catalyst loading (entry 5) were briefly investigated, however, these led to no improvement in the yield of **12**.

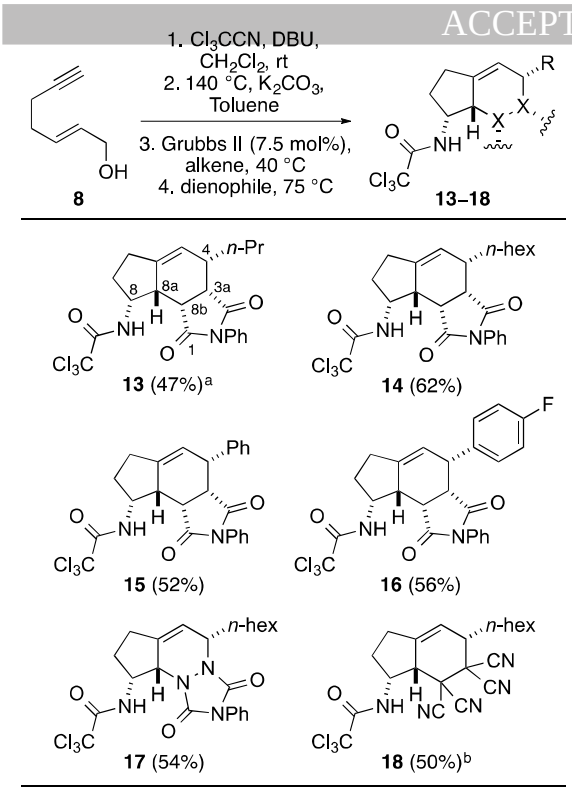
Table 1. Optimisation of the one-pot RCEYM/CM process.



Entry	Reaction Conc. (M)	Cat. Loading (mol%)[a]	Temp. (°C)	Yield (%) of **11**[b]	Yield (%) of **12**[b]
1	0.05	7.5	75	16	41
2	0.05	7.5	rt	9	74
3	0.025	7.5	rt	22	65
4	0.1	7.5	rt	30	53
5	0.05	10	rt	14	65

[a] Grubbs 2nd generation catalyst was added in two batches (5 and 2.5 mol% for entries 1–4 and 7.5 and 2.5 mol% for entry 5). [b] Isolated yield.

The optimised conditions for the RCEYM/CM sequence were then incorporated into the entire one-pot multi-reaction process for the preparation of aminobicyclo[4.3.0]nonanes from (2*E*)-hepta-2-en-6-yn-1-ol (**8**) (Scheme 3). Initially, allylic alcohol **8** was converted to the corresponding allylic trichloroacetimidate. The one-pot sequence was then initiated by Overman rearrangement under thermal conditions. The reaction mixture was cooled to room temperature and 1-pentene and Grubbs 2nd generation catalyst (5 mol%) were added. After addition of a second batch of the catalyst (2.5 mol%) and completion of the RCEYM/CM steps, the Diels-Alder reaction was instigated by the addition of *N*-phenyl maleimide and an increase in temperature to 75 °C. On purification, this gave aminobicyclo[4.3.0]nonane **13** as a single diastereomer in 47% yield over the five-steps. The relative stereochemistry of **13** was confirmed by difference NOE experiments which showed a *syn*-relationship of the hydrogen atoms at C-3a, C-4, C-8, C-8a and C-8b.[17] As observed previously with less substituted dienes,[12] the stereochemical outcome of the Diels-Alder reaction of diene **12** with *N*-phenyl maleimide is controlled by the formation of a hydrogen bonding directed *endo*-transition state between the trichloroacetamide hydrogen atom and the oxygen atom in the side-chain of the dienophile resulting in a highly diastereoselective process and the formation of five stereogenic centres. To explore the scope of this process, the one-pot procedure was repeated using 1-octene, styrene and 4-fluorostyrene as CM partners. Using these less volatile alkenes, it was found that the temperature of the RCEYM/CM sequence could be increased (40 °C), resulting in the isolation of aminobicyclo[4.3.0]nonanes **14**–**16** in improved yields over the five steps (52–62%). Further evidence of the relative stereochemistry of these compounds was achieved from the X-ray structure of **15** (Fig. 2).[18] Bicyclo[4.3.0]nonane **15** crystallises in the monoclinic space group $P2_1/n$ and the structure clearly shows the *syn*-relationship of the hydrogen atoms at the five stereocentres. Using 1-octene as the optimal CM partner, the scope of the dienophile was next investigated. The use of 4-phenyl-1,2,4-triazole-3,5-dione and tetracyanoethylene gave compounds **17** and **18** respectively, as single diastereomers in good overall yields.



Scheme 3. One-pot synthesis of aminobicyclo[4.3.0]nonanes **13**–**18**. [a] RCEYM/CM steps were conducted at room temperature. [b] Diels-Alder reaction was performed at 50 ºC.

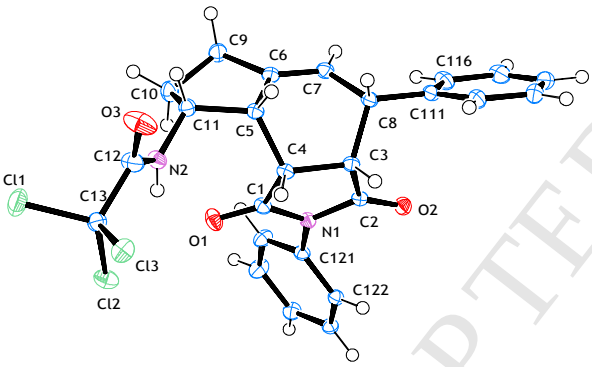
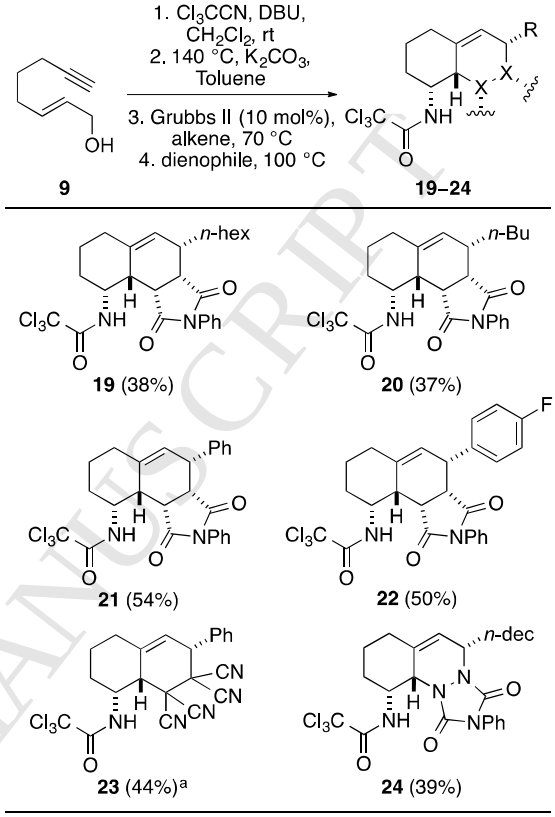


Fig. 2. ORTEP view of compound **15**. Thermal ellipsoids are drawn at 50% probability level and H-atoms are drawn with spheres of arbitrary radius.

To further expand the scope of the one-pot multi-reaction process, the use of (2*E*)-octa-2-en-7-yn-1-ol (**9**) for the diastereoselective synthesis of aminobicyclo[4.4.0]decanes was explored (Scheme 4). While imidate formation, Overman rearrangement and RCEYM proceeded as expected, the CM step of the resulting *exo*-diene with various alkenes showed poor conversion (29%). A better conversion (62%) could be achieved by increasing the temperature of the RCEYM/CM stage to 70 ºC and the loading of Grubbs 2nd generation catalyst to 10 mol%. The overall process using *N*-phenyl maleimide as the dienophile and with less reactive alkyl substituted alkenes such as 1-octene and 1-hexane gave the corresponding aminobicyclo[4.4.0]decanes **19** and **20** in modest yields (37–38%). The use of ^{1}H NMR spectroscopy and difference NOE experiments again confirmed the isolation of single diastereomers from each process and the relative stereochemistry of the five stereocentres formed during this one-pot process.[17] An improvement in yield was observed using more reactive CM partners. For example, the use of styrene and 4-fluorosytrene during the one-pot four-step process gave aminobicyclo[4.4.0]decanes **21** and **22** in 54% and 50% yields, respectively from allylic alcohol **9**. Other dienophiles were also utilised in combination with both alkyl and aryl derived CM partners giving aminobicyclo[4.4.0]decanes such as **23** and **24** in 39–44% yield over the five steps.

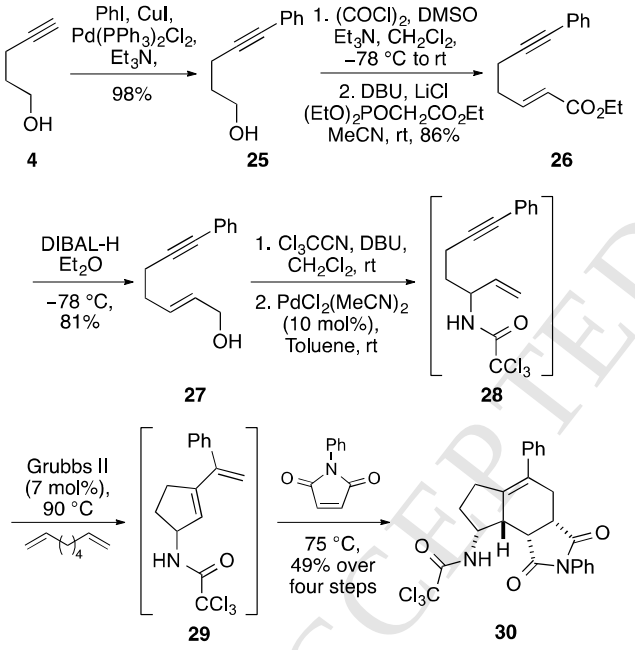


Scheme 4. One-pot synthesis of aminobicyclo[4.4.0]decanes **19**–**24**. [a] Diels-Alder reaction was performed at 50 ºC.

Having shown that aminobicyclo[4.3.0]nonanes could be substituted at the 4-position using a CM reaction as part of a one-pot multi-reaction process, we were also interested in developing an approach that would generate compounds with C-5 substitution. It was proposed that compounds with this substitution pattern could be generated using an allylic alcohol bearing a disubstituted alkyne. Another reason for investigating such substrates was to discover whether the Overman rearrangement step of disubstituted alkyne derived allylic alcohols could be performed using a Pd(II)-catalyst. All previous multi-step reaction processes involving mono-substituted alkyne derived allylic alcohols such as **8** and **9** have used a thermally mediated Overman rearrangement.[12,13] This was because preliminary studies with these compounds which investigated a Pd(II)-catalysed rearrangement showed that high catalyst loading (up to 25 mol%) and long reaction times were required for good conversion. This sluggish reactivity was attributed to catalyst binding to the alkyne. Therefore, we reasoned a hindered disubstituted alkyne would facilitate a more efficient Pd(II)-catalysed Overman rearrangement as part of a one-pot multi-step process. We were also interested to investigate how a disubstituted alkyne would affect the RCEYM step and the subsequent overall efficiency of these one-pot processes.

To investigate these aspects of the one-pot multi-reaction process, a four-step synthesis of a disubstituted alkyne derived allylic alcohol was developed (Scheme 5). A Sonogashira reaction of 4-pentyn-1-ol (**4**) with iodobenzene gave coupled

product **25** in 98% yield.[19] A one-pot Swern oxidation and Horner-Wadsworth-Emmons reaction gave (*E*)-α,β-unsaturated ester **26** in 86% yield and this was followed by reduction with DIBAL-H under standard conditions,[12] which gave allylic alcohol **27**. Before attempting a one-pot multi-reaction process with **27**, the key steps were optimised. Following allylic imidate formation, the Overman rearrangement was found to proceed using 10 mol% of bis(acetonitrile)palladium(II) chloride in 18 hours giving allylic trichloroacetamide **28** in 81% yield over the two steps. As expected, attempted RCEYM reaction with enyne **28** under typical conditions (75 ºC) using Grubbs 2nd generation catalyst showed minimal conversion. However, an increase in the reaction temperature to 90 ºC and the use of 1,7-octadiene as in situ source of ethylene to speed up the reaction,[20] gave diene **29** in 74% yield for this step. Using these optimised conditions for a one-pot process, which included a Diels-Alder reaction with *N*-phenyl maleimide gave 5-phenyl aminobicyclo[4.3.0]nonane **30** as a single diastereomer in 49% overall yield from allylic alcohol **27**. These preliminary results show that not only can this type of substitution pattern be formed but more importantly that with a relatively hindered alkyne, a Pd(II)-catalysed Overman rearrangement can be utilised during these one-pot multi-reaction processes. This is significant as the use of chiral Pd(II)-catalysts for the Overman rearrangement during these one-pot multi-reaction processes would allow for the first time, the asymmetric synthesis of these compounds using this approach.



Scheme 5. Synthesis of 5-phenyl aminobicyclo[4.3.0]nonane **30**.

3. Conclusions

In summary, a one-pot multi-step process involving a thermal Overman rearrangement, a tandem catalytic RCEYM/CM stage and a hydrogen bonding directed Diels-Alder reaction has been developed for the diastereoselective synthesis of aminobicyclo[4.3.0]nonanes. Variation of the CM partner and the dienophile allowed the preparation of a range of compounds with up to five stereogenic centres and in good overall yields. This process could be extended for the diastereoselective synthesis of aminobicyclo[4.4.0]decanes but a slow CM step meant that with less reactive alkyl substituted alkenes, overall yields were slightly lower compared to the nonane series. A one-pot multi-reaction process was also developed utilising a disubstituted alkyne derived allylic trichloroacetimidate. For the first time in these multi-step processes, the Overman rearrangement could be performed efficiently using a Pd(II)-catalyst, which gave a 5-aryl aminobicyclo[4.3.0]nonane in good overall yield. Work is currently underway to examine the scope of disubstituted alkyne derived allylic alcohols and the use of chiral Pd(II)-catalysts in these one-pot multi-reaction processes for the asymmetric synthesis of medicinally important compounds and natural products.

4. Experimental section

4.1 General Methods

All reagents and starting materials were obtained from commercial sources and used as received. All dry solvents were purified using a PureSolv 500 MD solvent purification system. All reactions were performed under an atmosphere of argon unless otherwise mentioned. Brine refers to a saturated solution of sodium chloride. Flash column chromatography was carried out using Fisher matrix silica 60. Macherey-Nagel aluminium-backed plates pre-coated with silica gel 60 (UV_{254}) were used for thin layer chromatography and were visualised by staining with $KMnO_4$. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 400 spectrometer with chemical shift values in ppm relative to TMS (δ_H 0.00 and δ_C 0.0) or residual chloroform (δ_H 7.28 and δ_C 77.2) as standard. Proton and carbon assignments are based on two-dimensional COSY and DEPT experiments, respectively. Mass spectra were obtained using a JEOL JMS-700 spectrometer. Infrared spectra were obtained neat using a Shimadzu IRPrestige-21 spectrometer. Melting points were determined on a Reichert platform melting point apparatus.

*4.1.1. Ethyl (2E)-hept-2-en-6-ynoate (**6**).*[21] Dimethyl sulfoxide (3.60 mL, 50.8 mmol) was added to a stirred solution of oxalyl chloride (2.49 mL, 28.4 mmol) in dichloromethane (100 mL) at −78 °C. The mixture was stirred for 0.3 h before 4-pentyn-1-ol (**4**) (1.70 g, 20.3 mmol) in dichloromethane (25 mL) was slowly added. The mixture was stirred for a further 0.3 h before triethylamine (14.1 mL, 102 mmol) was added. This reaction mixture was stirred for 0.5 h at −78 °C and then allowed to warm to room temperature and stirred for a further 3 h. A solution of lithium chloride (1.55 g, 36.5 mmol), triethyl phosphonoacetate (7.24 mL, 36.5 mmol) and 1,8-diazabicyclo[5,4,0]undec-7-ene (5.14 mL, 36.5 mmol) in acetonitrile (70 mL) was then prepared and stirred for 1 h. The Swern solution was concentrated *in vacuo*, then the Horner Wadsworth Emmons solution was added and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with a saturated solution of ammonium chloride (50 mL) and concentrated to give an orange residue, which was then extracted with diethyl ether (4 × 75 mL). The organic layers were combined, dried ($MgSO_4$), filtered and concentrated to give an orange oil. Purification by flash column chromatography (diethyl ether/petroleum ether, 1:9) gave ethyl (2*E*)-hept-2-en-6-ynoate (**6**) (2.95 g, 96%) as a yellow oil. Spectroscopic data was as reported in the literature.[21] R_f (25% diethyl ether/petroleum ether) 0.63; ν_{max} (neat) 3302 (C≡C−H), 2984 (CH), 1715 (CO), 1657 (C=C), 1445, 1368, 1267, 1155, 1038, 756 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.01 (1H, t, *J* 2.5 Hz, 7-H), 2.34–2.39 (2H, m, 5-H_2), 2.41–2.48 (2H, m, 4-H_2), 4.20 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.90 (1H, dt, *J* 15.7, 1.5 Hz, 2-H), 6.97 (1H, dt, *J* 15.7, 6.7 Hz, 3-H); δ_C (126 MHz, $CDCl_3$) 14.3 (CH_3), 17.4 (CH_2), 31.0 (CH_2), 60.3 (CH_2), 69.4 (CH), 82.7 (C), 122.6 (CH), 146.3 (CH), 166.4 (C); *m/z* (CI) 153 (MH^+, 100%), 139 (5), 113 (10), 97 (5), 81 (15), 69 (15).

*4.1.2. Ethyl (2E)-oct-2-en-7-ynoate (**7**).*[22] The reaction was carried out as described for the synthesis of ethyl (2*E*)-hept-2-en-6-ynoate (**6**) using 5-hexyn-1-ol (**5**) (3.00 g, 30.6 mmol). Purification by flash column chromatography (diethyl ether/petroleum ether, 1:9) gave ethyl (2*E*)-oct-2-en-7-ynoate (**7**) (4.99 g, 99%) as a yellow oil. Spectroscopic data was as reported in the literature.[22] R_f (50% diethyl ether/petroleum ether) 0.74; ν_{max} (neat) 3295 (C≡C−H), 2940 (CH), 1713 (CO), 1651 (C=C), 1265, 1188, 1150, 1042, 979, 756, 633 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.29 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.70 (2H, quin, *J* 6.9 Hz, 5-H_2), 1.98 (1H, s, 8-H), 2.23 (2H, t, *J* 6.9 Hz, 6-H_2), 2.33 (2H, q, *J* 6.9 Hz, 4-H_2), 4.18 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.86 (1H, d, *J* 15.6 Hz, 2-H), 6.94 (1H, dt, *J* 15.6, 6.9 Hz, 3-H); δ_C (101 MHz, $CDCl_3$) 14.3 (CH_3), 17.9 (CH_2), 26.7 (CH_2), 30.9 (CH_2), 60.2 (CH_2), 69.0 (CH), 83.5 (C), 122.1 (CH), 147.8 (CH), 166.6 (C); *m/z* (CI) 167 (MH^+, 100%), 139 (42), 113 (10), 97 (12), 81 (25), 71 (30).

*4.1.3. (2E)-Hept-2-en-6-yn-1-ol (**8**).*[23] Ethyl (2*E*)-hept-2-en-6-ynoate (**6**) (1.50 g, 9.87 mmol) was dissolved in diethyl ether (50 mL) and cooled to −78 °C. DIBAL-H (1 M in hexane) (21.7 mL, 21.7 mmol) was added dropwise and the reaction mixture was stirred at −78 °C for 3 h, before warming to room temperature overnight. The solution was cooled to 0 °C and quenched by the addition of a saturated solution of ammonium chloride (10 mL) and warmed to room temperature with vigorous stirring over 1 h, producing a white precipitate. The precipitate was filtered through a pad of Celite® and washed with diethyl ether (3 × 50 mL). The filtrate was then dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (diethyl ether/petroleum ether, 1:1) gave (2*E*)-hept-2-en-6-yn-1-ol (**8**) (1.01 g, 93%) as a yellow oil. Spectroscopic data was as reported in the literature.[23] R_f (50% diethyl ether/petroleum ether) 0.33; ν_{max} (neat) 3360 (OH), 3295 (C≡C−H), 2915 (CH), 1670 (C=C), 1433, 1084, 997, 968 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.42 (1H, br s, OH), 1.99 (1H, t, *J* 2.5 Hz, 7-H), 2.28–2.33 (4H, m, 4-H_2 and 5-H_2), 4.14 (2H, d, *J* 4.0 Hz, 1-H_2), 5.70–5.81 (2H, m, 2-H and 3-H); δ_C (126 MHz, $CDCl_3$) 18.5 (CH_2), 31.1 (CH_2), 63.5 (CH_2), 68.8 (CH), 83.7 (C), 130.5 (CH), 130.6 (CH); *m/z* (CI) 111 (MH^+, 3%), 107 (15), 93 (100), 81 (10), 69 (10).

*4.1.4. (2E)-Oct-2-en-7-yn-1-ol (**9**).*[24] The reaction was carried out as described for the synthesis of (2*E*)-hept-2-en-6-yn-1-ol (**8**) using ethyl (2*E*)-oct-2-en-7-ynoate (**7**) (4.10 g, 24.7 mmol). Purification by flash column chromatography (diethyl ether/petroleum ether, 1:1) gave (2*E*)-octa-2-en-7-yn-1-ol (**9**) (2.95 g, 97% yield) as a yellow oil. Spectroscopic data was as reported in the literature.[24] R_f (50% petroleum ether/diethyl ether) 0.29; ν_{max} (neat) 3361 (OH), 3302 (C≡C−H), 2932 (CH), 1674 (C=C), 1435, 1219, 1088, 972 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.29 (1H, br s, OH), 1.63 (2H, quin, *J* 6.9 Hz, 5-H_2), 1.96 (1H, t, *J* 2.6 Hz, 8-H), 2.15–2.25 (4H, m, 4-H_2 and 6-H_2), 4.09–4.15 (2H, m, 1-H_2), 5.63–5.74 (2H, m, 2-H and 3-H); δ_C (101 MHz, $CDCl_3$) 17.8 (CH_2), 27.8 (CH_2), 31.1 (CH_2), 63.7 (CH_2), 68.5 (CH), 84.2 (C), 129.9 (CH), 131.9 (CH); *m/z* (CI) 125 (MH^+, 20%), 107 (95), 97 (40), 81 (80), 71 (100).

*4.1.5. 3-(2',2',2'-Trichloromethylcarbonylamino)hept-1-en-6-yne (**10**).*[13] (2*E*)-Hept-2-en-6-yn-1-ol (**8**) (0.388 g, 3.53 mmol) was dissolved in dichloromethane (25 mL) and cooled to 0 °C. To the solution 1,8-diazabicyclo[5.4.0]undec-7-ene (0.099 mL, 0.706 mmol) and trichloroacetonitrile (0.530 mL, 5.29 mmol) were added. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The reaction mixture was filtered through a short pad of silica gel and the filtrate concentrated *in vacuo* to give the allylic trichloroacetimidate, which was used without further purification. The allylic trichloroacetimidate was dissolved in toluene (10 mL) and transferred to a Schlenk tube containing potassium carbonate (0.05 g, 0.362 mmol) and purged with Ar and sealed. The reaction mixture was heated to 140 °C and stirred for 36 h. The reaction mixture was then cooled to room temperature and the solvent was evaporated. Purification by flash column chromatography (petroleum ether/diethyl ether 10:1) gave 3-(2',2',2'-trichloromethylcarbonylamino)hept-1-en-6-yne (**10**) (0.866 g, 96%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.95; Mp 35–37 °C; ν_{max} (neat) 3304 (NH), 3055 (CH), 2361, 1713 (CO), 1510, 1265, 822, 733 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.84–2.00 (2H, m, 4-H_2), 2.05 (1H, t, *J* 2.7 Hz, 7-H), 2.26–2.39 (2H, m, 5-H_2), 4.56–4.63 (1H, m, 3-H), 5.27 (1H, d, *J* 10.5 Hz, 1-*H*H), 5.30 (1H, d, *J* 17.2 Hz, 1-H*H*), 5.82 (1H, ddd, *J* 17.2, 10.5, 5.6 Hz, 2-H), 6.93 (1H, br s, NH); δ_C (126 MHz, $CDCl_3$) 14.8 (CH_2), 32.5 (CH_2), 53.0 (CH), 69.9 (CH), 83.1 (C), 92.7 (C), 116.9 (CH_2), 135.4 (CH), 161.3 (C); *m/z* (CI) 254 (MH^+, 72%), 220 (55), 186 (42), 184 (37), 132 (12), 89 (100), 69 (27); HRMS (CI): MH^+, found 253.9901. $C_9H_{11}{}^{35}Cl_3NO$ requires 253.9906.

*4.1.6 4-(n-Pent-1"-ene)-1-(2',2',2'-trichloromethylcarbonylamino)cyclopent-4-ene (**12**).* 3-(2',2',2'-Trichloromethylcarbonylamino)hept-1-en-6-yne (**10**) (0.11 g, 0.42 mmol) was dissolved in toluene (8 mL) and Grubbs 2nd generation catalyst (0.016 g, 0.019 mmol) with 1-pentene (0.204 mL, 1.866 mmol) was then added. The reaction mixture was stirred at room temperature for 18 h. Further addition of Grubbs 2nd generation catalyst (0.008 g, 0.010 mmol) with 1-pentene (0.11 mL, 1.01 mmol) was then added and the reaction mixture stirred at room temperature for 22 h. The reaction mixture was then cooled and the solvent was evaporated. Purification by flash column chromatography (petroleum ether/diethyl ether 9:1) gave 4-(*n*-pent-1"-ene)-1-(2',2',2'-trichloromethylcarbonylamino)cyclopent-4-ene (**12**) (0.091 g, 74%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.82; Mp 56–58 °C; ν_{max} (neat) 3285 (NH), 2957 (CH), 2930, 1701, 1686 (CO), 1524, 1258, 1067, 964 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.4 Hz, 5"-H_3), 1.44 (2H, sextet, *J* 7.4 Hz, 4"-H_2), 1.75 (1H, ddt, *J* 13.0, 8.5, 4.1 Hz, 2-*H*H), 2.11 (2H, q, *J* 7.4 Hz, 3"-H_2), 2.40–2.55 (2H, m, 2-H*H* and 3-*H*H), 2.58–2.67 (1H, m, 3-H*H*), 4.96–5.03 (1H, m, 1-H), 5.53 (1H, br s, 5-H), 5.75 (1H, dt, *J* 15.7, 7.4 Hz, 2"-H), 6.27 (1H, d, *J* 15.7 Hz, 1"-H), 7.63 (1H, d, *J* 9.3 Hz, NH); δ_C (126 MHz, $CDCl_3$) 13.7 (CH_3), 22.4 (CH_2), 30.0 (CH_2), 31.1 (CH_2), 34.9 (CH_2), 57.8 (CH), 92.8 (C), 124.8 (CH), 125.9 (CH), 135.3 (CH), 147.3 (C), 161.1 (C); *m/z* (ESI) 318 ($[MNa]^+$, 86%), 296 (10), 236 (24), 184 (16), 135 (21); HRMS (ESI): $[MNa]^+$, found 318.0182. $C_{12}H_{16}{}^{35}Cl_3NNaO$ requires 318.0190.

4.1.7. (3aS,4S*,8R*,8aS*,8bR*)-4,6,7,8,8a,8b-Hexahydro-2-phenyl-4-n-propyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[e]isoindole-1,3(2H,3aH)-dione (**13**).* (2*E*)-Hept-2-en-6-yn-1-ol (**8**) (0.027 g, 0.24 mmol) was dissolved in dichloromethane (10 mL) and cooled to 0 °C. To the solution 1,8-diazabicyclo[5.4.0]undec-7-ene (0.007 mL, 0.048 mmol) and trichloroacetonitrile (0.036 mL, 0.36 mmol) were added. The reaction mixture was allowed to warm to room temperature before stirring for 3 h. The reaction mixture was filtered through a short pad of silica gel and the filtrate concentrated *in vacuo* to give the allylic trichloroacetimidate, which was used without further purification. The allylic trichloroacetimidate was dissolved in toluene (5 mL) and transferred to a Schlenk tube containing potassium carbonate (0.025 g, 0.18 mmol), purged with Ar and sealed. The reaction

mixture was then heated to 140 °C and stirred for 36 h. Grubbs 2nd generation catalyst (0.012 g, 0.014 mmol) was added with 1-pentene (0.13 mL, 1.21 mmol) and the reaction mixture was stirred for 24 h at room temperature. A further portion of Grubbs 2nd generation catalyst (0.005 g, 0.006 mmol) and 1-pentene (0.067 mL, 0.61 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. *N*-Phenyl maleimide (0.063 g, 0.36 mmol) was added with hydroquinone (0.005 g, 0.005 mmol). The reaction mixture was stirred for 24 h at 75 °C. The reaction mixture was then cooled and the solvent was evaporated. Flash column chromatography (petroleum ether/diethyl ether, 4:1) gave (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-4,6,7,8,8a,8b-hexahydro-2-phenyl-4-*n*-propyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**13**) (0.054 g, 47%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.59; Mp 145–147 °C; ν_{max} (neat) 3304 (NH), 2957 (CH), 1695 (CO), 1516, 1499, 1389, 1182 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.3 Hz, 3"-H_3), 1.37–1.50 (2H, m, 2"-H_2), 1.61–1.71 (1H, m, 1"-*H*H), 1.74–1.91 (2H, m, 1"-H*H* and 7-*H*H), 2.08 (1H, dt, *J* 12.4, 7.2 Hz, 7-H*H*), 2.23–2.33 (2H, m, 4-H and 6-*H*H), 2.39 (1H, dd, *J* 15.4, 8.1 Hz, 6-H*H*), 2.83–2.90 (1H, m, 8a-H), 3.20 (1H, dd, *J* 8.4, 6.9 Hz, 3a-H), 3.35 (1H, dd, *J* 8.4, 6.5 Hz, 8b-H), 4.75–4.85 (1H, m, 8-H), 5.52 (1H, br s, 5-H), 7.05–7.10 (2H, m, 2 × ArH), 7.30–7.35 (1H, m, ArH), 7.36–7.42 (2H, m, 2 × ArH), 8.90 (1H, d, *J* 9.7 Hz, NH); δ_C (126 MHz, $CDCl_3$) 14.1 (CH_3), 21.4 (CH_2), 28.2 (CH_2) 31.7 (CH_2), 33.2 (CH_2), 38.3 (CH), 42.1 (CH), 42.2 (CH), 42.8 (CH), 52.9 (CH), 92.9 (C), 123.1 (CH), 126.5 (2 × CH), 129.0 (CH), 129.3 (2 × CH), 131.5 (C), 145.1 (C), 162.3 (C), 175.7 (C), 179.3 (C); *m/z* (ESI) 491 ($[MNa]^+$, 75%), 413 (6), 301 (4), 236 (11), 228 (100); HRMS (ESI): $[MNa]^+$, found 491.0649. $C_{22}H_{23}{}^{35}Cl_3N_2NaO_3$ requires 491.0666.

*4.1.8. (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-4,6,7,8,8a,8b-Hexahydro-4-n-hexyl-2-phenyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[e]isoindole-1,3(2H,3aH)-dione (**14**).* (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-4,6,7,8,8a,8b-Hexahydro-4-*n*-hexyl-2-phenyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**14**) was synthesised according to the above procedure using (2*E*)-hept-2-en-6-yn-1-ol (**8**) (0.027 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.015 g, 0.018 mmol) and 1-octene (0.28 mL, 1.82 mmol) for 48 h at 40 °C before *N*-phenyl maleimide (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 24 h at 75 °C. Flash column chromatography (petroleum ether/diethyl ether, 5:1) gave (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-4,6,7,8,8a,8b-hexahydro-4-*n*-hexyl-2-phenyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**14**) (0.076 g, 62%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.62; Mp 145–147 °C; ν_{max} (neat) 3310 (NH), 2928 (CH), 1697 (CO), 1516, 1499, 1389, 1186 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.86–0.92 (3H, m, 6"-H_3), 1.25–1.53 (8H, m, 2"-H_2, 3"-H_2, 4"-H_2 and 5"-H_2), 1.73 (1H, dtd, *J* 14.1, 9.4, 5.4 Hz, 1"-*H*H), 1.86 (1H, qd, *J* 12.3, 7.8 Hz, 7-*H*H), 1.99–2.01 (1H, m, 1"-H*H*), 2.14 (1H, dt, *J* 12.3, 7.2 Hz, 7-H*H*), 2.25–2.39 (2H, m, 4-H and 6-*H*H), 2.46 (1H, dd, *J* 16.0, 7.8 Hz, 6-H*H*), 2.90–2.96 (1H, m, 8a-H), 3.27 (1H, dd, *J* 8.4, 6.9 Hz, 3a-H), 3.41 (1H, dd, *J* 8.4, 6.5 Hz, 8b-H), 4.81–4.92 (1H, m, 8-H), 5.57–5.61 (1H, m, 5-H), 7.13–7.17 (2H, m, 2 × ArH), 7.37–7.42 (1H, m, ArH), 7.43–7.48 (2H, m, 2 × ArH), 8.98 (1H, d, *J* 9.7 Hz, NH); δ_C (126 MHz, $CDCl_3$) 14.1 (CH_3), 22.6 (CH_2), 28.2 (CH_2), 28.3 (CH_2), 29.3 (CH_2), 31.0 (CH_2), 31.7 (CH_2), 31.8 (CH_2), 38.6 (CH), 42.1 (CH), 42.2 (CH), 42.8 (CH), 52.9 (CH), 92.2 (C), 123.1 (CH), 126.6 (2 × CH), 129.0 (CH), 129.3 (2 × CH), 131.5 (C), 145.0 (C), 162.2 (C), 175.7 (C), 179.4 (C); *m/z* (ESI) 533 ($[MNa]^+$, 100%), 413 (4), 301 (15), 236 (28), 228 (22), 218 (6), 141 (3); HRMS (ESI): $[MNa]^+$, found 533.1120. $C_{25}H_{29}{}^{35}Cl_3N_2NaO_3$ requires 533.1136.

4.1.9 (3aS,4S*,8R*,8aS*,8bR*)-2,4-Diphenyl-4,6,7,8,8a,8b-hexahydro-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[e]isoindole-1,3(2H,3aH)-dione (**15**).* (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-2,4-Diphenyl-4,6,7,8,8a,8b-hexahydro-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**15**) was synthesised according to the above procedure using (2*E*)-hept-2-en-6-yn-1-ol (**8**) (0.027 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.015 g, 0.018 mmol) and styrene (0.21 mL, 1.82 mmol) for 48 h at 40 °C before *N*-phenyl maleimide (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 48 h at 75 °C. Flash column chromatography (petroleum ether/diethyl ether, 1:1) gave (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-2,4-diphenyl-4,6,7,8,8a,8b-hexahydro-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**15**) (0.063 g, 52%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.32; Mp 154–156 °C; ν_{max} (neat) 3318 (NH), 2940 (CH), 1697 (CO), 1512, 1501, 1383, 1196, 1177, 822 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.99 (1H, qd, *J* 12.4, 7.9 Hz, 7-*H*H), 2.23 (1H, dq, *J* 12.4, 7.3 Hz, 7-H*H*), 2.38–2.49 (1H, m, 6-*H*H), 2.60 (1H, dd, *J* 16.5, 7.9 Hz, 6-H*H*), 3.08–3.16 (1H, m, 8a-H), 3.49–3.55 (2H, m, 3a-H and 8b-H), 3.75 (1H, br s, 4-H), 4.90–5.01 (1H, m, 8-H), 6.13–6.17 (1H, m, 5-H), 7.13 (2H, t, *J* 7.6 Hz, 2 × ArH), 7.25–7.32 (3H, m, 3 × ArH), 7.35–7.40 (3H, m, 3 × ArH), 7.41–7.46 (2H, m, 2 × ArH), 8.91 (1H, d, *J* 9.6 Hz, NH); δ_C (126 MHz, $CDCl_3$) 28.8 (CH_2), 31.8 (CH_2), 41.9 (CH), 42.1 (CH), 43.5 (CH), 46.1 (CH), 52.8 (CH), 92.8 (C), 120.3 (CH), 126.3 (2 × CH), 127.3 (CH), 128.4 (2 × CH), 128.7 (2 × CH), 128.9 (CH), 129.2 (2 × CH), 131.4 (C), 138.7 (C), 146.5 (C), 162.3 (C), 174.3 (C), 178.7 (C); *m/z* (ESI) 501 ($[M-H]^-$, 64%), 383 (100), 312 (15), 212 (22); HRMS (ESI): $[M-H]^-$, found 501.0533. $C_{25}H_{20}{}^{35}Cl_3N_2O_3$ requires 501.0545.

4.1.10. (3aS,4S*,8R*,8aS*,8bR*)-4-(4-Fluorophenyl)-4,6,7,8,8a,8b-hexahydro-2-phenyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[e]isoindole-1,3(2H,3aH)-dione (**16**).* (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-4-(4-Fluorophenyl)-4,6,7,8,8a,8b-hexahydro-2-phenyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**16**) was synthesised according to the above procedure using (2*E*)-hept-2-en-6-yn-1-ol (**8**) (0.027 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.015 g, 0.018 mmol) and 4-fluorostyrene (0.22 mL, 1.82 mmol) for 48 h at 40 °C before *N*-phenyl maleimide (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 24 h at 75 °C. Flash column chromatography (petroleum ether/diethyl ether, 1:1) gave (3a*S**,4*S**,8*R**,8a*S**,8b*R**)-4-(4-fluorophenyl)-4,6,7,8,8a,8b-hexahydro-2-phenyl-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**16**) (0.070 g, 56%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.24; Mp 146–148 °C; ν_{max} (neat) 3307 (NH), 2925 (CH), 1696 (CO), 1510, 1388, 1214, 1200, 1158, 822 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 2.00 (1H, qd, *J* 12.3, 7.9 Hz, 7-*H*H), 2.26 (1H, dq, *J* 12.3, 7.4 Hz, 7-H*H*), 2.39–2.52 (1H, m, 6-*H*H), 2.62 (1H, dd, *J* 16.4, 7.9 Hz, 6-H*H*), 3.09–3.16 (1H, m, 8a-H), 3.47 (1H, dd, *J* 15.5, 8.3 Hz, 3a-H), 3.54 (1H, dd, *J* 8.3, 6.0 Hz, 8b-H), 3.71–3.79 (1H, m, 4-H), 4.91–5.04 (1H, m, 8-H), 6.08–6.12 (1H, m, 5-H), 7.06–7.10 (2H, m, 2 × ArH), 7.13–7.16 (2H, m, 2 × ArH), 7.22–7.27 (2H, m, 2 × ArH), 7.38–7.43

(1H, m, ArH), 7.44–7.50 (2H, m, 2 × ArH), 8.92 (1H, d, *J* 9.6 Hz, NH); δ_C (126 MHz, $CDCl_3$) 28.7 (CH_2), 31.7 (CH_2), 41.8 (CH), 42.2 (CH), 42.8 (CH), 46.0 (CH), 52.8 (CH), 92.8 (C), 115.3 (d, $J_{C\text{-}C\text{-}F}$ 21.6 Hz, 2 × CH), 120.2 (CH), 126.3 (2 × CH), 129.0 (CH), 129.3 (2 × CH), 130.2 (d, $J_{C\text{-}C\text{-}C\text{-}F}$ 8.0 Hz, 2 × CH), 131.3 (C), 134.5 (C), 146.8 (C), 162.0 (d, $J_{C\text{-}F}$ 245.9 Hz, C), 162.3 (C), 174.4 (C), 178.6 (C); *m/z* (ESI) 543 ($[MNa]^+$, 100%), 449 (6), 413 (7), 352 (4), 227 (6), 159 (4); HRMS (ESI): $[MNa]^+$, found 543.0410. $C_{25}H_{20}{}^{35}Cl_3FN_2NaO_3$ requires 543.0416.

4.1.11. (5S,9R*,9aS*)-5-n-Hexyl-7,8,9,9a-tetrahydro-9-(2',2',2'-trichloromethylcarbonylamino)-1H,5H-cyclopent[c][2,4,10]-triazolo[1,2-a]pyridazine-1,3(2H)-dione (**17**).* (5*S**,9*R**,9a*S**)-5-*n*-Hexyl-7,8,9,9a-tetrahydro-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*,5*H*-cyclopent[*c*][2,4,10]-triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione (**17**) was synthesised according to the above procedure using (2*E*)-hept-2-en-6-yn-1-ol (**8**) (0.027 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.015 g, 0.018 mmol) and 1-octene (0.28 mL, 1.82 mmol) for 48 h at 40 °C before *N*-phenyl-1,2,4-triazoline-3,5-dione (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 18 h at 75 °C. Flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave (5*S**,9*R**,9a*S**)-5-*n*-hexyl-7,8,9,9a-tetrahydro-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*,5*H*-cyclopent[*c*][2,4,10]-triazolo[1,2-*a*]pyridazine-1,3(2*H*)-dione (**17**) (0.066 g, 54%) as a brown oil. R_f (50% diethyl ether/petroleum ether) 0.33; ν_{max} (neat) 3412 (NH), 2928 (CH), 1775 (CO), 1711 (CO), 1503, 1416, 1265, 1140, 820 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.9 Hz, 6"-H_3), 1.19–1.47 (8H, m, 2"-H_2, 3"-H_2 , 4"-H_2 and 5"-H_2), 1.73–1.94 (2H, m, 1"-H_2), 2.07–2.20 (1H, m, 8-*H*H), 2.34–2.43 (1H, m, 8-H*H*), 2.52–2.62 (2H, m, 7-H_2), 4.23–4.29 (1H, m, 9a-H), 4.62–4.68 (1H, m, 5-H), 4.87 (1H, br q, *J* 5.4 Hz, 9-H), 5.88–5.94 (1H, m, 6-H), 6.80 (1H, d, *J* 5.4 Hz, NH), 7.35–7.41 (1H, m, ArH), 7.45–7.50 (2H, m, 2 × ArH), 7.51–7.56 (2H, m, 2 × ArH); δ_C (126 MHz, $CDCl_3$) 14.0 (CH_3), 22.6 (CH_2), 24.9 (CH_2), 24.9 (CH_2), 27.7 (CH_2), 29.1 (CH_2), 31.5 (CH_2), 33.2 (CH_2), 52.6 (CH), 53.9 (CH), 60.7 (CH), 92.7 (C), 120.4 (CH), 125.2 (2 × CH), 128.2 (CH), 129.2 (2 × CH), 131.0 (C), 136.5 (C), 150.0 (C), 154.6 (C), 161.3 (C); HRMS (ESI): $[MNa]^+$, found 535.1023. $C_{23}H_{27}{}^{35}Cl_3N_4NaO_3$ requires 535.1041.

4.1.12. (1R,5S*,7aR*)-2,3,5,6,7,7a-Hexahydro-5-n-hexyl-6,6,7,7-tetracyano-1-(2',2',2'-trichloromethylcarbonylamino)indene (**18**).* (1*R**,5*S**,7a*R**)-2,3,5,6,7,7a-Hexahydro-5-*n*-hexyl-6,6,7,7-tetracyano-1-(2',2',2'-trichloromethylcarbonylamino)indene (**18**) was synthesised according to the above procedure using (2*E*)-hept-2-en-6-yn-1-ol (**8**) (0.027 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.015 g, 0.018 mmol) and 1-octene (0.28 mL, 1.82 mmol) for 48 h at 40 °C before tetracyanoethylene (0.046 g, 0.36 mmol) was added. The reaction mixture was stirred for 18 h at 50 °C. Flash column chromatography (petroleum ether/ethyl acetate, 4:1) gave (1*R**,5*S**,7a*R**)-2,3,5,6,7,7a-hexahydro-5-*n*-hexyl-6,6,7,7-tetracyano-1-(2',2',2'-trichloromethylcarbonylamino)indene (**18**) (0.057 g, 50%) as a white solid. R_f (50% ethyl acetate/petroleum ether) 0.80; Mp 163–165 °C; ν_{max} (neat) 3316 (NH), 2930 (CH), 1688 (CO), 1530, 1458, 1265, 841, 822 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 8.7 Hz, 6"-H_3), 1.25–1.49 (7H, m, 2"-*H*H, 3"-H_2, 4"-H_2 and 5"-H_2), 1.53–1.65 (1H, m, 2"-H*H*), 1.86–2.03 (2H, m, 1"-*H*H and 2-*H*H), 2.05–2.16 (1H, m, 1"-H*H*), 2.39–2.49 (1H, m, 2-H*H*), 2.51–2.64 (1H, m, 3-*H*H), 2.69–2.80 (1H, m, 3-H*H*), 2.97–3.06 (1H, m, 5-H), 3.29–3.37 (1H, m, 7a-H), 4.41–4.52 (1H, m, 1-H), 5.84–5.89 (1H, m, 4-H), 6.91 (1H, d, *J* 10.2 Hz, NH); δ_C (126 MHz, $CDCl_3$) 14.0 (CH_3), 22.5 (CH_2), 27.0 (CH_2), 27.9 (CH_2), 28.7 (CH_2), 28.8 (CH_2), 31.5 (CH_2), 32.8 (CH_2), 39.3 (C), 43.3 (CH), 44.5 (C), 49.0 (CH), 55.2 (CH), 91.8 (C), 109.1 (C), 110.1 (C), 110.9 (C), 111.6 (C), 119.8 (CH), 134.6 (C), 162.3 (C); *m/z* (ESI) 464 ($[M-H]^-$, 100%), 400 (2), 346 (10), 303 (22), 276 (8), 265 (4), 249 (4); HRMS (ESI): $[M-H]^-$, found 464.0806. $C_{21}H_{21}{}^{35}Cl_3N_5O$ requires 464.0817.

4.1.13. (3aS,4S*,9R*,9aS*,9bR*)-4-n-Hexyl-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1H-benz[e]isoindole-1,3(2H)-dione (**19**).* (2*E*)-Octa-2-en-7-yn-1-ol (**9**) (0.03 g, 0.24 mmol) was dissolved in dichloromethane (10 mL) and cooled to 0 °C. To the solution 1,8-diazabicyclo[5.4.0]undec-7-ene (0.007 mL, 0.048 mmol) and trichloroacetonitrile (0.036 mL, 0.36 mmol) were added. The reaction mixture was allowed to warm to room temperature before stirring for 3 h. The reaction mixture was filtered through a short pad of silica gel and the filtrate concentrated *in vacuo* to give the allylic trichloroacetimidate, which was used without further purification. The allylic trichloroacetimidate was dissolved in toluene (5 mL) and transferred to a Schlenk tube containing potassium carbonate (0.025 g, 0.18 mmol), purged with Ar and sealed. The reaction mixture was then heated to 140 °C and stirred for 36 h. Grubbs 2nd generation catalyst (0.010 g, 0.012 mmol) was added with 1-octene (0.19 mL, 1.21 mmol) and the reaction mixture was stirred for 24 h at 70 °C. A further portion of Grubbs 2nd generation catalyst (0.005 g, 0.006 mmol) and 1-octene (0.096 mL, 0.61 mmol) was added and the reaction mixture was stirred at 70 °C for 18 h. A further portion of Grubbs 2nd generation catalyst (0.005 g, 0.006 mmol) and 1-octene (0.096 mL, 0.61 mmol) was added and the reaction mixture was stirred at 70 °C for 18 h. *N*-Phenyl maleimide (0.063 g, 0.36 mmol) was added with hydroquinone (0.005 g, 0.005 mmol). The reaction mixture was stirred for 24 h at 100 °C. The reaction mixture was then cooled and the solvent was evaporated. Flash column chromatography (petroleum ether/diethyl ether, 3:1) gave (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-4-*n*-hexyl-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**19**) (0.048 g, 38%) as a colourless oil. R_f (50% diethyl ether/petroleum ether) 0.63; ν_{max} (neat) 3327 (NH), 2927 (CH), 2856 (CH), 1700 (CO), 1512, 1500, 1387, 1191, 845 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J* 6.8 Hz, 6"-H_3), 1.25–1.50 (8H, m, 2"-H_2, 3"-H_2, 4"-H_2 and 5"-H_2), 1.52–1.63 (1H, m, 7-*H*H), 1.64–1.78 (2H, m, 1"-*H*H and 7-H*H*), 1.81–2.00 (3H, m, 1"-H*H* and 8-H_2), 2.08–2.20 (1H, m, 6-*H*H), 2.25–2.36 (1H, m, 4-H), 2.46–2.56 (1H, m, 6-H*H*), 3.06 (1H, t, *J* 8.5 Hz, 9a-H), 3.27 (1H, dd, *J* 8.5, 6.0 Hz, 3a-H), 3.46 (1H, dd, *J* 8.5, 6.0 Hz, 9b-H), 4.58–4.69 (1H, m, 9-H), 5.61–5.66 (1H, m, 5-H), 7.13–7.19 (2H, m, 2 × ArH), 7.37–7.43 (1H, m, ArH), 7.44–7.51 (2H, m, 2 × ArH), 8.40 (1H, d, *J* 9.4 Hz, NH); δ_C (126 MHz, $CDCl_3$) 13.1 (CH_3), 20.9 (CH_2), 21.6 (CH_2), 27.2 (CH_2), 28.0 (CH_2), 28.2 (CH_2), 28.7 (CH_2), 29.8 (CH_2), 30.8 (CH_2), 36.1 (CH), 36.7 (CH), 41.1 (CH), 43.4 (CH), 47.2 (CH), 91.9 (C), 125.4 (2 × CH), 127.4 (CH), 127.9 (CH), 128.2 (2 × CH), 130.5 (C), 136.9 (C), 160.7 (C), 175.3 (C), 178.2 (C); HRMS (ESI): $[M-H]^-$, found 523.1319. $C_{26}H_{30}{}^{35}Cl_3N_2O_3$ requires 523.1327.

4.1.14. (3aS,4S*,9R*,9aS*,9bR*)-4-n-Butyl-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1H-benz[e]isoindole-1,3(2H)-dione (**20**).* (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-4-*n*-Butyl-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**20**) was synthesised according to the above procedure using (2*E*)-octa-2-en-7-yn-1-ol (**9**) (0.030 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.020 g, 0.024 mmol) and 1-

hexene (0.30 mL, 2.41 mmol) for 72 h at 70 °C before *N*-phenyl maleimide (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 24 h at 100 °C. Flash column chromatography (petroleum ether/diethyl ether, 3:1) gave (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-4-*n*-butyl-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**20**) (0.045 g, 37%) as a colourless oil. R_f (50% diethyl ether/petroleum ether) 0.59; ν_{max} (neat) 3328 (NH), 2929 (CH), 1698 (CO), 1499, 1387, 1191, 820 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.1 Hz, 4"-H_3), 1.33–1.49 (4H, m, 2"-H_2 and 3"-H_2), 1.51–1.62 (1H, m, 7-*H*H), 1.65–1.77 (2H, m, 1"-*H*H and 7-H*H*), 1.82–2.01 (3H, m, 1"-H*H* and 8-H_2), 2.09–2.19 (1H, m, 6-*H*H), 2.26–2.35 (1H, m, 4-H), 2.48–2.54 (1H, m, 6-H*H*), 3.06 (1H, t, *J* 8.5 Hz, 9a-H), 3.27 (1H, dd, *J* 8.5, 6.0 Hz, 3a-H), 3.45 (1H, dd, *J* 8.5, 6.0 Hz, 9b-H), 4.58–4.69 (1H, m, 9-H), 5.61–5.66 (1H, m, 5-H), 7.13–7.18 (2H, m, 2 × ArH), 7.37–7.42 (1H, m, ArH), 7.43–7.49 (2H, m, 2 × ArH), 8.39 (1H, d, *J* 9.4 Hz, NH); δ_C (126 MHz, $CDCl_3$) 14.0 (CH_3), 21.9 (CH_2), 22.6 (CH_2), 29.0 (CH_2), 29.7 (CH_2), 30.5 (CH_2), 30.6 (CH_2), 37.1 (CH), 37.8 (CH), 42.1 (CH), 44.4 (CH), 48.3 (CH), 92.9 (C), 126.4 (2 × CH), 128.4 (CH), 128.9 (CH), 129.3 (2 × CH), 131.5 (C), 138.0 (C), 161.7 (C), 176.4 (C), 179.2 (C); *m/z* (CI) 497 (MH^+, 31%), 463 (100), 429 (41), 379 (32), 335 (39), 174 (38), 122 (12), 69 (40); HRMS (CI): MH^+, found 497.1167. $C_{24}H_{28}{}^{35}Cl_3N_2O_3$ requires 497.1166.

4.1.15. (3aS,4S*,9R*,9aS*,9bR*)-2,4-Diphenyl-3a,4,6,7,8,9,9a,9b-octahydro-9-(2',2',2'-trichloromethylcarbonylamino)-1H-benz[e]isoindole-1,3(2H)-dione (**21**).* (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-2,4-Diphenyl-3a,4,6,7,8,9,9a,9b-octahydro-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**21**) was synthesised according to the above procedure using (2*E*)-octa-2-en-7-yn-1-ol (**9**) (0.030 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.020 g, 0.024 mmol) and styrene (0.27 mL, 2.41 mmol) for 72 h at 70 °C before *N*-phenyl maleimide (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 24 h at 100 °C. Flash column chromatography (petroleum ether/diethyl ether, 13:7) gave (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-2,4-diphenyl-3a,4,6,7,8,9,9a,9b-octahydro-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**21**) (0.067 g, 54%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.47; Mp 153–155 °C; ν_{max} (neat) 3336 (NH), 2937 (CH), 1698 (CO), 1511, 1499, 1386, 1192, 819 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.61–1.86 (3H, m, 7-H_2 and 8-*H*H), 2.01 (1H, dq, *J* 12.5, 5.6 Hz, 8-H*H*), 2.23–2.34 (1H, m, 6-*H*H), 2.58–2.66 (1H, m, 6-H*H*), 3.21–3.28 (1H, m, 9a-H), 3.53–3.60 (2H, m, 3a-H and 9b-H), 3.70 (1H, br s, 4-H), 4.66–4.76 (1H, m, 9-H), 6.23–6.28 (1H, m, 5-H), 7.11–7.16 (2H, m, 2 × ArH), 7.26–7.46 (8H, m, 8 × ArH), 8.43 (1H, d, *J* 9.4 Hz, NH); δ_C (126 MHz, $CDCl_3$) 21.7 (CH_2), 28.7 (CH_2), 29.9 (CH_2), 38.2 (CH), 41.8 (CH), 41.9 (CH), 47.3 (CH), 48.2 (CH), 92.9 (C), 125.2 (CH), 126.3 (2 × CH), 127.2 (CH), 128.3 (2 × CH), 128.8 (2 × CH), 128.9 (CH), 129.2 (2 × CH), 131.4 (C), 138.6 (C), 139.1 (C), 161.9 (C), 175.0 (C), 178.6 (C); *m/z* (ESI) 539 ($[MNa]^+$, 100%), 413 (10), 383 (8), 301 (6), 236 (3); HRMS (ESI): $[MNa]^+$, found 539.0652. $C_{26}H_{23}{}^{35}Cl_3N_2NaO_3$ requires 539.0666.

4.1.16. (3aS,4S*,9R*,9aS*,9bR*)-4-(4-Fluorophenyl)-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1H-benz[e]isoindole-1,3(2H)-dione (**22**).* (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-4-(4-Fluorophenyl)-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**22**) was synthesised according to the above procedure using (2*E*)-octa-2-en-7-yn-1-ol (**9**) (0.030 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.020 g, 0.024 mmol) and 4-fluorostyrene (0.29 mL, 2.41 mmol) for 72 h at 70 °C before *N*-phenyl maleimide (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 48 h at 100 °C. Flash column chromatography (petroleum ether/diethyl ether, 5:2) gave (3a*S**,4*S**,9*R**,9a*S**,9b*R**)-4-(4-fluorophenyl)-3a,4,6,7,8,9,9a,9b-octahydro-2-phenyl-9-(2',2',2'-trichloromethylcarbonylamino)-1*H*-benz[*e*]isoindole-1,3(2*H*)-dione (**22**) (0.065 g, 50%) as a white solid. R_f (50% diethyl ether/petroleum ether) 0.35; Mp 144–146 °C; ν_{max} (neat) 3324 (NH), 2927 (CH), 1699 (CO), 1510, 1386, 1264, 1188, 820 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.61–1.86 (3H, m, 7-H_2 and 8-*H*H), 2.02 (1H, dq, *J* 11.8, 5.4 Hz, 8-H*H*), 2.22–2.33 (1H, m, 6-*H*H), 2.58–2.66 (1H, m, 6-H*H*), 3.24 (1H, t, *J* 6.8 Hz, 9a-H), 3.51 (1H, dd, *J* 8.5, 5.7 Hz, 3a-H), 3.57 (1H, dd, *J* 8.5, 6.8 Hz, 9b-H), 3.68 (1H, br s, 4-H), 4.65–4.76 (1H, m, 9-H), 6.15–6.21 (1H, m, 5-H), 7.02–7.08 (2H, m, 2 × ArH), 7.11–7.15 (2H, m, 2 × ArH), 7.29–7.47 (5H, m, 5 × ArH), 8.41 (1H, d, *J* 9.7 Hz, NH); δ_C (126 MHz, $CDCl_3$) 21.7 (CH_2), 28.6 (CH_2), 29.8 (CH_2), 38.2 (CH), 41.2 (CH), 41.8 (CH), 47.3 (CH), 48.2 (CH), 92.9 (C), 115.2 (d, $J_{C\text{-}C\text{-}F}$ 21.4 Hz, 2 × CH), 125.1 (CH), 126.3 (2 × CH), 129.0 (CH), 129.3 (2 × CH), 130.3 (d, $J_{C\text{-}C\text{-}C\text{-}F}$ 8.0 Hz, 2 × CH), 131.3 (C), 134.3 (C), 139.4 (C), 161.9 (C), 162.0 (d, $J_{C\text{-}F}$ 245.9 Hz, C), 175.1 (C), 178.5 (C); *m/z* (ESI) 557 ($[MNa]^+$, 100%), 413 (23), 345 (8), 242 (34), 142 (3); HRMS (ESI): $[MNa]^+$, found 557.0586. $C_{26}H_{22}{}^{35}Cl_3FN_2NaO_3$ requires 557.0572.

4.1.17. (1R,6R*,8aR*)-1,2,3,4,6,7,8,8a-Octahydro-6-phenyl-7,7,8,8-tetracyano-1-(2',2',2'-trichloromethylcarbonylamino)naphthalene (**23**).* (1*R**,6*R**,8a*R**)-1,2,3,4,6,7,8,8a-Octahydro-6-phenyl-7,7,8,8-tetracyano-1-(2',2',2'-trichloromethylcarbonylamino)naphthalene (**23**) was synthesised according to the above procedure using (2*E*)-octa-2-en-7-yn-1-ol (**9**) (0.030 g, 0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.020 g, 0.024 mmol) and styrene (0.27 mL, 2.41 mmol) for 72 h at 70 °C before tetracyanoethylene (0.046 g, 0.36 mmol) was added. The reaction mixture was stirred for 24 h at 50 °C. Flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave (1*R**,6*R**,8a*R**)-1,2,3,4,6,7,8,8a-octahydro-6-phenyl-7,7,8,8-tetracyano-1-(2',2',2'-trichloromethylcarbonylamino)naphthalene (**23**) (0.050 g, 44%) as a colourless oil. R_f (50% diethyl ether/petroleum ether) 0.68; ν_{max} (neat) 3332 (NH), 2946 (CH), 2254 (CN), 1696 (CO), 1513, 1455, 1275, 1082, 820 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.57–1.70 (1H, m, 3-*H*H), 1.95–2.10 (2H, m, 2-*H*H and 3-H*H*), 2.21–2.35 (2H, m, 2-H*H* and 4-*H*H), 2.63 (1H, br d, *J* 13.2 Hz, 4-H*H*), 3.68 (1H, d, *J* 11.3 Hz, 8a-H), 4.21–4.31 (1H, m, 1-H), 4.32–4.37 (1H, m, 6-H), 5.85–5.90 (1H, m, 5-H), 7.10–7.18 (1H, m, NH), 7.44–7.49 (5H, m, 5 × ArH); δ_C (126 MHz, $CDCl_3$) 24.2 (CH_2), 32.1 (CH_2), 35.2 (CH_2), 40.3 (C), 44.3 (C), 46.2 (CH), 46.4 (CH), 54.6 (CH), 92.0 (C), 108.8 (C), 110.2 (C), 111.5 (C), 112.4 (C), 119.8 (CH), 129.0 (2 × CH), 130.5 (CH), 130.7 (2 × CH), 131.3 (C), 136.1 (C), 161.8 (C); *m/z* (ESI) 470 ($[M-H]^-$, 100%), 352 (21), 309 (20), 282 (15), 257 (8), 212 (4); HRMS (ESI): $[M-H]^-$, found 470.0332. $C_{22}H_{15}{}^{35}Cl_3N_5O$ requires 470.0348.

4.1.18. (5S,10R*,10aS*)-5-n-Decyl-5,7,8,9,10,10a-hexahydro-10-(2',2',2'-trichloromethylcarbonylamino)-1H-[2,4,11]-triazolo[1,2-a]cinnoline-1,3(2H)-dione (**24**).* (5*S**,10*R**,10a*S**)-5-*n*-Decyl-5,7,8,9,10,10a-hexahydro-10-(2',2',2'-trichloromethylcarbonylamino)-1*H*-[2,4,11]-triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (**24**) was synthesised according to the above procedure using (2*E*)-octa-2-en-7-yn-1-ol (**9**) (0.030 g,

0.24 mmol). The reaction mixture was stirred with Grubbs 2nd generation catalyst (0.020 g, 0.024 mmol) and 1-dodecene (0.54 mL, 2.41 mmol) for 72 h at 75 °C before *N*-phenyl-1,2,4-triazoline-3,5-dione (0.063 g, 0.36 mmol) was added. The reaction mixture was stirred for 24 h at 100 °C. Flash column chromatography (petroleum ether/ethyl acetate, 7:3) gave (5*S**,10*R**,10a*S**)-5-*n*-decyl-5,7,8,9,10,10a-hexahydro-10-(2',2',2'-trichloromethylcarbonylamino)-1*H*-[2,4,11]-triazolo[1,2-*a*]cinnoline-1,3(2*H*)-dione (**24**) (0.055 g, 39%) as a colourless oil. R_f (50% diethyl ether/petroleum ether) 0.49; ν_{max} (neat) 3415 (NH), 2923 (CH), 1709 (CO), 1503, 1416, 1141, 818 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.0 Hz, 10"-H_3), 1.15–1.59 (17H, m, 8-*H*H, 2"-H_2, 3"-H_2, 4"-H_2, 5"-H_2, 6"-H_2, 7"-H_2, 8"-H_2 and 9"-H_2), 1.77–1.91 (3H, m, 8-H*H*, 9-*H*H and 1"-*H*H), 2.14–2.28 (3H, m, 7-*H*H, 9-H*H* and 1"-H*H*), 2.49–2.57 (1H, m, 7-H*H*), 4.31–4.38 (1H, m, 5-H), 4.49 (1H, br s, 10a-H), 5.11–5.18 (1H, m, 10-H), 5.88–5.93 (1H, m, 6-H), 6.79 (1H, d, *J* 8.1 Hz, NH), 7.33–7.39 (1H, m, ArH), 7.44–7.53 (4H, m, 4 × ArH); δ_C (126 MHz, $CDCl_3$) 14.1 (CH_3), 21.6 (CH_2), 22.7 (CH_2), 25.2 (CH_2), 28.0 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 31.9 (CH_2), 33.2 (CH_2), 33.5 (CH_2), 50.0 (CH), 54.4 (CH), 57.5 (CH), 92.8 (C), 122.7 (CH), 125.8 (2 × CH), 128.2 (CH), 128.3 (C), 129.1 (2 × CH), 131.1 (C), 151.6 (C), 151.9 (C), 161.2 (C); *m/z* (ESI) 605 ($[MNa]^+$, 100%), 413 (9), 301 (4), 236 (5); HRMS (ESI): $[MNa]^+$, found 605.1796. $C_{28}H_{37}{}^{35}Cl_3N_4NaO_3$ requires 605.1823.

*4.1.19. 5-Phenylpent-4-yn-1-ol (**25**).*[25] Bis(triphenylphosphine)palladium(II) dichloride (0.022 g, 0.0312 mmol) and copper iodide (0.012 g, 0.062 mmol) were dissolved in triethylamine (43 mL) and iodobenzene (0.42 mL, 3.75 mmol) was added and stirred at room temperature for 0.1 h. 4-Pentyn-1-ol (0.26 g, 3.12 mmol) (**4**) was added and the reaction mixture was stirred at room temperature for 48 h. The reaction mixture was concentrated *in vacuo* and flash column chromatography (petroleum ether/ethyl acetate, 3:1) gave 5-phenylpent-4-yn-1-ol (**25**) (0.49 g, 98%) as a colourless oil. The spectroscopic data was as reported in the literature.[25] R_f (50% petroleum ether/ethyl acetate) 0.43; δ_H (500 MHz, $CDCl_3$) 1.63 (1H, s, OH), 1.85 (2H, quin, *J* 6.5 Hz, 2-H_2), 2.53 (2H, t, *J* 6.5 Hz, 3-H_2), 3.81 (2H, t, *J* 6.5 Hz, 1-H_2), 7.24–7.29 (3H, m, 3 × ArH), 7.36–7.40 (2H, m, 2 × ArH); δ_C (126 MHz, $CDCl_3$) 16.0 (CH_2), 31.4 (CH_2), 61.8 (CH_2), 81.2 (C), 89.3 (C), 123.7 (C), 127.7 (CH), 128.2 (2 × CH), 131.6 (2 × CH); *m/z* (EI) 160 (M^+. 39%), 141 (100), 128 (38), 115 (71), 104 (32), 85 (35).

*4.1.20. Ethyl (2E)-7-phenylhept-2-en-6-ynoate (**26**).*[26] The reaction was carried out as described for the synthesis of ethyl (2*E*)-hept-2-en-6-ynoate (**6**) using 5-phenylpent-4-yn-1-ol (**26**) (1.62 g, 10.1 mmol). Purification by flash column chromatography (diethyl ether/petroleum ether, 3:17) gave ethyl (2*E*)-7-phenylhept-2-en-6-ynoate (**26**) (1.97 g, 86%) as a yellow oil. The spectroscopic data was as reported in the literature.[26] R_f (50% petroleum ether/diethyl ether) 0.66; δ_H (500 MHz, $CDCl_3$) 1.30 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.48–2.55 (4H, m, 4-H_2 and 5-H_2), 4.20 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.93 (1H, dt, *J* 15.7, 1.5 Hz, 2-H), 7.04 (1H, dt, *J* 15.7, 6.6 Hz, 3-H), 7.26–7.31 (3H, m, 3 × ArH), 7.36–7.41 (2H, m, 2 × ArH); δ_C (126 MHz, $CDCl_3$) 14.3 (CH_3), 18.4 (CH_2), 31.4 (CH_2), 60.3 (CH_2), 81.6 (C), 88.3 (C), 122.5 (CH), 123.6 (C), 127.8 (CH), 128.2 (2 × CH), 131.6 (2 × CH), 146.7 (CH), 166.5 (C); HRMS (ESI): $[MNa]^+$, found 251.1040. $C_{15}H_{16}NaO_2$ requires 251.1043.

*4.1.21. (2E)-7-Phenylhept-2-en-6-yn-1-ol (**27**).*[27] The reaction was carried out as described for the synthesis of (2*E*)-hept-2-en-6-yn-1-ol (**8**) using ethyl (2*E*)-7-phenylhept-2-en-6-ynoate (**26**) (1.97 g, 8.64 mmol). Purification by flash column chromatography (ethyl acetate/petroleum ether, 7:13) gave (2*E*)-7-phenylhept-2-en-6-yn-1-ol (**27**) (1.30 g, 81%) as a colourless oil. R_f (50% petroleum ether/diethyl ether) 0.43; ν_{max} (neat) 3329 (OH), 2918 (CH), 2324, 2110, 1597, 1489, 1441, 1084, 966 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.36 (1H, br s, OH), 2.36 (2H, dt, *J* 7.2, 6.8 Hz, 4-H_2), 2.50 (2H, t, *J* 6.8 Hz, 5-H_2), 4.13 (2H, t, *J* 4.5 Hz, 1-H_2), 5.72–5.85 (2H, m, 2-H and 3-H), 7.25–7.31 (3H, m, 3 × ArH), 7.36–7.42 (2H, m, 2 × ArH); δ_C (126 MHz, $CDCl_3$) 19.5 (CH_2), 31.5 (CH_2), 63.6 (CH_2), 81.2 (C), 89.4 (C), 123.8 (C), 127.6 (CH), 128.2 (2 × CH), 130.4 (CH), 131.0 (CH), 131.6 (2 × CH); *m/z* (CI) 169 (MH^+-H_2O, 100%), 143 (14), 123 (46), 105 (17), 91 (6); HMRS (CI): MH^+-H_2O, found 169.1018. $C_{13}H_{13}$ requires 169.1017.

4.1.22. (3aS,8R*,8aS*,8bR*)-2,5-Diphenyl-4,6,7,8,8a,8b-hexahydro-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[e]isoindole-1,3(2H,3aH)-dione (**30**).* (2*E*)-7-Phenylhept-2-en-6-yn-1-ol (**27**) (0.075 g, 0.40 mmol) was dissolved in dichloromethane (10 mL) and cooled to 0 °C. To the solution 1,8-diazabicyclo[5.4.0]undec-7-ene (0.011 mL, 0.008 mmol) and trichloroacetonitrile (0.062 mL, 0.60 mmol) were added. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The reaction mixture was filtered through a short pad of silica gel with diethyl ether (300 mL) and the filtrate concentrated *in vacuo* to give the allylic trichloroacetimidate, which was used without further purification. The allylic trichloroacetimidate was dissolved in toluene (10 mL) and bis(acetonitrile)palladium chloride (0.011 g, 0.040 mmol) was then added and the reaction mixture was stirred at room temperature for 18 h. Grubbs 2nd generation catalyst (0.024 g, 0.028 mmol) was added with 1,7-octadiene (0.24 mL, 1.60 mmol) and the reaction mixture was stirred for 18 h at 90 °C. *N*-Phenyl maleimide (0.104 g, 0.60 mmol) was added with hydroquinone (0.005 g, 0.005 mmol). The reaction mixture was stirred for 18 h at 75 °C. The reaction mixture was then cooled and the solvent was evaporated. Flash column chromatography (petroleum ether/ethyl acetate, 1:1) gave (3a*S**,8*R**,8a*S**,8b*R**)-2,5-diphenyl-4,6,7,8,8a,8b-hexahydro-8-(2',2',2'-trichloromethylcarbonylamino)cyclopent[*e*]isoindole-1,3(2*H*,3a*H*)-dione (**30**) (0.099 g, 49%) as a yellow solid. R_f (50% petroleum ether/ethyl acetate) 0.76; Mp 151–153 °C; ν_{max} (neat) 3358 (NH), 2936 (CH), 1695 (CO), 1517, 1498, 1387, 1154, 822 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.75 (1H, dq, *J* 12.3, 10.2 Hz, 7-*H*H), 2.10–2.20 (1H, m, 7-H*H*), 2.53–2.66 (3H, m, 4-*H*H and 6-H_2), 3.12 (1H, dd, *J* 9.1, 5.8 Hz, 8a-H), 3.30 (1H, dd, *J* 15.2, 1.4 Hz, 4-H*H*), 3.46–3.56 (2H, m, 3a-H and 8b-H), 4.88–5.01 (1H, m, 8-H), 7.06–7.10 (2H, m, 2 × ArH), 7.23–7.47 (8H, m, 8 × ArH), 8.96 (1H, d, *J* 9.6 Hz, NH); δ_C (126 MHz, $CDCl_3$) 28.4 (CH_2), 29.9 (CH_2), 31.6 (CH_2), 40.3 (CH), 41.7 (CH), 43.7 (CH), 52.8 (CH), 92.9 (C), 126.5 (2 × CH), 127.2 (CH), 127.5 (2 × CH), 128.5 (2 × CH), 129.2 (CH), 129.4 (2 × CH), 130.3 (C), 131.4 (C), 139.0 (C), 139.6 (C), 162.3 (C), 178.5 (C), 179.7 (C); *m/z* (ESI) 525 ($[MNa]^+$, 100%), 481 (18), 454 (7), 413 (7), 345 (24), 323 (21), 297 (9), 236 (11), 218 (7), 196 (6); HRMS (ESI): $[MNa]^+$, found 525.0497. $C_{25}H_{21}{}^{35}Cl_3N_2NaO_3$ requires 525.0510.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.XXXXX.

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Supporting Information for:

Diastereoselective synthesis of highly substituted polycyclic scaffolds via a one-pot four-step tandem catalytic process

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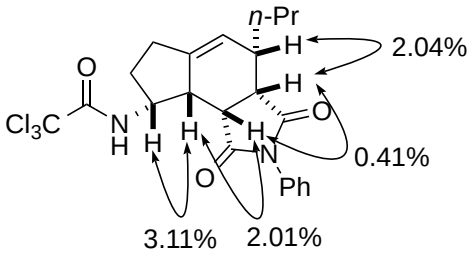
Table of Contents

1. Key NOE enhancements for compounds 13–24 and 30.



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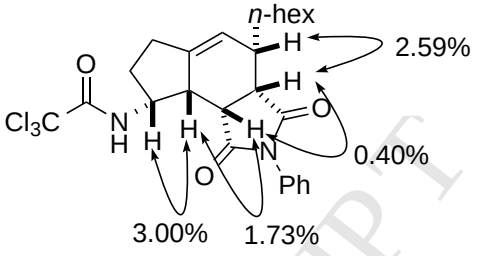

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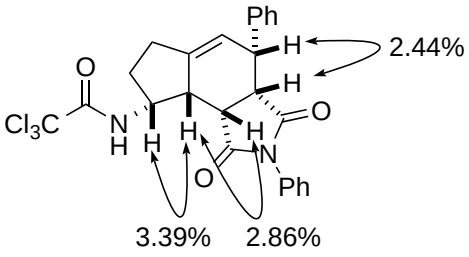

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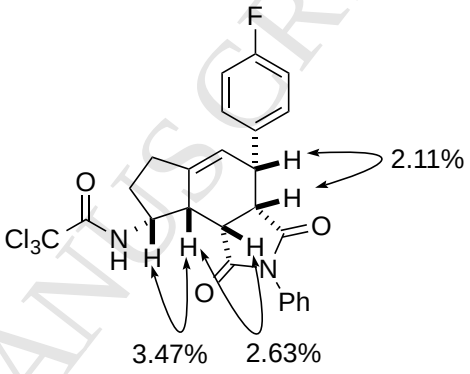

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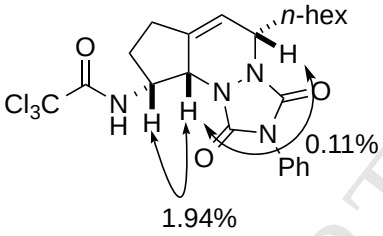

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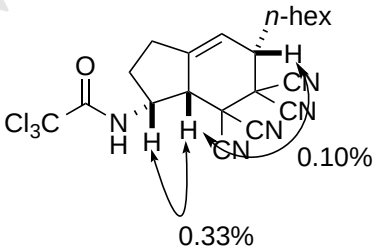

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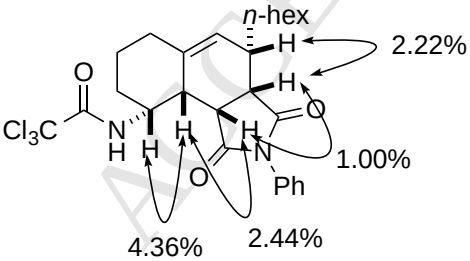

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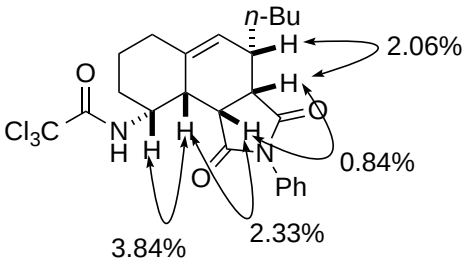

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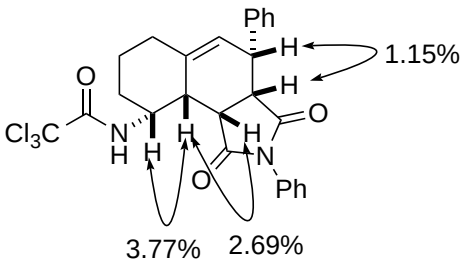

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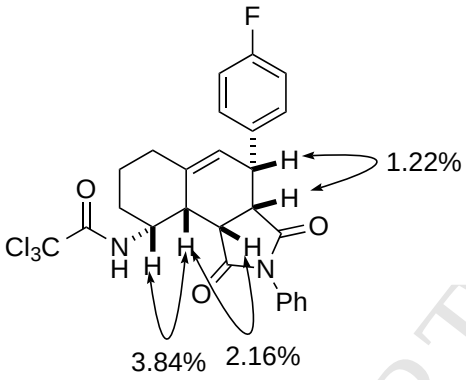

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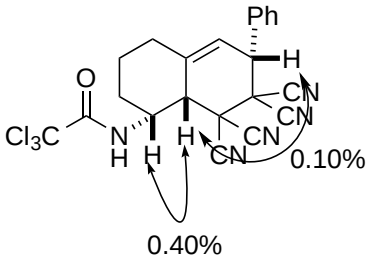

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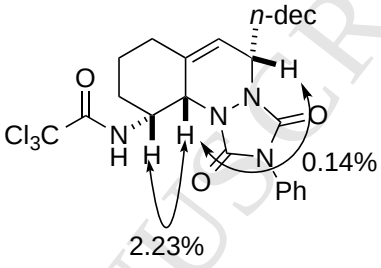

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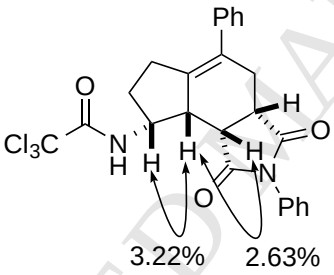

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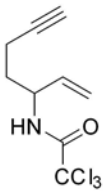

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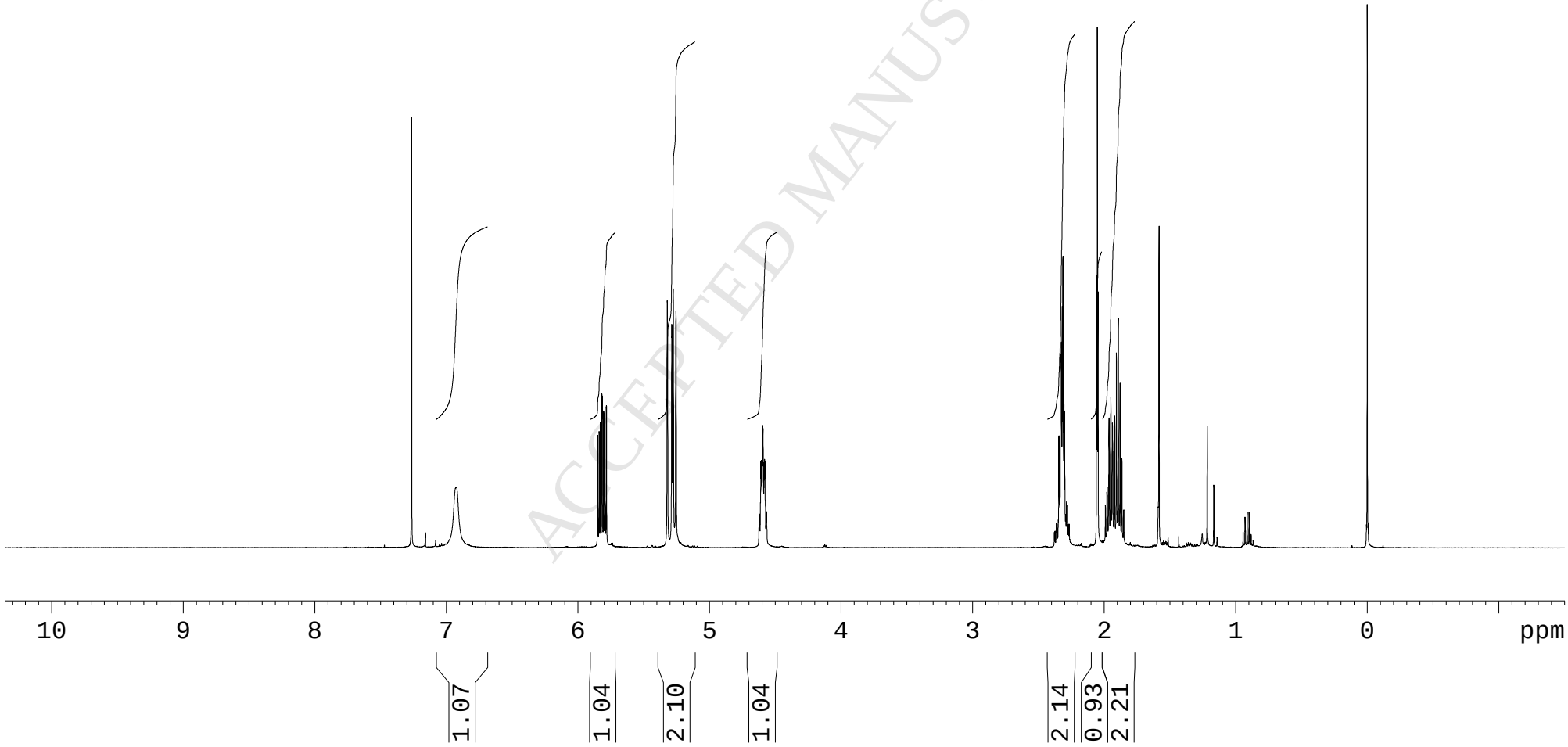

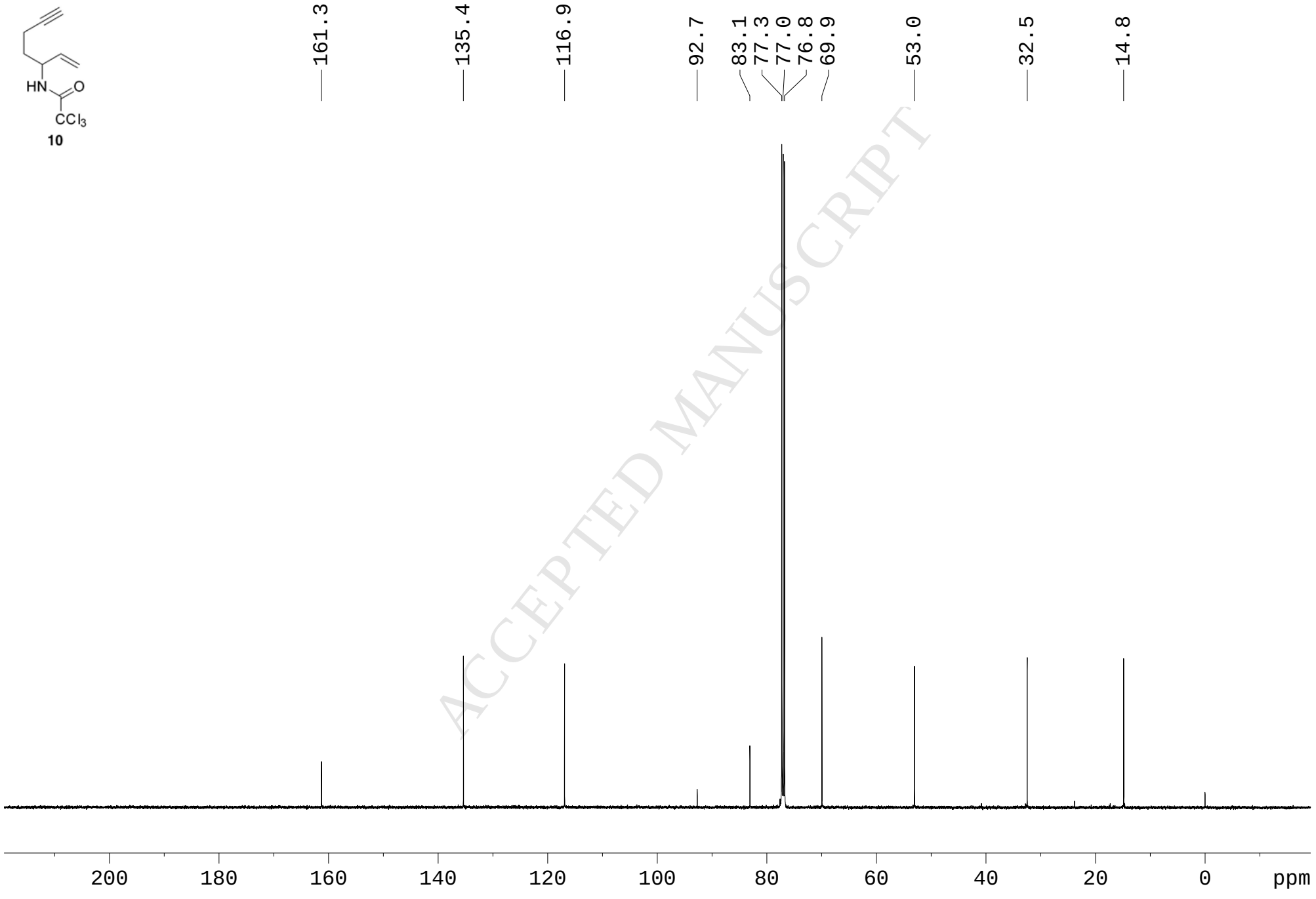

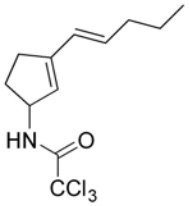

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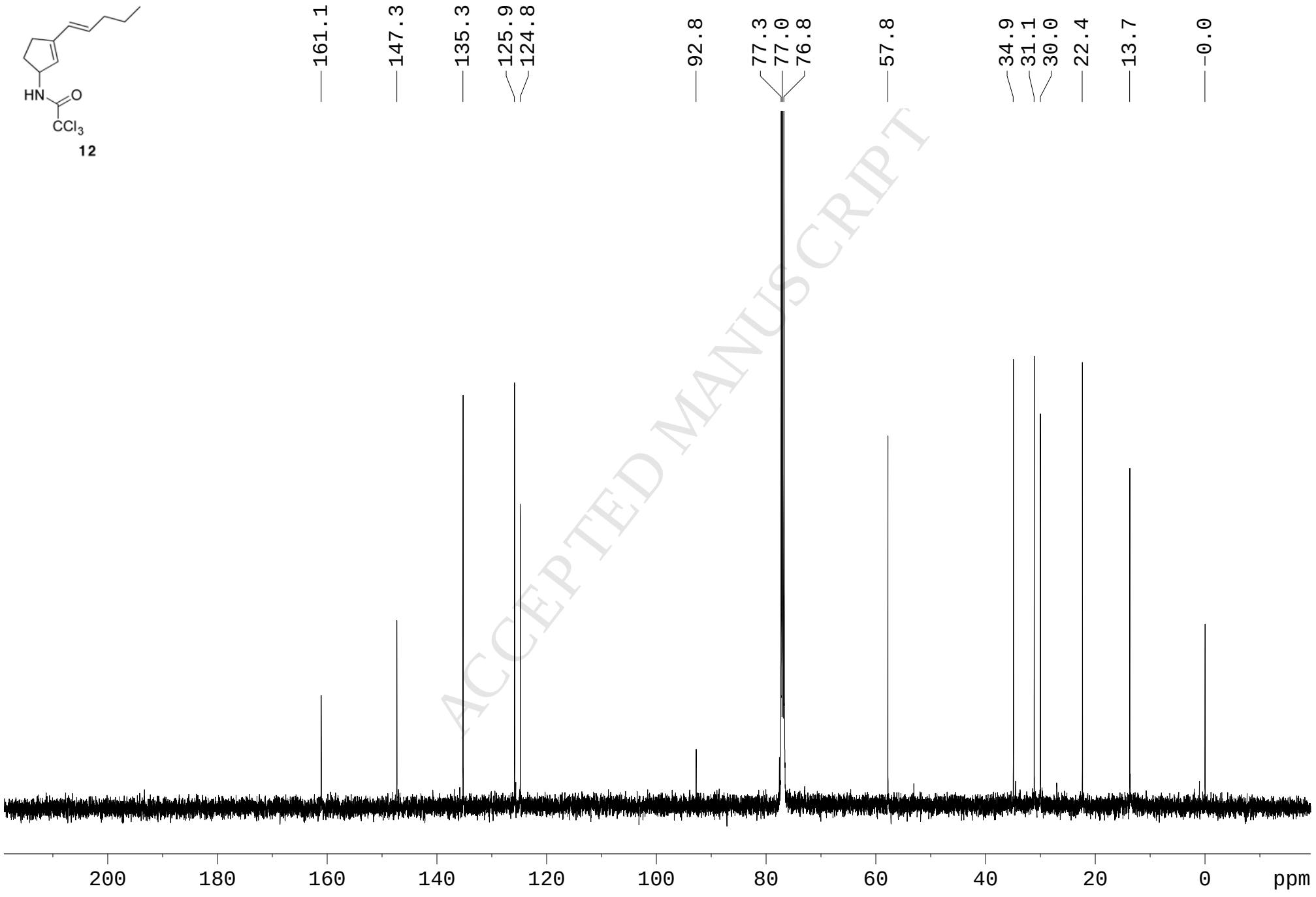

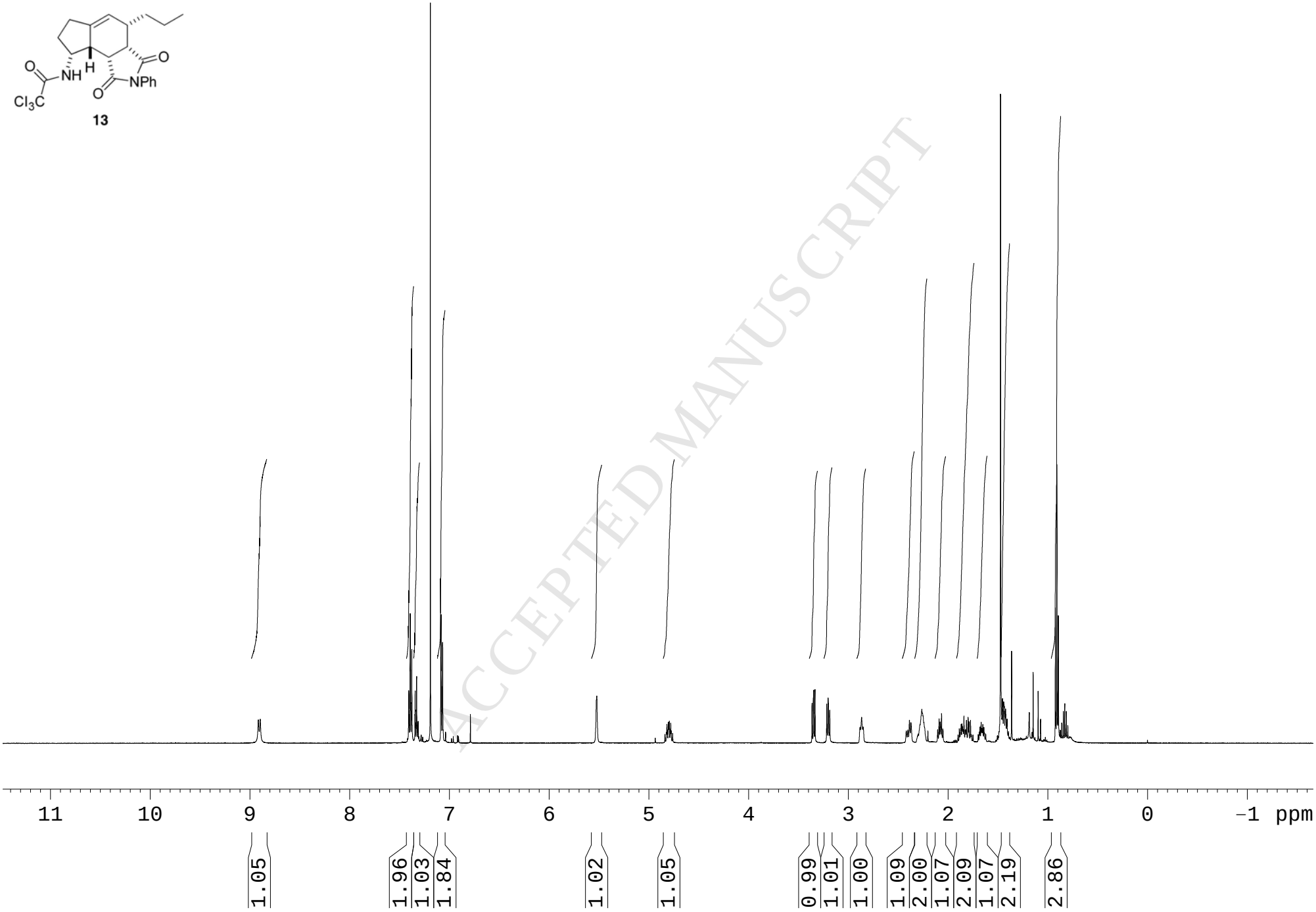

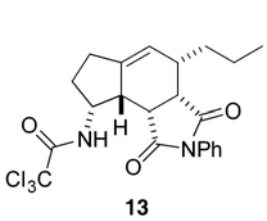

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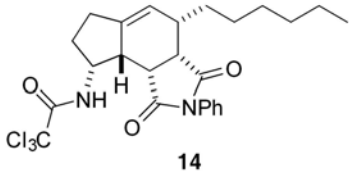

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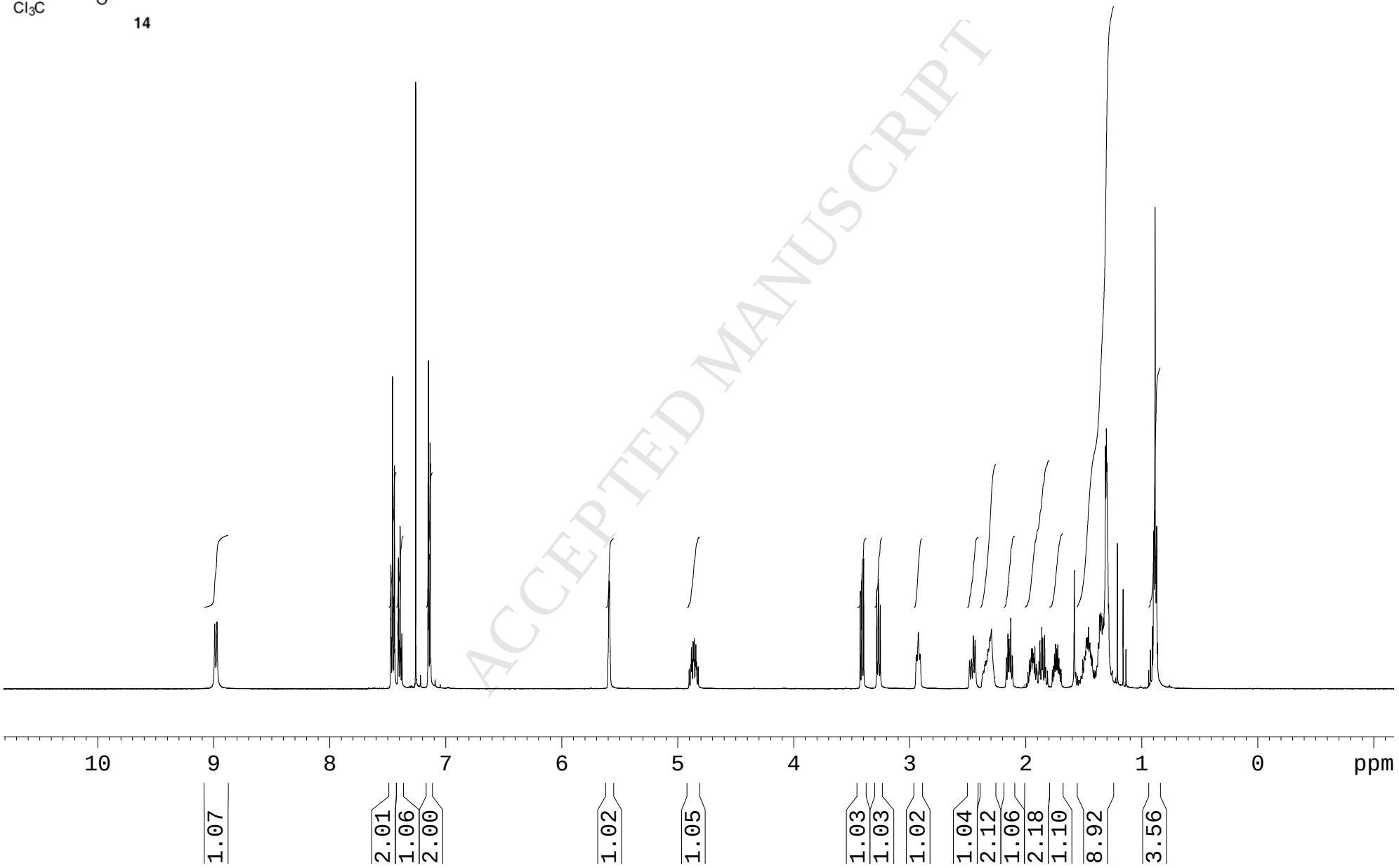

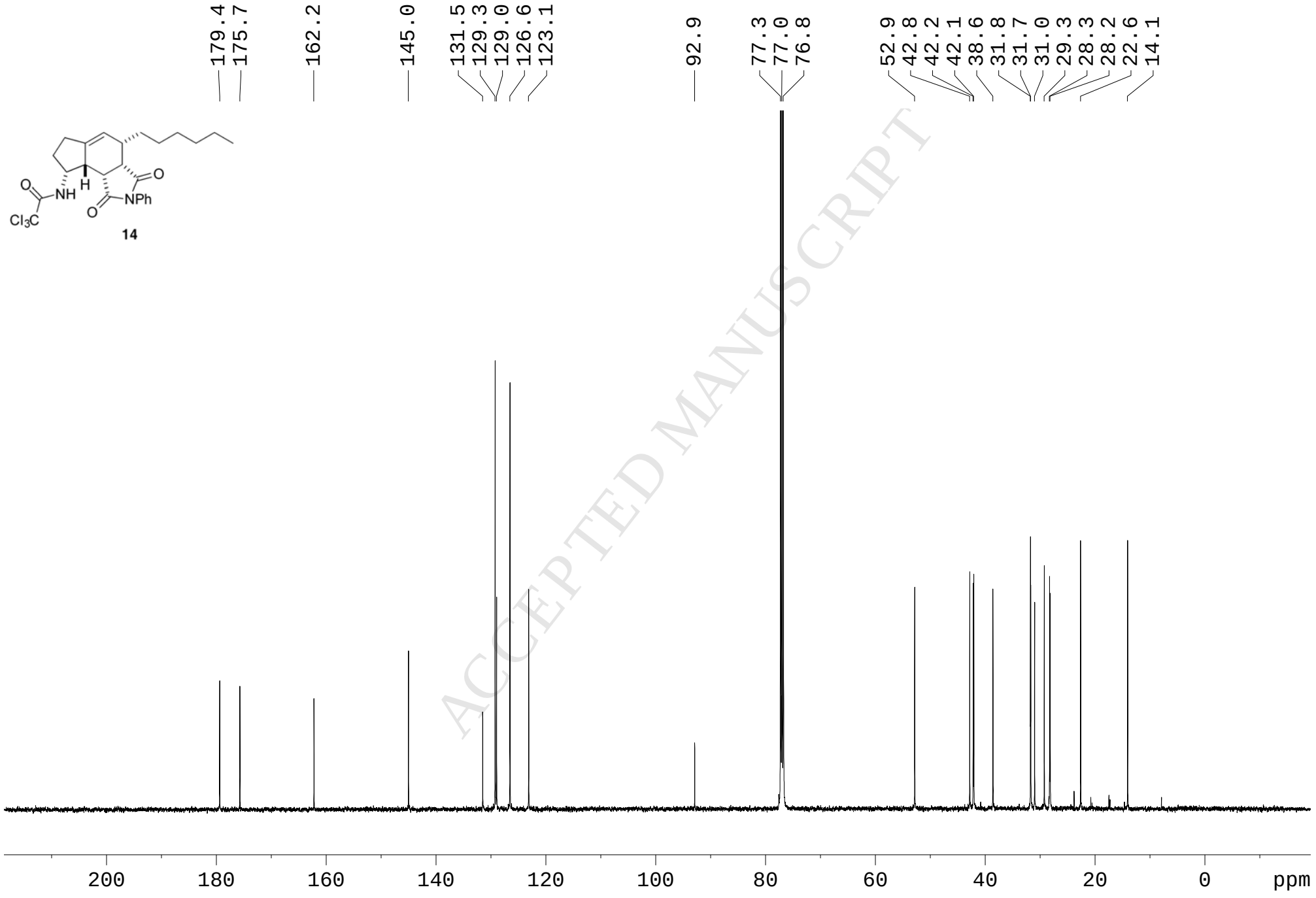

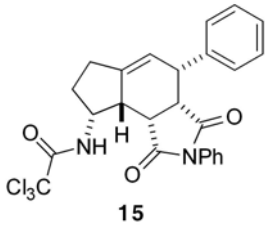

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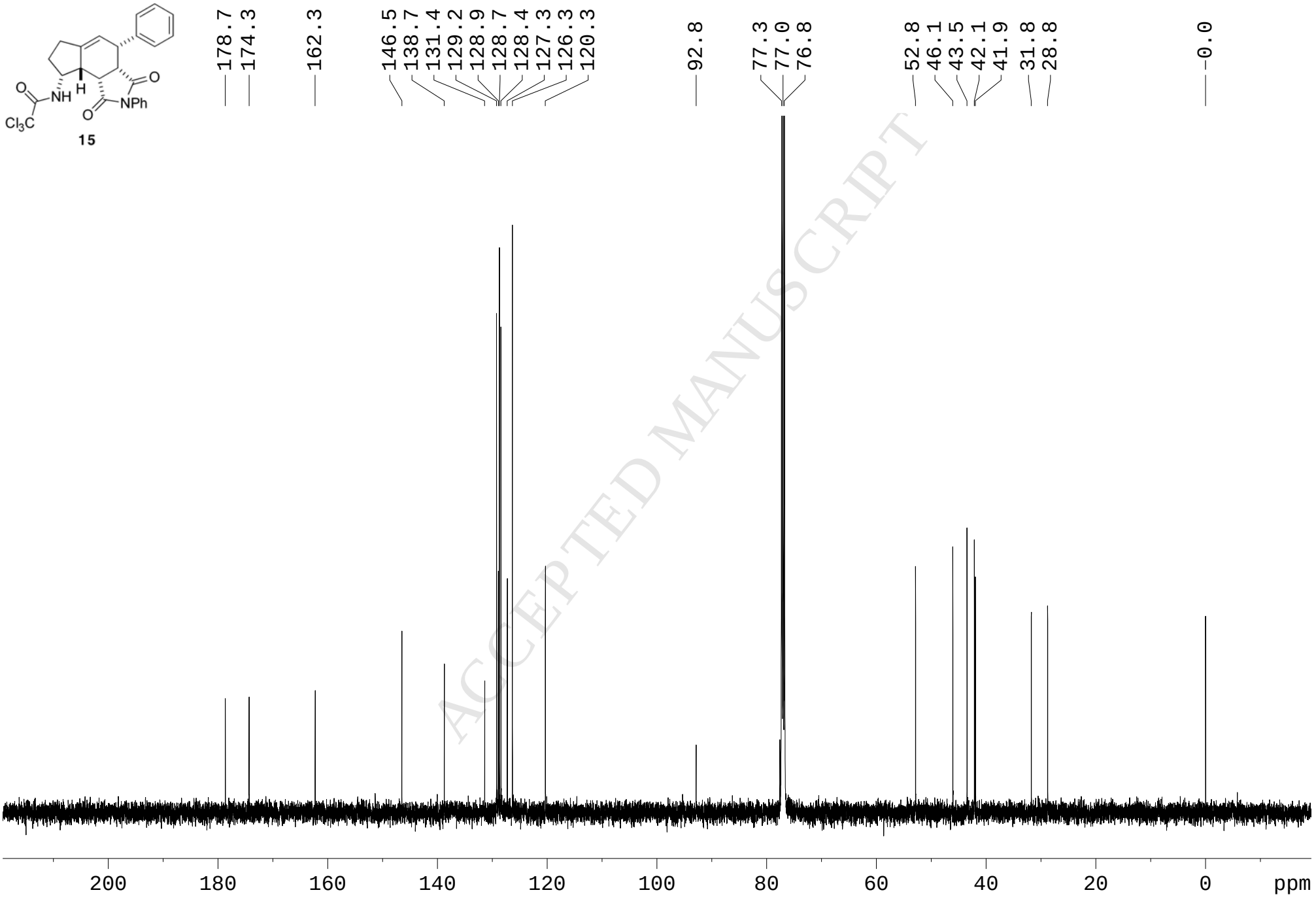

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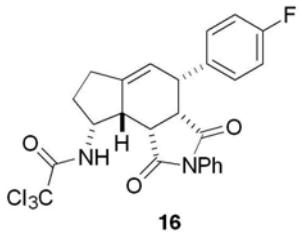

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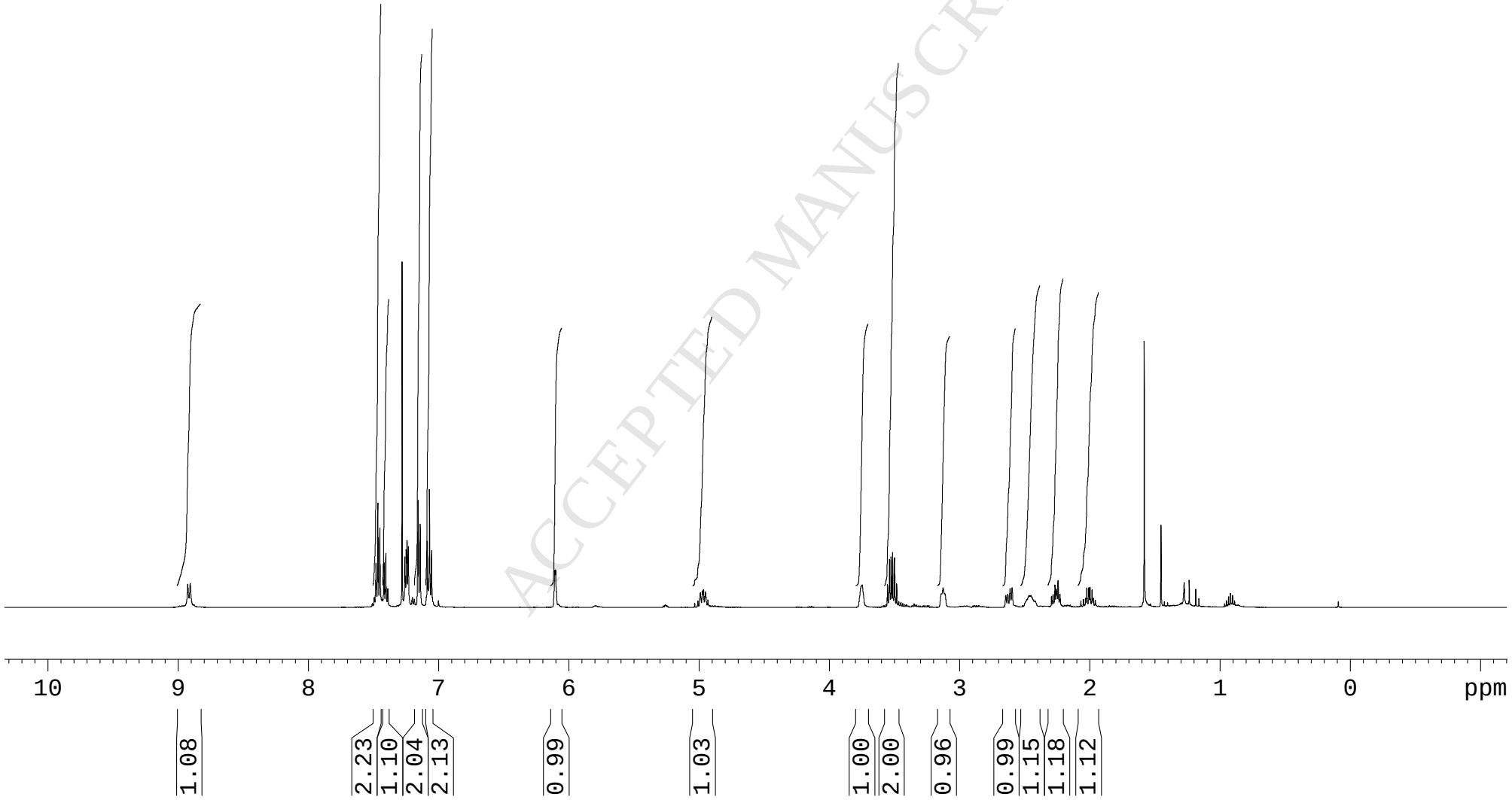

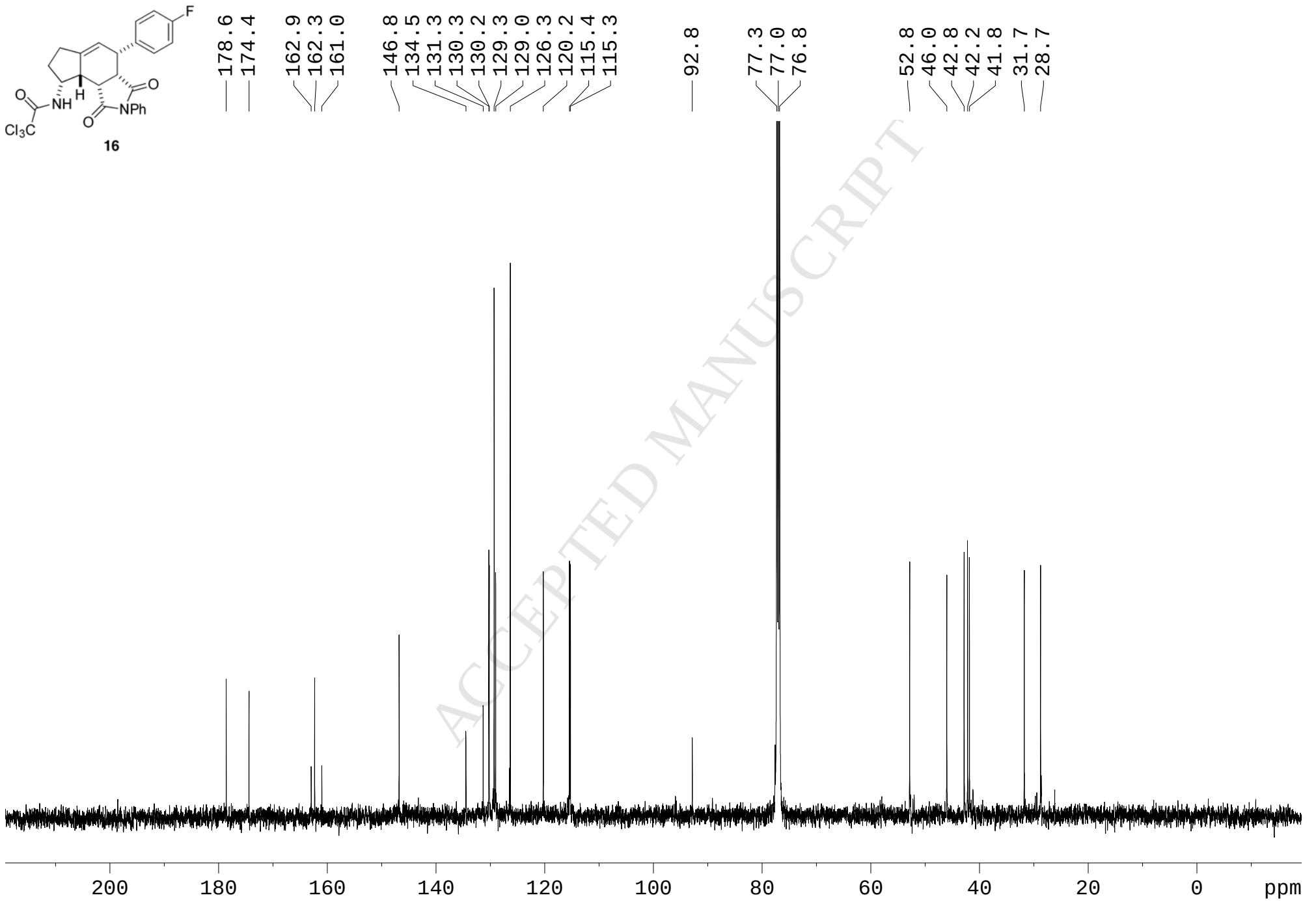

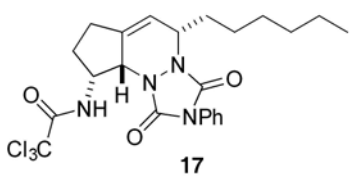

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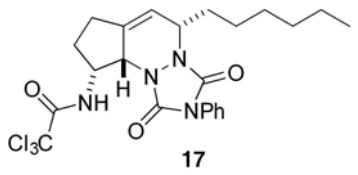

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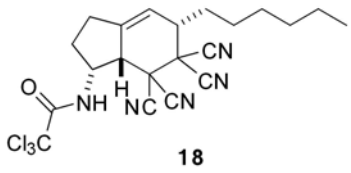

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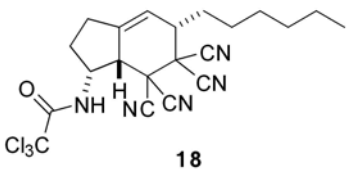

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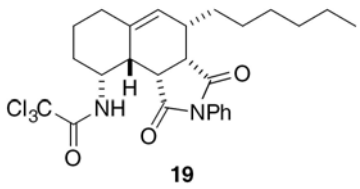

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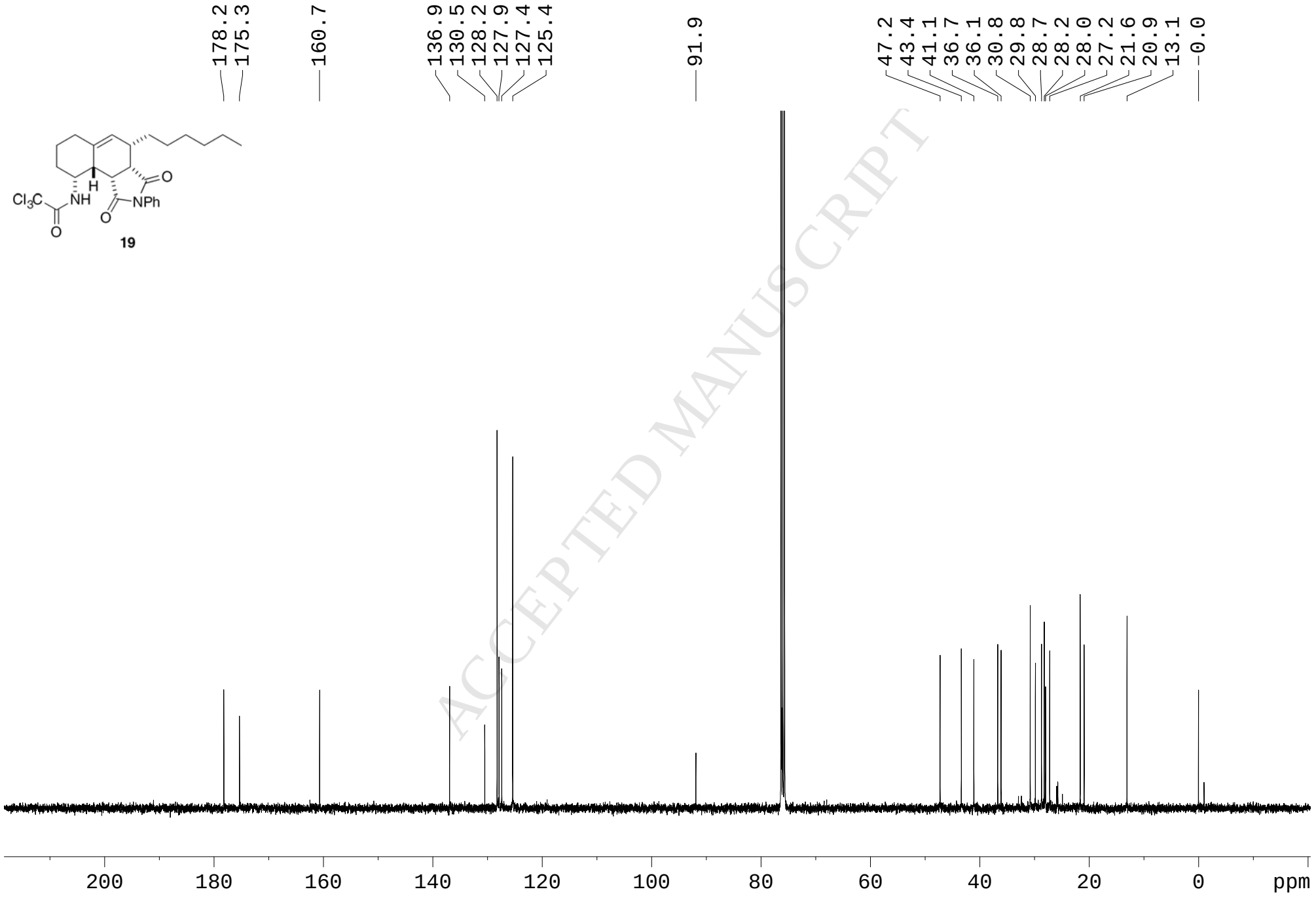

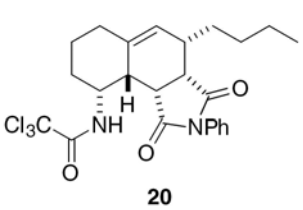

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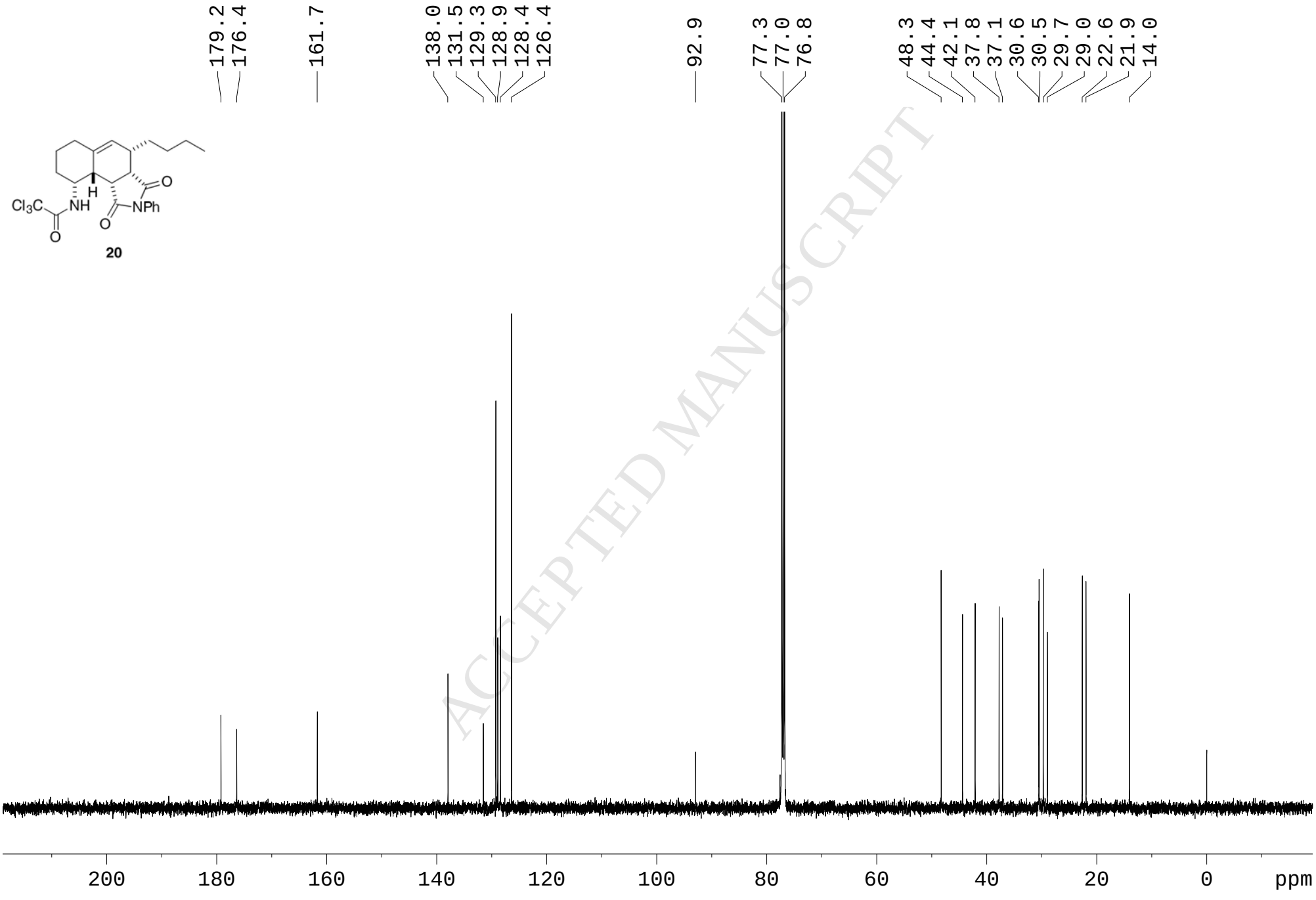

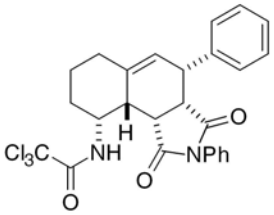

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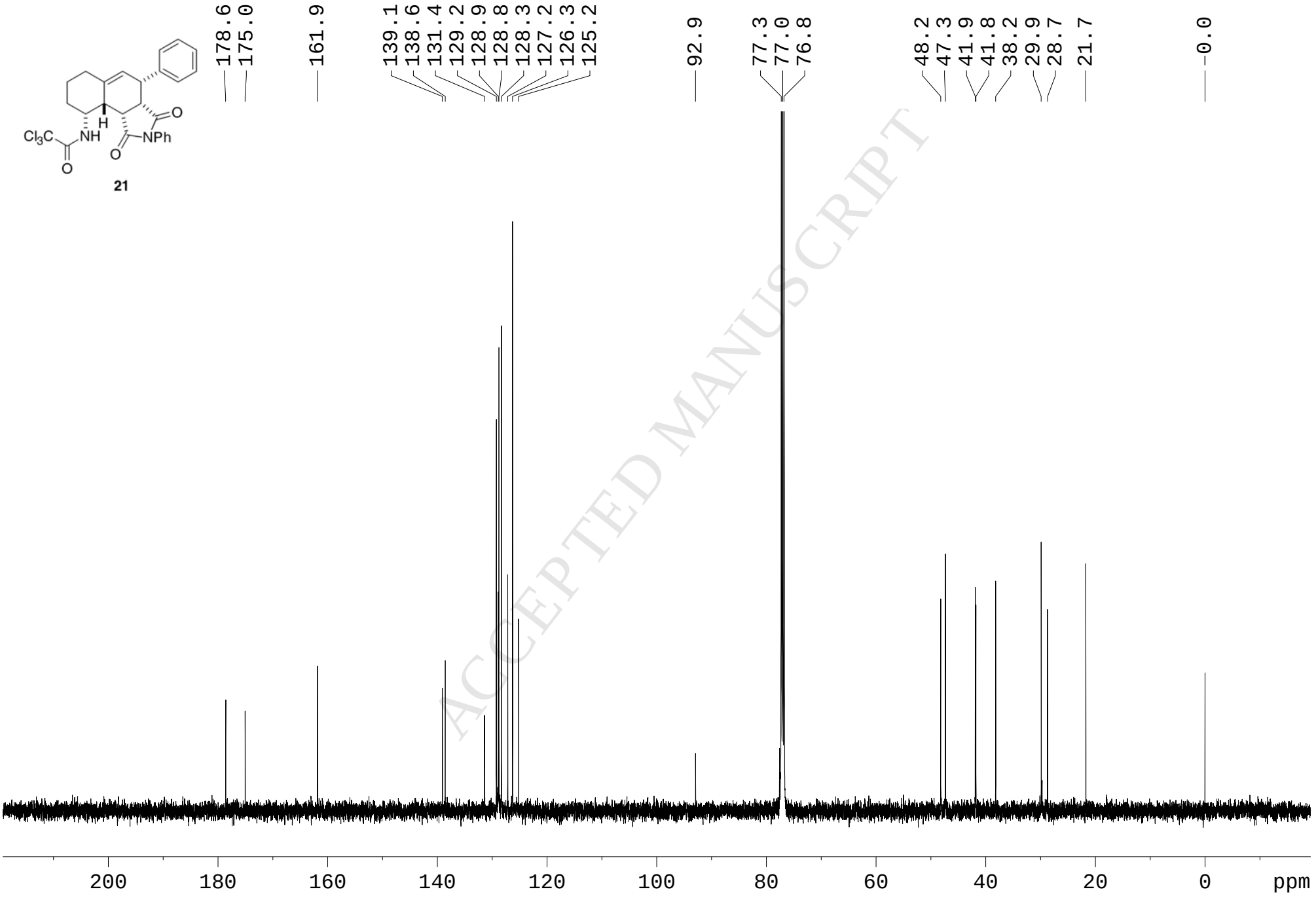

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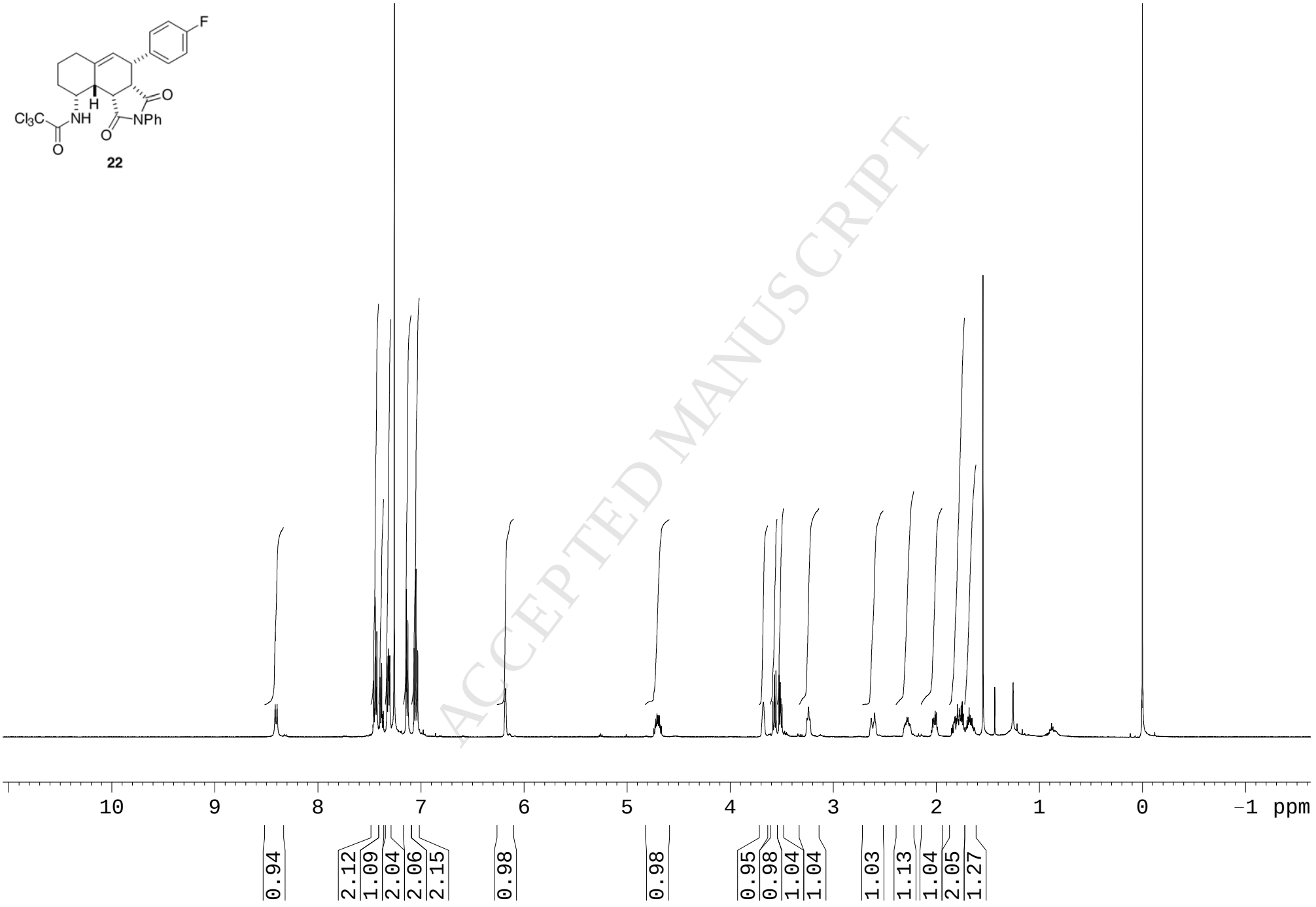

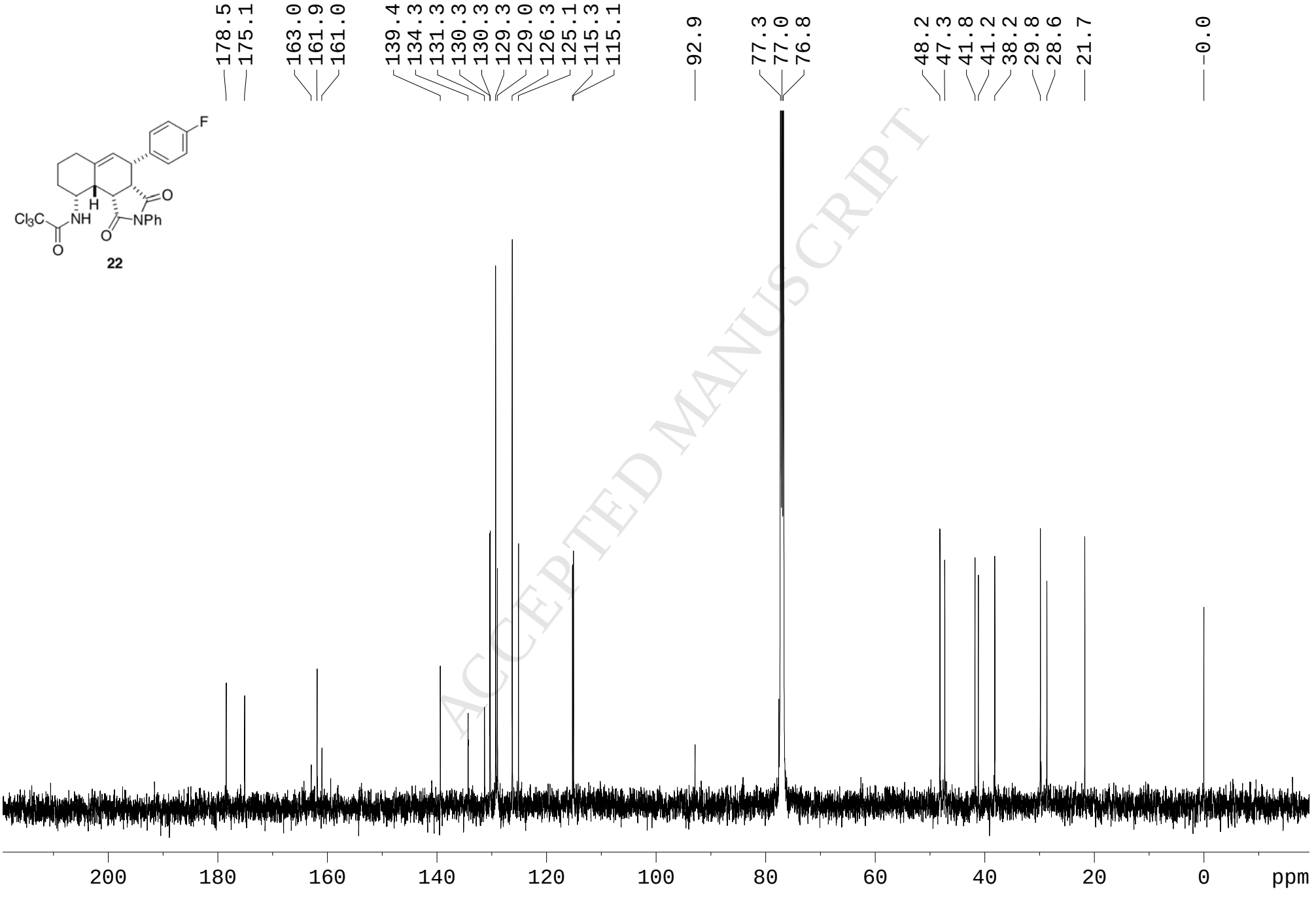

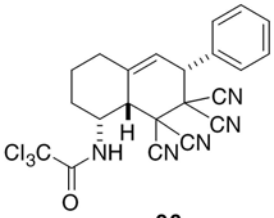

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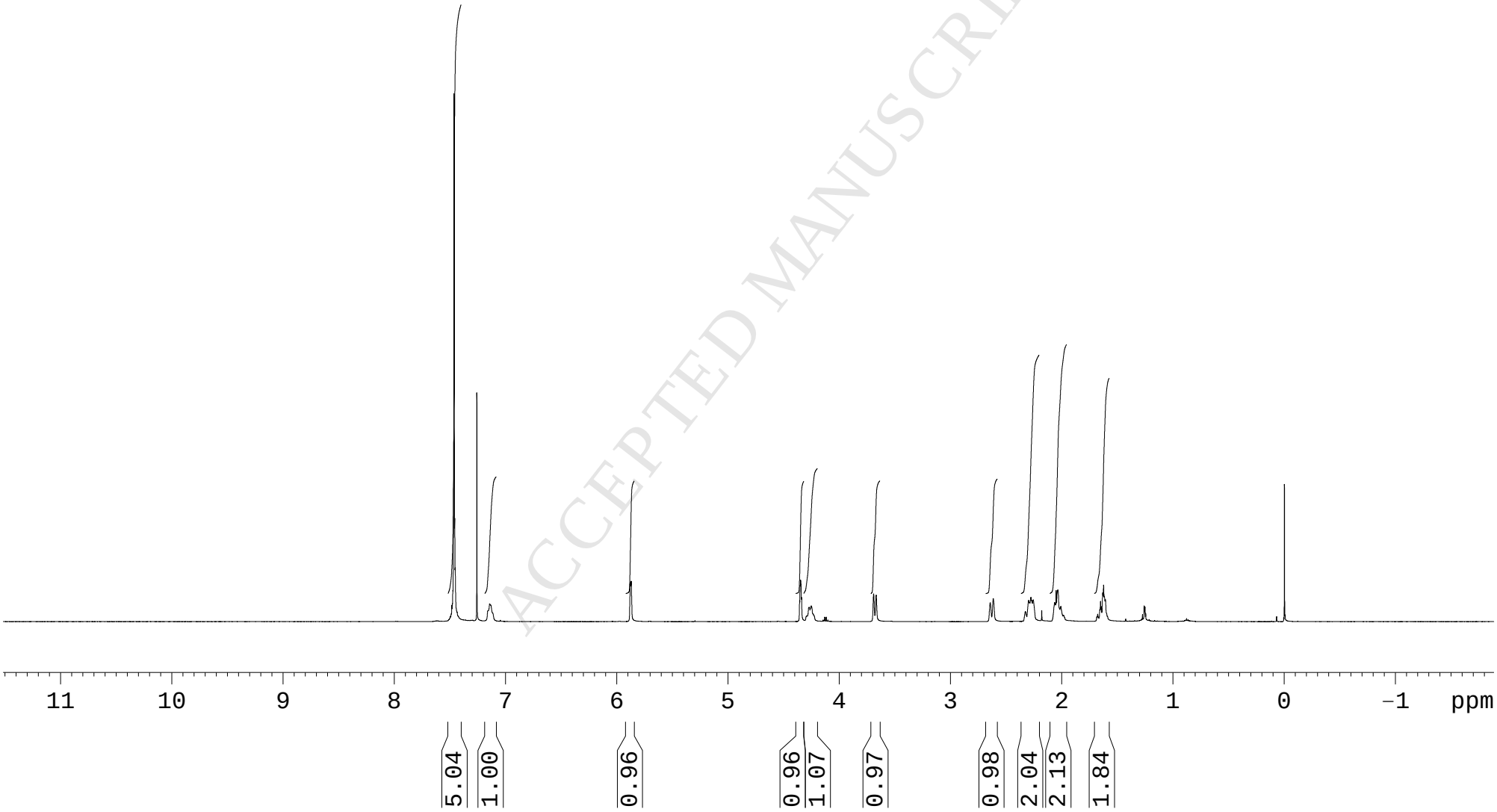

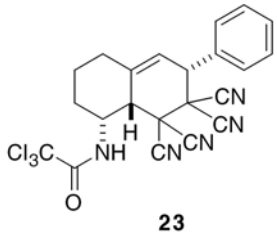

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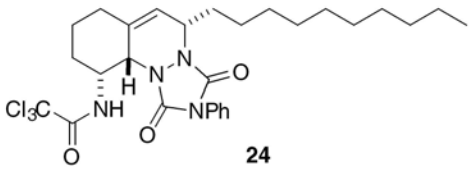

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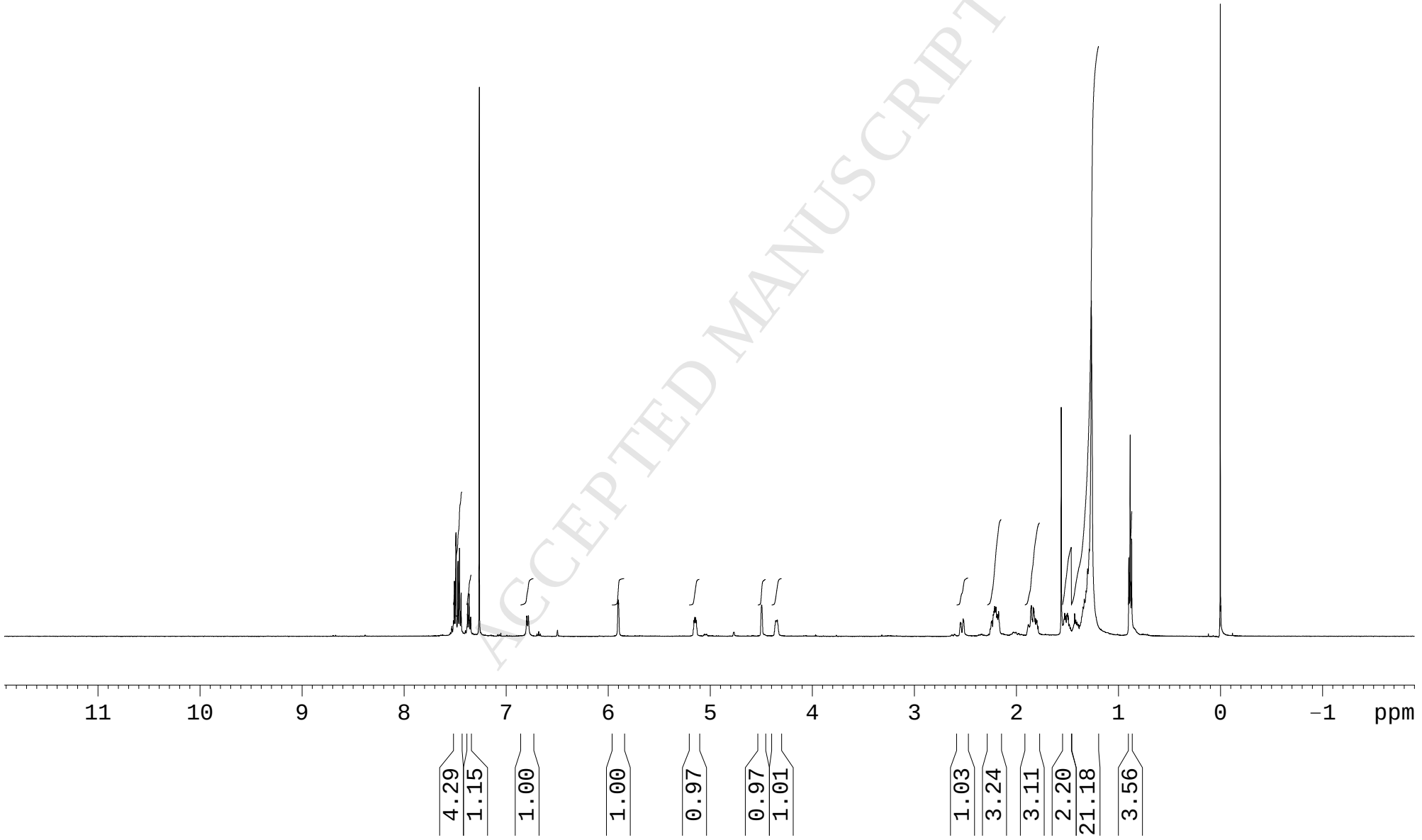

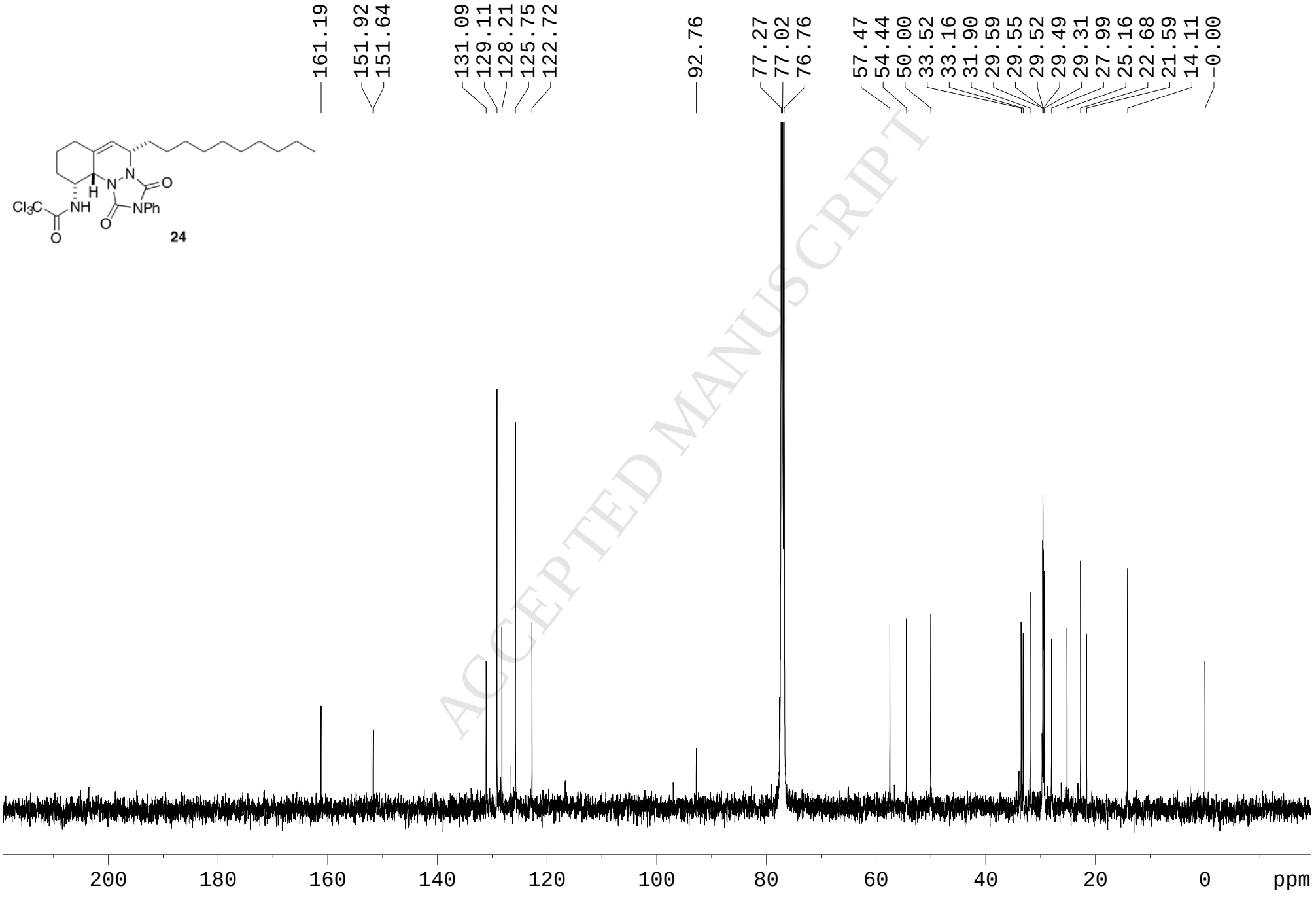

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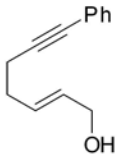

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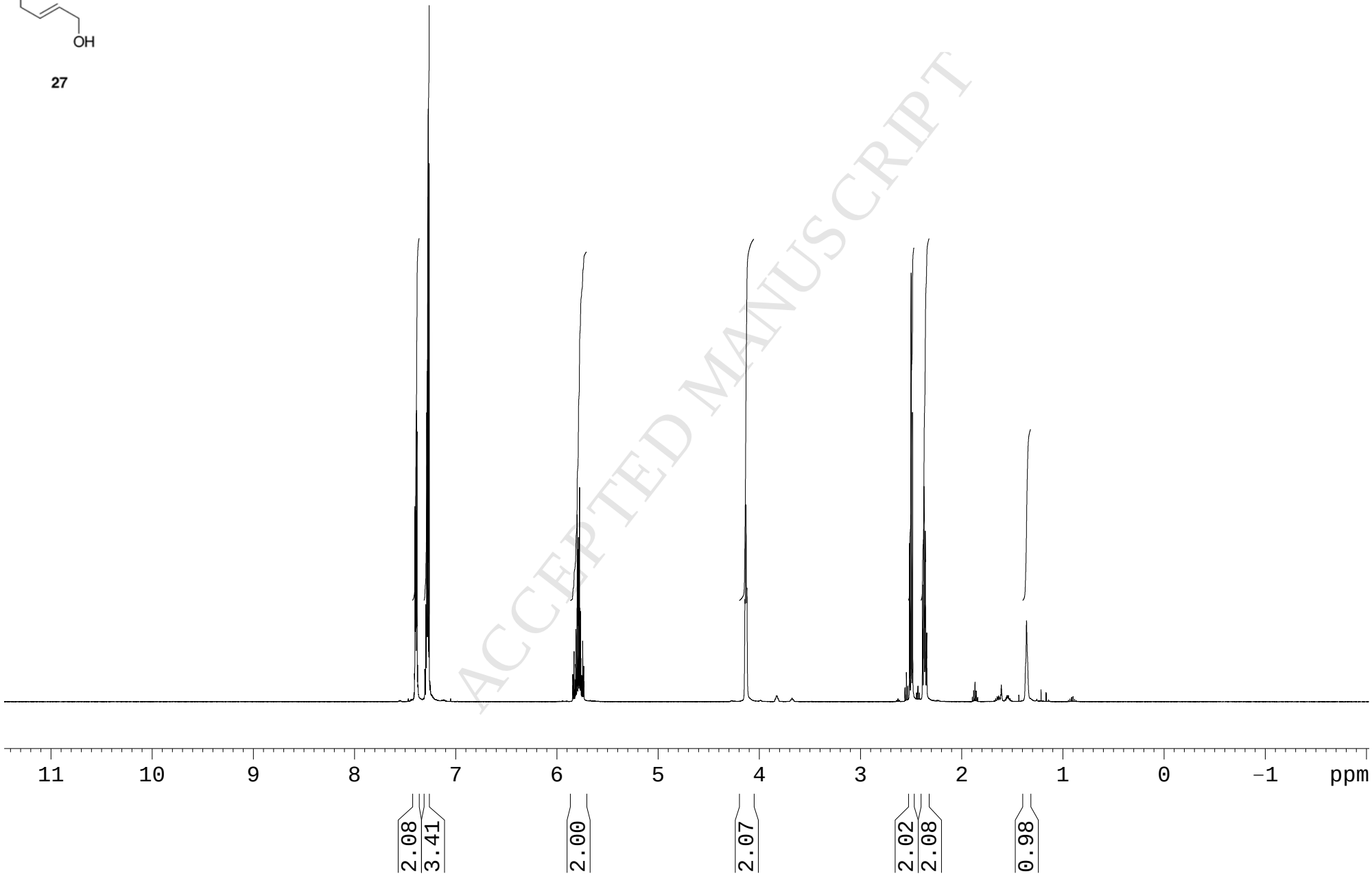

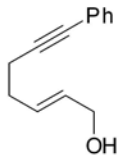

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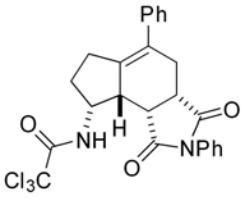

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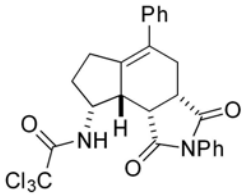

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